STIFEL | Healthcare

Women's Health

Volume I:

The History of Female Well-Being

A report prepared by

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Figure of woman from Andreas Vesalius, *De humani corporis fabrica librorum epitome*. Basel: Johannes Oporinus, June 1543.

"How many things are looked upon as quite impossible until they have been actually effected?"

Pliny the Elder (23 CE – 79 CE)

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Preface

This report reviews the history of women's health research and discusses areas where progress has been most significant. I identify contributions that have mattered most in reducing suffering and mortality of women over the centuries.

I have illustrated contributions to women's health with books and journal articles selected from my collection of historical medical publications.

As will soon become apparent, the topic of women's health far predates the printed word. Fortunately, most of the known major ancient contributions were reprinted after the appearance of the printing press in the 1460s.

This report is the first of three on the topic of women's health. Volume I (this one) covers women's well-being and gynecology. Volume II covers female reproduction – topics like obstetrics, IVF, sexuality and contraception. Volume III covers the future of women's health and current biopharma efforts underway in the area.

This report is part of a regular series of publications on the markets in the life sciences. An appendix provides a guide to other related reports that we issued in 2025, including a piece on the history of breast cancer research.

To maintain some semblance of brevity I focus on the high points in women's health innovation. My hope is to give you a sense of the stories of the many remarkable people that have made a difference for women over the years. At times, the effort to synthesize and condense 3000 years of science has felt hopeless as the literature and list of important contributors is understandably vast.

But I hope that this report captures a lot of what really mattered. The adversity, courage and ingenuity of past innovators has been towering. The insights and developments in women's health innovation have been remarkable – with profound positive implications for our species and its long-term future.

My ultimate hope is to inspire you to participate in and invest in a critical area for humanity: the health of women.

Best,

Tim Opler
Managing Director, Healthcare Investment Banking, Stifel
January 2026

Acknowledgements

In preparing this publication I have benefited from the advice and comments of many and am grateful for excellent suggestions along the way.

I would like to thank Arlene Shaner, Historical Collections Reference Librarian, of the New York Academy of Medicine, for spending several afternoons with me introducing publications that mattered in the history of women's health. I most remember a sense of wonder when Arlene shared a first illustrated edition of Angélique Marguerite Le Boursier du Coudray's *Abrégé de l'Art des Accouchements.* Arlene has also been a great conversation partner in thinking through some of the rather complex characters who have transformed the lives of women in the 19th and 20th centuries including Margaret Sanger and Marion Sims.

I would also like to thank Svetlana Kochkina and Rolando F. Del Maestro for spending a similar afternoon with me showing off books relevant to the history of women's health from the Osler Library at McGill University. Rolando encouraged me to write this book.

Dr. Mario Molina, Overseer of the Huntington Library, provided some useful suggestions on current trends in female health. I have benefitted from advice and input from a variety of medical experts including Stephen Kennedy (Oxford) and Hugh Taylor (Yale) in the field of gynecology and endometriosis; Marlena Fejzo (USC) in the field of pregnancy complications and Laura Esserman (UCSF) in the field of breast cancer.

This survey has further benefitted from much work on the history of women's health prepared by those that have come before me, and I have included a section of bibliographic references at the end.

There has been no shortage of scholarly work on the history of women's health although most of it tends to focus on a specific era or country.

The works that were most helpful included *The Women's Booke* by Owe Hagelin (1990), *A History of Gynecology* by Richard Leonardo (1944), Michael O'Dowd and Elliot Philipp's *The History of Obstetrics and Gynaecology* (1994), Walter Radcliffe's *Milestones in Midwifery* (1967), James Ricci's *The Genealogy of Gynaecology* (1943) and Harold Speert's *Obstetric and Gynecologic Milestones* (1994).

I have spent many hours poring over these books and comparing their observations about different eras and authors.

There have been several important collectors of books on the history of women's health who left behind a record of what they owned. I have reviewed the records of these collections to understand what each saw as important. Larry Longo left over 2900 books to the Huntington Library and his collection is intact and unparalleled. Elis Essen-Möller accumulated quite a large collection and left it to the Lund University Library. I spent a magical morning reviewing his collection at Lund last year and had a delightful lunch afterwards with his grandson (and biotech entrepreneur) Anders Essen-Möller.

Other collectors whom I tracked carefully included James Hardman and John Studd. Several collectors published on the literature before their deaths. I have read these carefully and would particularly note Larry *Longo's Wombs with a View* (2016), Herbert Spencer's *The Renaissance of Midwifery* (1924) and Alfred Hellman's *A Collection of Early Obstetrical Books* (1952).

A modern genre has emerged focused on medieval medicine, women and feminist themes. I have read widely in this literature and have particularly benefitted from Mary Fissell's *Vernacular Bodies* (2004); Katharine Park's *Secrets of Women* (2006) and a series of publications by the extraordinary Monica Green. Her 2008 book *Making Women's Medicine Masculine*: The Rise of Male Authority in Pre-Modern Gynaecology is a *tour de force* of scholarship and, very helpfully, for me, provided a full list of printed gynecologic and obstetric texts from 1474 to 1600.

Any collector of antique medical books will soon develop symbiotic relationships with the various dealers who help to hunt down long forgotten works on a topic of interest.

In the field of women's health, I have particularly benefitted from the help of Robert Chevalier, Wolfgang Friebes, Cynthia Greene, Jörn Koblitz, Malcolm Kottler, Jeremy Norman and Fritz-Dieter Söhn.

Finally, I would particularly like to thank Catherine Smith who spends many hours each week acquiring new items for me and Annabelle Seeliger, who has become quite the cataloguer and is a budding rare book librarian. Both have helped to build my collection of publications in women's health which is partially catalogued here.

1

The Changing Lives of Women

Over the past thousand years, women's health has undergone a profound transformation, moving from a domain shaped by tradition, superstition, and social control to one grounded—however imperfectly—in scientific evidence, professional medicine, and increasing patient autonomy.

In the early sixteenth century, women's health was largely defined by the exigencies of childbirth and reproductive capacity, overseen by midwives whose knowledge was experiential rather than formally anatomical.

Disease was interpreted through humoral theory, religious belief, moral judgment, and female suffering—especially pain related to menstruation, pregnancy, or childbirth—was largely considered to be inevitable.

Life expectancy for women was less than half its current level. A thousand years ago, a woman in England could expect to live, on average, to age thirty at birth – although much of this brevity was due to maternal mortality. By the year 1500, life expectancy at birth had risen to thirty-four – not much of an improvement.

Commonplace conversations about women's health today, involving topics like dealing with polycystic ovary syndrome or menopause, were absent, at least in the literature, as more pressing issues involving survival from the scourges of infectious disease, starvation and the risks of childbirth were front of mind. Concepts of gynecologic disease which are enormously important today for female wellness were completely absent from medical practice, such as it was.

History Was Not Kind to Women

Throughout history women's diseases have been undertreated, misunderstood or, worse yet, treated in a gender-biased manner that was unkind to women's interests.

To illustrate, two conditions that have historically been poorly understood are life threatening vomiting in pregnancy (hyperemesis gravidarum) and endometriosis.

Both conditions today are understood to have a biological origin. It appears likely based on work of Marlena Fejzo that hypersensitivity to elevations in a nausea-causing hormone, GDF-15, is principally responsible for hyperemesis gravidarum in pregnancy. This disease is life-threatening if not treated appropriately and remains undertreated today. Similarly, endometriosis is understood to have a proliferative origin linked to both genetic factors, inflammation and, potentially, infectious agents. The condition causes severe pain and exacts a heavy burden on women.

However, as illustrated on the opposite page, hyperemesis gravidarum was typically seen as psychological in origin. Patients were seen as hysterical and capricious.

A similar story can be told of many other diseases, including endometriosis. In a 2012 paper, Nezhat et al. studied the history of endometriosis and wrote:

> "By applying this broader set of criteria we were able to uncover substantial, if not irrefutable, evidence that hysteria, the now discredited mystery disorder presumed for centuries to be psychological in origin, was most likely endometriosis in the majority of cases. If so, then this would constitute one of the most colossal mass misdiagnoses in human history, one that over the centuries has subjected women to murder, madhouses, and lives of unremitting physical, social, and psychological pain. The number of lives that may have been affected by such centuries-long misdiagnoses is staggering to consider, likely involving figures in the multiple millions."

This type of hysteria diagnosis is a recurring one. Dr. Kate Young from Monash University has researched this. A story in *The Guardian* by Gabrielle Jackson on Nov 13, 2019 wrote:

> "Young's research has uncovered how doctors fill knowledge gaps with hysteria narratives. This is particularly prevalent when women keep returning to the doctor, stubbornly refusing to be saved. 'Rather than acknowledge the limitations of medical knowledge, medicine expected women to take control (with their minds) of their disease (in their body) by accepting their illness, making 'lifestyle' changes and conforming to their gendered social roles of wife and mother.'"

Obviously, scientific advances are of the highest priority to advance women's health. There is an opportunity to do much better and, clearly, the historical bar has been set fairly low.

Hospital Clinics.

HYPEREMESIS GRAVIDARUM.

By SIR J. HALLIDAY CROOM, M.D., F.R.C.P., F.R.C.S., Professor of Midwifery, Edinburgh University.

(A Clinical Lecture delivered at the Royal Maternity Hospital, Edinburgh.)

Gentlemen,—Within the last few weeks there have been several cases of well-marked hyperemesis gravidarum in this hospital, and as one has proved fatal I wish to draw your attention this afternoon to the whole condition.

Morning sickness, as you all know, is a very common concomitant of pregnancy in its earlier months. As a rule it begins after the first menstrual suppression, and continues more or less until the third month. It generally manifests itself in three varieties: (1) that in which there is vomiting and no nausea; (2) that in which there is nausea and no vomiting, and (3) where there are both. The condition is troublesome, but generally gives rise to no serious symptoms. Its treatment is various, and no one form presents any special value over another.

This afternoon I am not concerned with that form of vomiting. I wish to draw your attention to it when it has ceased to become a symptom, and has developed into a more or less grave disorder; where the vomiting has gone on to such an extent as to impair the patient's nutrition, and seriously compromise her life. Such a condition of matters is by no means infrequent, and our first object ought to be to distinguish the form of vomiting with which we have to deal. You saw some time ago a well-marked case of retroversion of the gravid uterus between the third and fourth month, associated with very well-marked vomiting which had lasted for six weeks. The patient was sent in solely on this account, because she could retain nothing, and was getting exhausted. And you will recollect that after replacing the gravid uterus the vomiting ceased, and she went out in a few weeks quite well.

Such a form of vomiting one would place under the heading of reflex; and this reflex variety is accounted for in various ways—not only by displacement, but in cases by over-distension of the uterus with hydramnios or twins; or, under some circumstances, with hydatidiform degeneration of the chorion—the so-called "hydatid mole." From want of any better classification such cases may be very conveniently ranged in the class of reflex. Whether the condition is produced by simple over-distension, or by some alteration in the metabolism, is a matter which at present seems to be somewhat shrouded in mystery. But, be the cause what it may, the fact remains that in such cases the removal of the apparent cause brings the hyperemesis to a conclusion. If in hydramnios with twins the uterus is emptied the symptoms cease, and in retroversion, if the uterus be replaced, in the majority of cases hyperemesis ends. Some have associated this condition with rigidity of the cervix and inflammation of the endometrium. I think in all probability these conditions are merely coincident; they may aggravate, but I do not think they cause the symptom which we are discussing.

The second variety of hyperemesis would fall, as Williams and Kaltenbach have both pointed out, under the heading of hysterical or neurotic. This class of cases is fairly easily recognised by the facts that there is no abnormality about the uterus or appendages; that the patient is probably of a neurotic or hysterical temperament; and that there is no abnormality in the urine, and no manifestation of any change in the liver. As a matter of fact, such cases usually get well, although I should like to mention to you a case in which this form of vomiting reduced the patient almost to the last extremity. Those who were attendant upon her as well as myself were very averse to interference, yet there was no alternative; with the emptying of the uterus the symptoms ceased. Such cases are extremely capricious. Assuming that they are hysterical in their origin, or at any rate due to increased nervous irritability, or diminished reflex control, they can ordinarily be managed by medicinal treatment and moral control, and they lend themselves to treatment by suggestion and the rest cure.

These two varieties to which I have referred seldom cause any very grave anxiety, because they can in the majority of cases, as I have already pointed out, be satisfactorily dealt with.

But the third variety—toxic vomiting—is quite another matter. And here I must refer you to the case that has been the text of this afternoon's lecture. The patient, a married woman, aged 33, primigravid, menstruated last at the end of May 1907. Two months after that she began to suffer from vomiting, which at first occurred only after meals, but after a few weeks became aggravated, and during October she vomited at short intervals during the day, irrespective of meals. In the beginning of November the vomiting and retching became almost constant, and she brought up mucus and blood. She came to this hospital when she was six months pregnant. On admission she was anæmic and emaciated, her lips were pallid, and the sclerotics somewhat jaundiced. There was no dropsy or cyanosis. The temperature was 96°, and the pulse 152 per minute, thin and very irregular. The stomach was not dilated, and there was no apparent abnormal condition of the alimentary tract. The liver dulness was normal. There was no erosion of the cervix nor any obvious pelvic abnormality to be made out on examination. Four ounces of urine were drawn off and examined carefully. It contained quantities of albumen, blood, and bile, while urates and granular blood casts were found in the deposit; there was no leucin or tyrosin. On the night of admission she was so weak and exhausted that one could not think of procuring abortion. It was decided to treat her with injections of saline solution and plenty of warm bottles. Afterwards she was given some bismuth and salol, followed by dilute milk, but she continued to vomit persistently. She was stimulated with strophanthus and strychnine, as the pulse indicated from time to time, but she died within twenty-four hours after admission.

Life-threatening vomiting seen as capricious and a sign of hysteria.

Patient unresponsive and eventually died in treatment.

Source: https://pmc.ncbi.nlm.nih.gov/articles/PMC5211004/

Women's Life Expectancy Has Improved Massively

A critical metric of a women's health is life expectancy. While not a perfect proxy, life expectancy is highly correlated with health and welfare overall, a point we documented in our Nov 2025 report on aging biology.

Several countries have reasonably good data on life expectancy going back hundreds of years. These include Sweden, France and the UK.

We have used data from the UK as a key proxy for progress everywhere in women's health. In general, the UK has been ahead of other countries so this will give a sense of the maximal outcomes at a point of time.

Figure 1 (opposite page) shows life expectancy at birth in the UK from 1200 to the present by gender. Also shown is the difference in life expectancy between women and men.

In general, women tend to live longer than men - across time and place. This itself is an interesting and not fully explained fact.

Thus, it is quite notable that women's life expectancy in the UK was less than that of men a thousand years ago. This was related to high maternal mortality and the lack of any meaningful gynecological care.

Both men and women had short expected lives. By 1500 CE things had evened out with women and men both living, on average, to age 34 - roughly the life expectancy of a horse today.

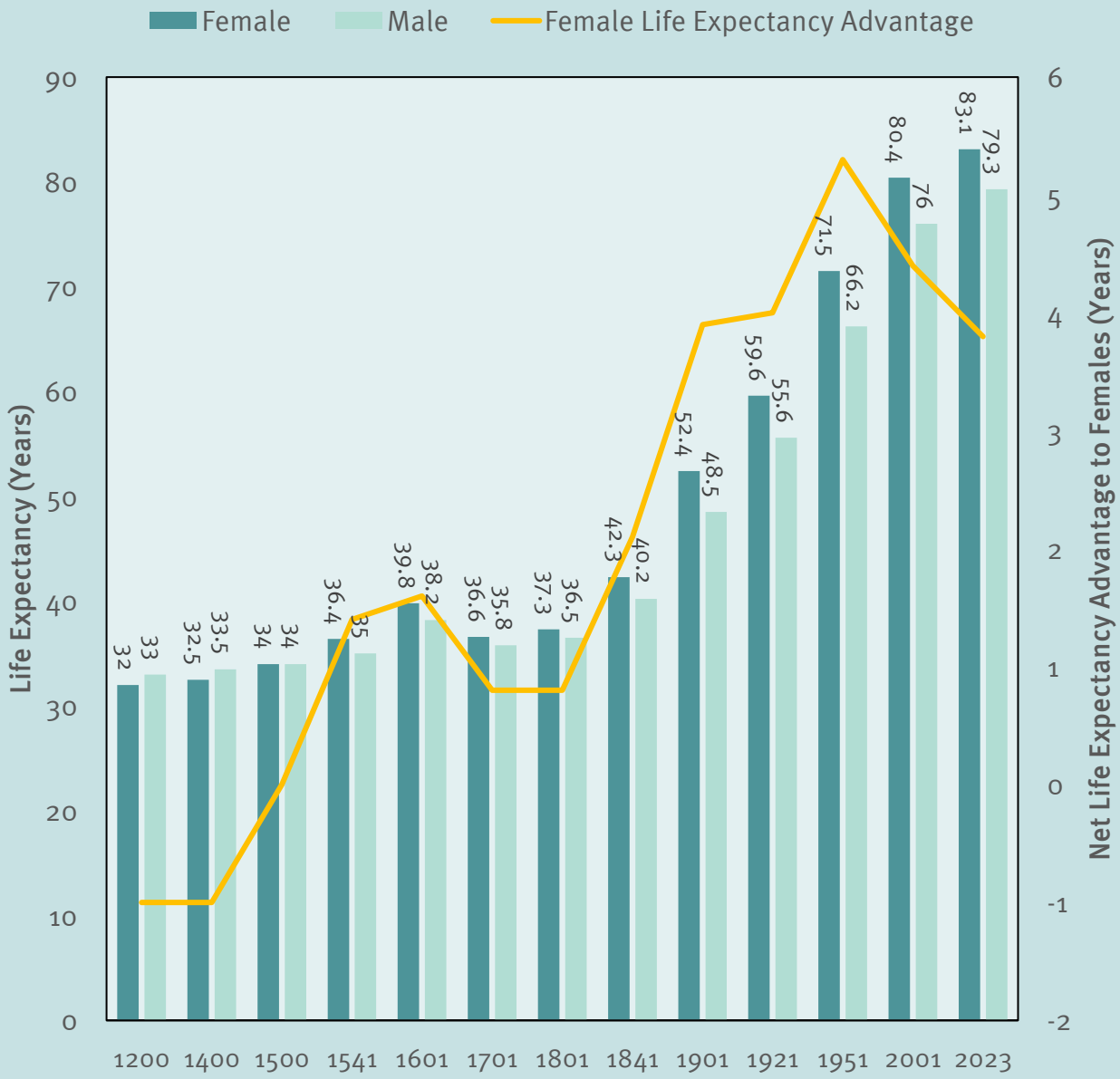
Life expectancy did not change much for both sexes until the 1800s when major changes in public health took place: the smallpox vaccine, improved sanitation, better nutrition, and lower maternal mortality.

As will be evident throughout this report, the quality of gynecologic care improved steadily throughout the 1800s with better outcomes for a range of life-threatening conditions such as inverted uterus, vesico-vaginal fistula and various female cancers.

By 1841 women could expect to live more than two years longer than men despite ongoing deaths in childbirth.

Figure 1. Life Expectancy at Birth in Years, 1200 to 2023

United Kingdom



Data sources: 1000–1540 AD: Bioarchaeological and Manorial Reconstruction Data for the medieval period is derived from osteological analysis from the London Museum's Osteological Database. which catalogs age-at-death data from over 5,000 skeletons in medieval London cemeteries. These are cross-referenced with Manorial Court Rolls and ecclesiastical records, as analyzed by Zvi Razi (*Life, Marriage and Death in a Medieval Parish*) and John Hatcher (*Mortality in the Fifteenth Century*). For 1541–1836 the data are derived from Parish Register Back-Projection Data published by E.A. Wrigley and R.S. Schofield, *The Population History of England 1541–1871: A Reconstruction* (Cambridge University Press). For 1841–1921 the data are from *Historical Life Tables* from the Office for National Statistics (ONS), based on the mandatory civil registration of births and deaths established by the Births and Deaths Registration Act 1836. Figures for 1922–2023 are from National Life Tables (UK) provided by the ONS and the Human Mortality Database (HMD).

Change in Nutrition and Sanitation Highly Relevant

One of the key changes that impacted women was the Industrial Revolution in the 1800s. As more women moved to urban areas for factory jobs, the quantity and quality of food that was available went down compared to what had been available in the average rural diet, in say, 1750.

The quality of sanitation also wasn't great in urban areas and communicable diseases like cholera were rampant in UK cities in the first half of the 19th century.

Economists, like Robert Fogel, point out that one way to measure how a population is doing on nutrition is to look at average height. Today, the average height of a well-fed woman is somewhere around 5' 4" – perhaps a smidge less. But, as noted in Figure 2, in 1850, the average height of a woman in the UK had fallen to as low as 5 feet, indicating severe nutritional stress for a portion of the population.

Some time in the second half of the 1800s nutritional status started to get materially better. Wealth improved and food became more available. This is evident in the UK height data above which show a steady improvement from 1880 to today.

Change in Rates of Partner Violence

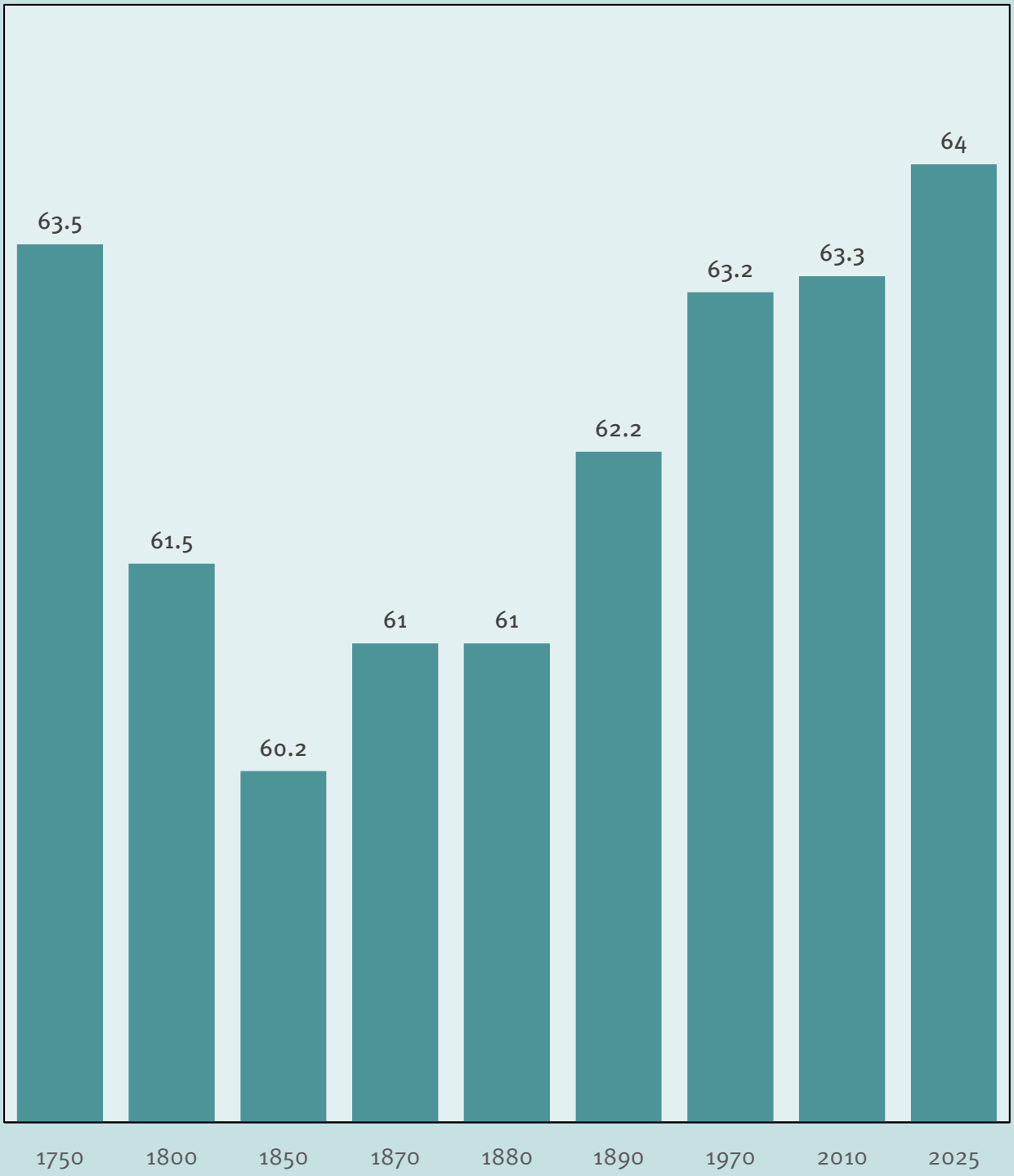
Another important area of change that has impacted the health of women is the rate of partner violence.

The World Health Organization reports that nearly 1 in 3 women – estimated to be 840 million globally – have experienced partner or sexual violence during their lifetime.

The Violence Against Women Act (VAWA) became law in 1994 in the United States. The act provides funds toward investigation and the prosecution of violent crimes against women, imposed automatic and mandatory restitution on those convicted, and allowed civil redress when prosecutors chose not to prosecute cases.

Rates of domestic violence have fallen steadily in recent decades. NCVS statistics show that domestic violence rates are down more than 50% since 1994 – although most would agree that rates today are still far too high.

Figure 2. Average Height of a UK Female in Inches 1750 to 2025



Source: Quantumrun and UK ONS.

Women's Lives Have Improved - Recently

For all the progress in the 18th and 19th centuries, it has been mainly in the last 100 years that things have really started to improve for women. This is readily apparent as you leaf through this report. You will note how many life-changing innovations have hit the market in the second half of the 20th century.

Figure 3. Count of Innovations Impacting Women's Health by Importance, 1550 to 2025 (N=66)

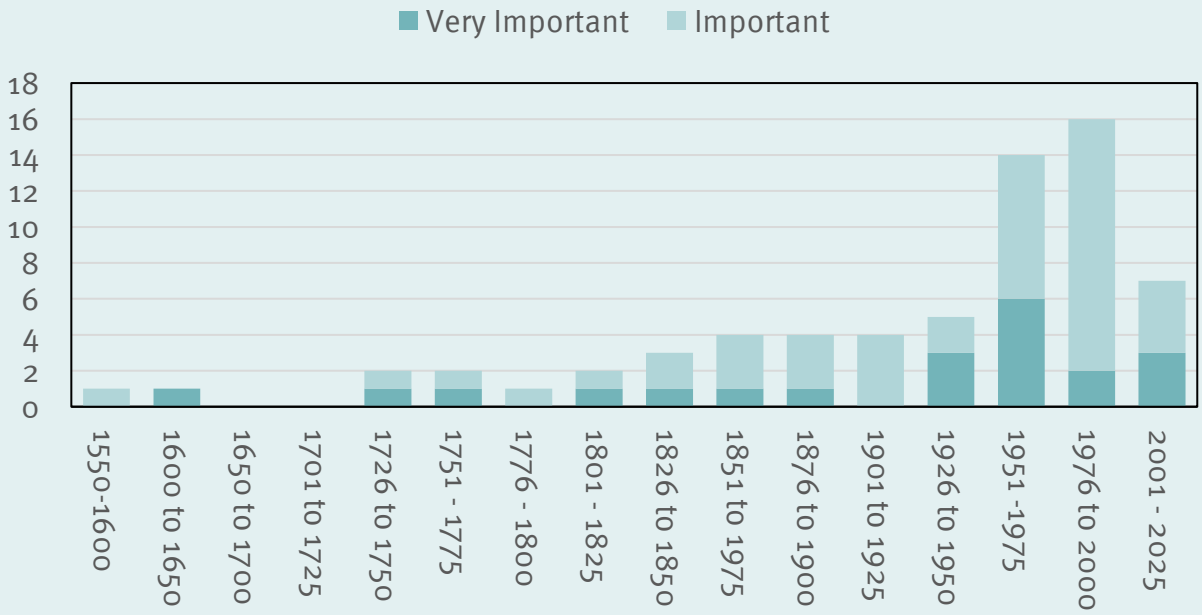


Figure 3 is built from the table on the opposite page which chronicles innovations that have mattered for women's health – as discussed in the literature. It's notable how many such innovations appeared in just a fifty-year period (1951 to 2000). This is the time when science methods had vastly improved, when funding for research was strong and when the interest in innovations for women's health had risen.

The chart would give one the impression that the pace of innovation has fallen in the last 25 years. Our own guess is that timidity by historians (and ourselves) is the main factor at play here. Most of our list comes from Speert's book on milestones in obstetrics and gynecology and he last updated his work in 2000. Recent events are so fresh it's hard to look back and nominate events that mattered. For example, we don't include the introduction of many drugs (think IBRANCE®) because it's a little soon to make the judgement call of history. Undoubtedly, there remains plenty of room for improvement in women's health, but at the same time it is hard to avoid the conclusion that the tools available for a woman to lead a healthy life are far better today than they were in 1950.

Table 1. Landmark Innovations in Women's Health, 1550 - 2025

Date	Innovation / Market Change	Date	Innovation / Market Change
1550	Podalic Version Reintroduced by Paré	1960	Birth control pill
1600	UK/Germany/France begin to train midwives	1962	Oral SERMS and hormones for fertility
1750	Forceps widely available for obstructed birth	1965	HRT for menopause widely used (Premarin)
1750	Much greater entry of obstetricians in UK/France	1969	Clomiphene approved for PCOS infertility
1760	Major improvements in managing labor mechanics	1969	Widespread Mammography
1770	Rapid growth of lying-in hospitals in France/UK	1970	Prenatal test for genetic defects
1781	Pelvimeter available for the first time	1972	Title IX opens sports to more women
1813	Ergot becomes widely used for labor induction	1973	Roe vs Wade legalizes abortion
1821	Auscultation used for fetal monitoring	1975	First hormonal therapy for breast cancer
1840	Half of rural English women can read	1975	Widespread adoption of C-section
1843	Cause of eclampsia understood for first time	1981	Acyclovir available for herpes
1847	Anesthesia in surgery and birth room	1990	Laparoscopy for endometriosis
1852	The speculum used widely	1990	Norplant - long-acting contraceptive widely used
1860	Braxton Hicks introduces bimanual version	1990	GnRH agonists approved for endometriosis
1866	Condom becomes widely available in US / Europe	1992	Good IVF available
1870	Good treatment for vesico-vaginal fistula	1992	Widespread use of prenatal vitamins
1882	Uterine sutures for hemorrhage	1992	First good migraine drug (sumatriptan)
1890	Better nutrition for women	1992	Less use of radical mastectomy for breast cancer
1900	Good treatment for uterine prolapse	1994	Violence Against Women Act bans partner violence
1900	Adoption of hand washing by obstetricians	1994	Aleve available OTC for menstrual headache
1915	Blood transfusion SOC for PP hemorrhage	1995	Alendronate approval for osteoporosis
1920	Diaphragm for contraception introduced in US/UK	1995	Uterine fibroid embolization available
1925	Endometriosis named for the first time	1996	Letrozole (aromatase inhibitor) for BC available
1925	Good treatment for eclampsia adopted	1997	Plan B (emergency contraception) approved
1935	Sulfa drugs (PRONTOSIL) become available	1998	Herceptin approved for breast cancer
1935	Ergometrine available for labor induction	2000	Mirena (good IUD) approved
1943	Penicillin available for STD's	2000	Mifepristone approved for abortion
1943	Pap smear introduced for uterine cancer	2004	Robotic surgery available for gynecologic issues
1948	Link between estrogen and endometriosis	2006	HPV vaccine / Gardasil
1952	Amniocentesis introduced	2021	Wegovy approved for weight management
1952	Apgar score introduced	2022	Half of US gynecologists are female
1953	First good drug for UTI available	2023	First NK antagonist for menopause
1956	Chemo for cancer introduced for the first time	2025	Removal of boxed warnings on HRT

Source: This list of events was obtained through interviews, from reviewing Speert's book *Obstetric and Gynecologic Milestones*, from reviewing other books on key events in women's health cited in this report and from reviewing our topics in women's health identified in our own collection of historical publications on the topic.

Women's Lives Have Improved Vastly in Last Century

Eight "very important" innovations that impacted women's health and obstetrics in the period from 1950 to 2000 were:

Date	Innovation
1952	Apgar Score Introduced
1960	Birth Control Pill Introduced
1965	HRT for menopause widely used (Premarin)
1969	Mammography becomes widely used
1975	First hormonal therapy for breast cancer
1975	Widespread adoption of C-Section
1990	Norplant – Long-Acting Reversible Contraception
1990	GnRH Agonists Approved for Endometriosis

We should add that unmet need and dissatisfaction with the quality of women's health care remains.

Roughly two thirds of women worldwide are satisfied with the healthcare that they get.

A 2022 global Gallup poll conducted in 143 countries reports that nearly 70 percent of women worldwide are satisfied with the availability of quality health care where they live and believe most pregnant women in their communities receive quality prenatal care.

The poll found that 68% of women worldwide in 2022 were satisfied with the availability of quality healthcare.

Perspective matters, of course. If 68% are satisfied with their healthcare that means that 32% are not.

The poll also revealed that billions of women aren't getting tested for deadly diseases, are continuing to suffer from physical or emotional health issues and are struggling to afford food.

A large fraction of American women struggle with mental and emotional health.

A similar poll of U.S. women in 2024 (run by Gallup and sponsored by Hologic) found that 74% of younger women struggle to make healthcare a priority – mainly for financial reasons. Other factors were lack of time or the sense that healthcare can be overwhelming.

Half of women in the U.S. said that their mental and emotional health is their top concern, followed by sleep (47%), weight (40%), nutrition/diet (37%) and chronic conditions (35%).

McKinsey Study: Women Spend Substantial Time in Poor Health

For all of the positive change in lifespan and nutrition, women continue to suffer disproportionately from poor health. A January 2024 report by the McKinsey Health Institute reported:

> "Over the past two centuries, the rise in life expectancy—for both men and women—has been a tremendous success story. Global life expectancy increased from 30 years to 73 years between 1800 and 2018. But this is not the full picture. Women spend more of their lives in poor health and with degrees of disability (the "health span" rather than the "life span"). A woman will spend an average of nine years in poor health, which affects her ability to be present and/or productive at home, in the workforce, and in the community and reduces her earning potential."

The authors of the report argue that poor health in women represents a major economic opportunity: "Addressing the 25 percent more time that women spend in "poor health" relative to men not only would improve the health and lives of millions of women but also could boost the global economy by at least $1 trillion annually by 2040."

More than half of the excess female health burden is experienced in women's working years. And more than 40% of the excess health burden is related to diseases that impact women disproportionately (what we will term female-predominant diseases in the next section). These include depression, autoimmunity and headache.

Women's diseases are a burden for their own well-being and society.

A key part of the story is neglect of solutions for conditions that are not life threatening but, nonetheless, challenging. Of particular note, McKinsey data show that conditions like PCOS, endometriosis, menopause and PMS get relatively little investment compared to their burden.

We should note that methodology matters greatly in studies of the relative gender burden of disease. In November 2025, the IQVIA Institute released a study entitled "Quantifying Differences in Female and Male Healthcare" which found that the burden of women's diseases was not disproportionately high relative to men.

They also found that the pharmaceutical industry is, if anything, generating more new drugs for female prevalent conditions than those of men. An interesting additional fact is that women are substantially higher users of pharmaceuticals for female-prevalent disease than are men for male-prevalent disease.

What is clear from both the McKinsey and IQVIA studies is that women's diseases are a major burden and that there remains a substantial opportunity for improvement.

Concerns About Gender Bias in Healthcare Persist in the United States

Some countries are much more attuned than others to building good practices for women's healthcare.

It is, of course, more than the care itself. Patients respond to biases from providers and can often feel that their complaints are dismissed.

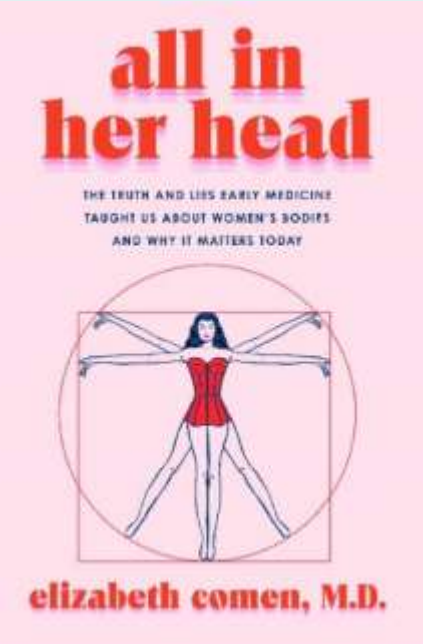
Substantially more U.S. women today report the healthcare providers dismiss their concerns than men.

In the United States, the 2022 KFF Women's Health Survey found that significant numbers of women report negative interactions with providers—including feeling dismissed, disbelieved, or assumed about before being asked—suggesting notable dissatisfaction with aspects of care even among those who have access to services.

In the KFF survey, 29% of women aged 18 to 64 reported that a health care provider dismissed their concerns while 21% of men said the same thing.

Likewise, 19% of physicians assumed something about the patient without asking while 16% of men had the same experience.

A recent book that addresses gender bias in medicine is Elizabeth Comen's 2024 *All in Her Head*.



Comen is a practicing medical oncologist and notes that:

> "For as long as medicine has been a practice, women's bodies have been treated like objects to be practiced on: examined and ignored, idealized and sexualized, shamed, subjugated, mutilated, and dismissed. The history of women's healthcare is a story in which women themselves have too often been voiceless—a narrative written from the perspective of men who styled themselves as authorities on the female of the species, uninformed by women's own voices, thoughts, fears, pain, and experiences. This continuing cultural and societal legacy results in the (mis) treatment and care of women. While the modern age has seen significant advancements in the medical field, the notion that female bodies are flawed inversions of the male ideal lingers on — as do the pervasive societal stigmas and ignorance that shape women's health and relationships with their own bodies."

Progress of Women in Medical Profession Has Been Exceedingly Slow

In the 19th century, women seeking medical careers faced systemic barriers rooted in legal restrictions and cultural beliefs that medicine was a male domain.

Women were often barred from formal medical education and licensing, prompting the creation of separate women's medical colleges and alternative training paths such as in homeopathy or osteopathy.

Mary Roth Walsh documented a *decline* in women physicians in the US in the first half of the twentieth century, such that there were fewer women physicians in 1950 than there were in 1900.

Her analysis highlighted how formal professionalization, gendered norms, and institutional exclusion worked together to limit women's opportunities.

Mary Roth Walsh

Historian of Medical Profession

As late as 1970 many women received pelvic exams by doctors on their wedding night and were told about sex while this was happening.

In the United States, anti-discrimination laws opened doors to medical school admission starting in 1972, contributing to a rapid increase in women entering the field. Through the 1970s and 1980s, women's representation in medical schools grew from a small minority to near parity, and by the early 21st century women formed the majority of medical school matriculants.

Today, slightly over a third of doctors are women but 87% of nurses are women. Women nurses are paid less than their male counterparts.

Today, 62% of obstetricians and gynecologists in the United States are women. This is up from 7% in 1970. A recent study in Germany found quite similar numbers.

A 2025 report from AAMC noted that 88% of residents in OB/GYN programs are now female. This implies that in ten to fifteen years that, overwhelmingly, this profession will be female.

Given the choice most women would prefer a female OB/GYN. This implies that male OB/GYNs are going to be in a fight for relevance in the years ahead. Quite the reversal.

2

Women's Health: Antiquity and Onwards

Unlike many medical specialties such as cardiology or neurosurgery, the treatment of diseases specific to women and the practice of woman's health has been with us since the very beginning of humanity. Medical practitioners, midwives and women themselves have by necessity had to care for the various problems that arise in the course of a woman's life.

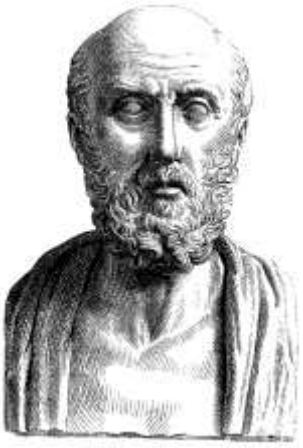
Our collection of books and journal articles on this topic begins with the advent of the printing press. Our earliest holding is dated 1478, some twenty-three years after Gutenberg printed his first bible in Mainz.

But because the written word on treatments for women dates to the Egyptians and Babylonians, our study begins at least four thousand years after knowledge accumulation had begun. Indeed, a recent BBC series *Human* traces the origins of our ancestors back three million years. Thus, the practice of obstetrics and gynecology dates from the very beginning and, in a sense, you could say, our book collection starts late in the course of events.

Fortunately, our understanding of the woman's body and appropriate medical interventions to deal with associated pathologies was quite primitive in the 1400s. As shall soon become apparent, almost all the progress has taken place since then.

Indeed, we must look at the concepts that have guided medicine in general through the millennia. And, in this background, some very specific developments can be identified – such as the moment when anesthesia first became available or the moment when the Cesarean Section could be first applied without ending a mother's life.

Greek Writings Pioneered the Study of Women's Health



Hippocrates

In the gynecological and obstetrical treatises of Hippocrates (notably *Diseases of Women*, *On the Nature of Woman*, and *On the Generation of the Child*), women's health is interpreted through humoral balance, with menstruation understood as a necessary physiological evacuation of excess blood rather than a moral or supernatural phenomenon.

Hippocratic authors described disorders of menstruation, infertility, uterine inflammation, prolapse, pregnancy complications, and childbirth in mechanical and bodily terms.

While the infamous concept of the "wandering womb" emerged from this tradition, Hippocratic medicine nonetheless represented a major advance by treating gynecologic disease as subject to observation, regimen, and therapy rather than divine punishment as had been the thinking in Ancient Mesopotamia.

The foundation of Western embryology was laid by Aristotle (384-322 BCE), the first scientist to gather biological evidence through observation.

Despite these insights, the views of Aristotle and Hippocrates were severely limited by a lack of anatomical knowledge.

Pliny the Elder

Roman Thinkers Were the First to Advance Women's Care

Following the Greeks, the Roman era introduced a more practical, albeit error-laden, approach. Celsus (c. 25 BCE - 50 CE) produced *De Medicina*, the oldest surviving major medical treatise written in Latin. Celsus integrated gynecology into general medicine, subtly affirming that female physiology was driven by the same rational principles as males.

Conversely, Pliny the Elder (23-79 CE) presented a world governed by magical thinking. He described a menstruating woman as a "destructive force of nature" capable of souring wine or killing bees by touch, yet he acknowledged menstruation as a necessary natural purgation.

A bright light in the late Roman era was Soranus of Ephesus, who was the best gynecologist to live perhaps until Guillemau or Smellie (1400 years later). He understood the problems of women, devised ingenious solutions for them and understood the women's perspective. He wrote of the women's view about male doctors in Latin: "Vos de qualibet levissima vestrarum affectionum libros ex libris facientes, bibliothecas voluminibus oneratis, et nostris interea diris ac difficillimis cruciatibus nulla vel exigua mentione facta." See translation at right.

"You, who make books out of books on even the slightest of your own afflictions, burden libraries with volumes, while meanwhile no mention at all—or only the slightest—is made of our dreadful and most difficult sufferings."

Soranus of Ephesus

(as quoted by Gianna Pomata in *Was there a Querelle des Femmes in early modern medicine?*, 2013).

The Medieval Era

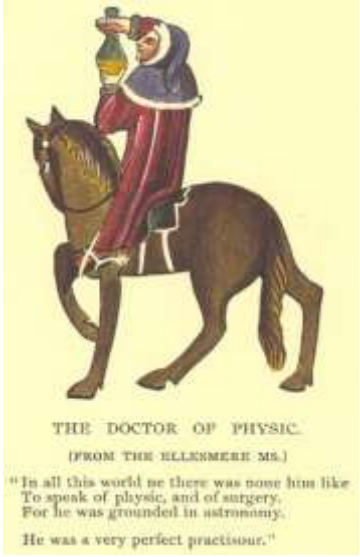
The Medieval Era was defined by the consolidation of insights from antiquity, the growth of Islamic medicine, and the gradual advent of empiricism.

Albertus Magnus (c. 1200-1280) was a pivotal figure who expanded on Aristotelian embryology. In *De Animalibus*, he refined Aristotle's theories by incorporating Galenic and Arabic insights, granting the female a more physiologically substantive role in gestation than Aristotle had allowed.

However, the era also produced Pseudo-Albertus Magnus and the text *De secretis mulierum* ("On the Secrets of Women"). Arguably the most misogynistic mainstream book of all time, it portrayed women's bodies as mysterious, imperfect, and requiring male control. It is a depressing thought that *De Secretis Mulierum* went through more printings in its day than, say, today's most read book on pregnancy – *What to Expect When You're Expecting*.

Despite frequent regression, practical medicine advanced through figures like Gilbert Anglicus (1203-1272), the first Englishman to discuss gynecology comprehensively in print. Similarly, John of Gaddesden (c. 1280-1361) authored the *Rosa Anglica*, the first printed medical book by an English writer. While he offered practical protocols for childbirth, he famously propagated the ancient "wandering womb" theory – that argued that a woman's pathologies were driven by the uterus and its peregrinations around the human body.

In the Middle Ages women themselves occasionally emerged as producers of medical knowledge. Figures such as Hildegard of Bingen and the authors associated with the Trotula corpus demonstrate that when women held positions of authority—religious, intellectual, or courtly—they could shape discourse on women's health in experiential and pragmatic ways.



Gilbert Anglicus was featured in the Canterbury Tales by the "Doctor of Physic"

The Renaissance Brought Fresh Observation

Mundinus and an assistant dissectionist

As the Middle Ages gave way to the Renaissance, the focus shifted toward observation and dissection. Mundinus (Mondino de Luzzi, c. 1270-1326) set a new standard with his *Anatomia*, reintroducing dissection as a vital part of medical training.

However, the grip of authority was so strong that, despite dissecting two women, Mundinus could not shake Galenic tradition and incorrectly described the uterus as having seven compartments. Nonetheless, humanist scholarship, renewed interest in classical texts, and expanding anatomical practice created conditions for re-examining inherited doctrines. Gynecology and obstetrics did not yet become autonomous specialties, but the conceptual terrain began to shift.

Johannes de Ketham's *Fasciculus Medicinae* exemplifies the late medieval–early Renaissance period. Its textual content largely reiterated traditional humoral and embryological theories, but its visual program was revolutionary. The woodcut images of fetal positions, the pregnant uterus, and female reproductive anatomy circulated widely and profoundly shaped medical imagination.

More explicitly humanistic works followed. Sponsored by Lucrezia Borgia, Ludovico Bonaccioli's *Enneas Muliebris*, represented a discursive survey of ancient opinions on generation rather than a therapeutic manual. His work illustrates both the promise and limitations of Renaissance humanism: textual recovery advanced anatomical description, yet deference to authority constrained interpretation.

One of the oddities of scholarship in the Renaissance era is that most of the works of Hippocrates had been almost entirely lost in the Middle Ages and were not rediscovered and published until 1525. As a result, scholarship was shaped by writers with a different perspective including Galen, Aristotle and Avicenna.

Early Renaissance women's health research remained constrained by social and intellectual structures as most authors continued to frame female physiology in relation to reproduction and male lineage.

Yet the cumulative effect of anatomical observation, humanist critique, and visual representation weakened the absolute authority of Galen and Aristotle. The female body began to emerge not merely as a vessel for reproduction but as an object of systematic anatomical and clinical inquiry.

Today's Scientific Approach to Women's Diseases Emerged Gradually

Despite these magic moments, much of the progress in women's health has come in small increments that were barely recognized at the time. While severely lacking in both scientific and technical information, early practitioners of gynecology and obstetrics nonetheless faced the imperative to treat the patients in their care.

And they did so as best as they could – with very limited information and resources – at least as seen in the current context.

Today's modern disciplines of obstetrics, gynecology and the broader care of women emerged gradually. To understand our discipline of treating women's health one must look back quite far. These disciplines have a heritage that goes back at least to the Renaissance.

The Medical Imperative Was Frequently Defined by Gender Roles and Suppression of Women's Interests

Because it is tied up with conceptions of gender and the efforts of men to elevate themselves in the emerging profession of medicine, the history of women's health involves a complex narrative of suppression, misunderstanding and gradual, if halting, enlightenment.

As described in historical texts, it is often hard to even call the medical discipline at the "women's health" during its earliest inception, as authors were not always focused on the health of the women at all. Instead, medicine up through the Enlightenment frequently saw women as "breeders," with the purpose of delivering male heirs.

Discourse in obstetrics and gynecology through the 1700s overwhelmingly focused on topics like infertility and the exigencies of birth. Much of the attempt to move beyond this and bring a broader context to women's lives was anticipated by the celebrated French philosopher and novelist Simone de Beauvoir in 1949 in her book *The Second Sex*.

While not fully progressive, today's discourse on women's health is populated by a much broader set of topics, including how endometriosis and menopause impact women's well-being.

Simone de Beauvoir's *The Second Sex* (1949) is one of the most influential works ever written on women's lives, bodies, and social position. In it, de Beauvoir argues that woman has been historically constructed as the "Other"—defined not in her own right but in relation to man—and that biology, while real, has been systematically used to justify social subordination. A central theme of *The Second Sex* is de Beauvoir's critique of the historical reduction of women to reproductive function.

Women, of course, were rarely in positions of power to influence the direction of medicine. Female literacy rates were appallingly low throughout the Middle Ages and early modernity.

Sweden, for example, was the first country to meaningfully invest in women's primary education. It was not until 1780 that more than half of the Swedish female population could read.

Even when reading was possible, women were systematically excluded from the medical profession and men started to take over traditional female caretaking roles – particularly midwifery – by the mid 1600's.

In this section, we address broad topics in women's health and spend a fair bit of time on the antecedents of female-prevalent disease and menstruation.

The Role of Menstruation

Theories of menstruation have evolved alongside broader medical understanding of the female body, moving from humoral and symbolic interpretations in antiquity to modern endocrine and systems-based models.

Women in a fifteenth century Italian breviary

In ancient medicine, Hippocratic writers viewed menstruation primarily as a necessary purgation, preventing illness by eliminating excess blood from women's bodies, which were thought to be wetter and more prone to imbalance than men's.

When menstruation was suppressed, it was associated with systemic disease and mental disturbance. Aristotle reframed menstruation within reproduction, arguing that menstrual blood supplied the material for the embryo while male semen provided form and motion, though he also treated menstruation as evidence of women's physiological imperfection due to insufficient bodily heat.

In Roman medicine, especially in the work of Galen, menstruation was further medicalized and partially normalized. Galen described menstrual blood as excess nourishment that women could not fully convert into semen, making menstruation the female analogue of male emission rather than a toxic process.

Disorders of menstruation were treated as clinical problems, an approach that strongly influenced later medical traditions.

During the medieval period, these physiological models persisted in medical texts, particularly in Islamic medicine, but in Christian Europe menstruation increasingly acquired moral and symbolic meanings, often associated with impurity, even as physicians continued to treat it medically.

The early modern period saw gradual erosion of humoral explanations as anatomical research and discoveries such as blood circulation undermined the idea of menstruation as simple cleansing.

Menstruation became more closely tied to reproduction, though its precise mechanism remained unclear. In the 19th century, modern gynecology and emerging endocrinology reframed menstruation as a cyclical uterine process linked to ovulation and the shedding of the endometrial lining, yet Victorian medicine often pathologized menstruation psychologically, reinforcing restrictive gender norms.

In the 20th century and beyond, hormonal regulation of the menstrual cycle became well understood, with estrogen and progesterone recognized as central drivers. Today, menstruation is seen as a normal physiological process with implications for overall health, not merely reproduction.

Contemporary medicine increasingly emphasizes variability, destigmatization, and equity, marking a major break from ancient theories that framed menstruation as excess, danger, or defect, while still contending with their long cultural legacy.

Female-Predominant Diseases

In 2021, the National Institutes of Health (NIH) began to discuss a shift in its research framework by discussing the concept of “Female-Predominant Disease."

The key idea is that there are some diseases which are far more common in women than men.

Illustrative conditions are depression (twice as common in women); lupus (eight times more common in women than men); fibromyalgia (two to four times as common in women than men); and migraine (three times as common in women than men).

We return to the topic of female-predominant disease in the final section of this report.

HIPPOCRATIS COI, MEDICORVM PRINCIPIS, LIBER prior de morbis mulierum.

AD

HENRICVM III. GALLIARum & Polonia Regem Christianissimum.

MAVRICIO CORDÆO RHEMO INTERprete & explicatore.

Cum tribus Indicibus copiosissimis calci subiectis.

A. T. T.

ΙΠΠΟΚΡΑΤΗΣ ΠΕΡΙ ΚΡΙΣΙΜΩΝ.

Μέγα μέρος ἡγέομαι τῆς τέχνης εἶ), τὸ διώασθαι καὶ διασκοπέεσθαι ἐπὶ τῇ γεγραμμένων ὁρθῶς.

PARISIIS,

Apud Dionysium Duvallium, sub Bucephalo, in vico Bellouaco.

M. D. LXXXV.

Cum priuilegio Regis ad decennium.

AD HENRICVM III. GALLIARVM ET POLONIAE REGEM Christianissimum.

IANVM Lascarim è principibus Byzantinis ortum, & quidem perditum, fuisse, & polliciturum accepimus magno Regi FRANCISCO imperanti, vt qua Græcus ille Medicorum princeps vernacule quondam loquutus erat Hippocrates, traderet consuetudini Latinæ: eidemque etiam quantumuis ad hoc munus temporis esset impensurus, interroganti: cõsulto quàm maxime quinquennium respondisse. Firmauit enim intersuadendo, totum se arti medicæ tradi prius oportere, vt minimum, annos tres: ne parum id quidem, dignè & illotis (quod aiunt) manibus ag gredereturus. Idque sanè merito.

IN HIPP. LIB. I. DE MVLIERB. 19

SENTENTIA SEXTA.

Ergo pessimum malum quod illiquam pepercit, manifestum in secula latet, nec vnam posset inuenire facta, & morbus tacite cuique contrahitur.

Accidit autem illud, si consistat vsqueadeo vitet, aut diffugiatur, aut quidem denuntiatur pars quadam pudendi.

Eorum si quid eorum adfit, nil prius petentur mentes vnam inuenire facta, quam sensigrant vitrea ad conflationem ferrum.

Atque hic morbus in eas præsertim cadit quæ primogenam habent vitrum, aut petiam eius cernit cum extra pudendum.

Si enim ex ea alterutram adfit, & vna confundunt mulier ut vitatur, & vacuetur alius plus æquo, ab insuendi affectibus vitrea facile perueniunt.

Neque enim in se vitrea mulier, quæ vitrea & vitrea mulier non vitatur.

Est & ipsi vitrea amplitudo fluxa, præsertim quam se alius nimis vitrea, vt facile possit inuenti, minimque quam se facier & inuiter.

Accidit vero nonnunquam, vt ipsamet intersis enfiamm quoque eius perueniatur, & pollit subiect cruoris extra prodiisse.

Si enim vitrea Vitrea ipsa mulierum, & alius non vacuatur prædicto modo, non ita è facile perueniretur.

Hæc igitur causa est cur contingat vitrei, quod nisi vitrea esset rebus Vitrea non vitatur, ut in Virginibus menstrualibus et Vi

EXPLICATIO.

HIPPOCRATES (c. 460 BCE to 377 BCE)

Medicorum Principis, Liber Prior de Morbis Mulierum

Interpreted and explained by Cordaeus. Paris: Denis Duval, 1585.

De Mulierum Morbis (Diseases of Women) is the core gynecological treatise of the Hippocratic Corpus and represents the earliest systematic medical work devoted exclusively to women's diseases. The text itself is much older, dated to the late 5th or early 4th century BCE.

This is a compilation of Hippocratic works on women's diseases, focused on disorders of menstruation, fertility, pregnancy, and the uterus. The work treats women's illness almost entirely through the lens of reproductive physiology, reflecting the assumption that female health is inseparable from menstruation, conception, and childbirth.

Medically, the treatise is grounded in humoral and mechanical explanations rather than theology or superstition – as had been the pattern in ancient Mesopotamia. Menstrual retention is identified as the central pathological driver of many female diseases, with retained blood thought to migrate or corrupt other organs, producing systemic symptoms. The uterus is portrayed as a responsive, quasi-autonomous organ whose dryness, moisture, fullness, or emptiness determines health or disease, giving rise to theories such as uterine displacement or "wandering." Treatments emphasize regimen and local therapy: diet, baths, exercise, sexual activity, pessaries, fumigations, suppositories, and evacuative measures designed to restore flow and balance. The text also provides practical guidance on pregnancy complications, miscarriage, postpartum disorders, and abnormal discharges. Helen King (2018) in her essay "Woman and Doctors in Ancient Greece" reviews the extensive contemporary discourse on Hippocratic writings on women's diseases and notes that, universally, the idea of the Greeks was to keep women health for the purpose of generation.

Book Notes: The text consists of sections of Hippocrates' writings in Greek and Latin, interspersed with Cordaeus's commentary in Latin. [20], 361, [1] blank, [12] index pp. Tall 4to, contemporary vellum. As evident on the previous page, our copy is annotated in a contemporary hand.

References: Adams H615; Durling 2412; Hirsch II 76; Radcliffe p. 2; Thoms p. 34.

CL.

GALENI PERGAMENI DE MORBORVM ET SYMPTOMATVM differentijs & causis libri Sex,

Gulielmo Copo Basileiēsi interprete, accuratax cum Vetustis codicibus collatione quamplurimis in locis diligentus quam Vnquam antehac castsigati.

Presixa sunt singulis capitibus argumenta, quibus eorum quæ traduntur, methodus indicatur: accesit & index copiosissimus.

LVGDVNI,
Apud Gulielmum Rouillium,
1560.

Humoral framework for women's diseases dominated thinking for over a thousand years

CLAUDIUS GALENUS (129 CE - 216 CE)

De Morborum et Symptomatum Differentiis et Causis, Libri Sex

Lyon: Gulielmum Rouillium, 1560.

Galen's systematic categorization of disease by its causa (cause), locus (location), and symptoma (manifestation) offered physicians a comprehensive humoral framework for diagnosis and prognosis—one that would dominate European medical thought for nearly two millennia.

In his classification of symptoms, Galen had to categorize "hysterical suffocation" (the wandering womb). Unlike earlier physicians who thought the womb literally moved like an animal, Galen argued in his pathological works that the womb remained stationary but caused symptoms through toxic retention (e.g., "retained seed" or menstrual blood). This book's rigorous classification of "causes" (antecedent, continent) would provide the theoretical framework for explaining why a retained fluid in the uterus could cause convulsions in the brain (via the nerves/sympathy).

Galen discusses how different bodies are predisposed to different diseases. He categorizes sex (gender) as a key differentiator, arguing that the female body's "imperfection" (lack of heat) predisposes it to accumulation diseases (like edema or menses retention), whereas the hotter male body burns off these superfluities.

Galen's impact on women's health, reinforced by the theoretical authority of texts like this, was profound and dominating, described by historians as a "chokehold... on thought for 1500 years". This theoretical dogmatism led to the persistence of significant anatomical errors, such as the belief that the uterus contained seven compartments. This specific fallacy was so entrenched that even Renaissance anatomists like Mondino de Luzzi who performed actual dissections, continued to repeat Galen's error rather than trust their own observations.

Book Notes: Copus's learned Latin translation, praised for its clarity and fidelity to the Greek, helped to circulate Galenic medicine through the universities of Paris, Padua, and Basel, influencing physicians and scholars long after its publication.

Provenance: Lucien d'Ursin, Antwerp (armorial bookplate). Early manuscript notes to endpapers.

Si non satis iunguntur: ultra lineas quas ante fecimus/alias du as lunatas & ad plagam conuersas immittere: quibus summa tantum cutis diducatur. sic enim fit ut facilius quod adduci tur sequi possit. quod non ui cogendum est: sed ita adducen dum: ut exfacili subsequatur: et dimissum non multum rece dat. Interdum autem abaltera parte cutis haud omnino addu cta: deformem quem reliquit locum: reddit. Huiusmodi loci altera pars incidenda: altera intacta habenda est. Ergo neque eximis auribus: neq; exmedio naso imis uenarum partibus: ne que exangulis labrorum quicquã attrahere tentabimus. Vtrin que autem petemus: siquid summis auribus: siquid imis: siquid aut medio naso: aut mediis naribus. aut mediis labris deerit. Quæ tamen interdum etiam duobus locis curata esse consue runt. Sed eadem ratio curandi est: si cartilago ineo quod inci sum est eminet: excidenda est. Neq; enim aut glutinatur. aut a acu tuto traiicitur. Neque longe tamen excidi debet. ne inter duas oras liberæ cutis/utrinq; coitus puris fieri possit. Tum iu nctæ oræ inter se suendæ sunt utrinq; cute apprehensa: & qua priores lineæ sunt: ea quoq; suturae iniiciendae sunt. Siccis lo cis/ut innaribus/illita spuma argenti satis proficit. In ulterio res uero lunatasq; plagas linamentum dandum est: ut caro in crescens/vulnus impleat. summaq; cura quod ita sutum est: tu endum esse: apparere exeo potest: quod decancro supra posui Ergo etiam tertio quoq; die fouendum erit uapore aquæ cali dae. rursusq; idem medicamentum iniiciendum: fereque septi mo die glutinatum est. Tum suturae eximi: & ulcus ad sanita tem perduci debent.

De polypi curatione per ferrum.

Caput. X.

POlypum uero: qui innaribus nascitur: praecipue ferro cura ri iam alias posui. Ergo etiam hunc ferramento acu to inmodum spathae facto resoluere abosse oportet adhibita diligentia ne infra cartilago laedatur: iqua difficilis curatõ è

Roman physician provided an early discussion of gynecology

AURELIUS CELSUS (c. 25BCE - 50 CE)

De Medicina

Florence: Nicolaus Laurentii, Alamanus, 1478.

De medicina remains the oldest medical document written after the Hippocratic writings, the earliest surviving major medical treatise written in Latin, and the earliest Western history of medicine.

It is the only extant work of Roman encyclopedist and presumed physician Aulus Cornelius Celsus who likely lived in Gallia Narbonensis, a Roman province located in what is now the Languedoc.

Celsus discussed women's diseases primarily in Books IV and VI, integrating gynecology into general medicine rather than isolating it as a purely obstetrical discipline, an approach that subtly affirmed that female physiology operated under the same rational principles as male bodies. He devoted particular attention to menstrual disorders, treating both suppressed and excessive menstruation as serious medical conditions linked to systemic illness rather than moral or mystical disturbance, and he discussed uterine inflammation, ulceration, and displacement using largely mechanical and humoral explanations rather than invoking supernatural uterine behavior. He was one of the first to acknowledge menopause, although the topic received little attention.

Celsus provided some of the earliest and clearest descriptions of gynecological treatments, including vaginal pessaries, suppositories, medicated oils, and fumigations, while emphasizing moderation and warning against overly aggressive or harmful interventions, reflecting an early awareness of iatrogenic risk. His treatment of pregnancy and fertility focused on prevention of miscarriage, avoidance of physical strain, and management of uterine pain, framing infertility as a physiological problem rather than divine judgement.

Book Notes: Our copy of the *Editio Princeps* of De Medicina was based on text edited for the printing press by Bartolomeo Fonzio from Laurentian Library manuscript copy 73.4 in Florence. Chancery folio and royal half-sheet 4to (270 x 198mm). 196 leaves. Extensive notes from various previous owners.

References: Dibner 119; Grolier Medicine 4; GMN 20; Goff C-364; Norman 424; Osler 147; Radcliffe p. 3; Reynolds 5; Waller 44; Wellcome 1392.

AETII MEDICI GRAECI CONTRACTAE MEDICINAE TETRABIBLI PRIMAE SERMO PRIMVS, PER IANVM CORNARIVM Medicum Physicum latinè conscriptus.

De simplicibus pharmacis ex plantis, iuxta ordinem literarum græcarum. Item de multorum oleorum præparatione.

DE SIMPLICIVM MEDICAMENTORVM VIRIBVS.

DIFFERENTIAE particularum actionum in singulis pharmacis fiunt, ex eo quod singula ex ipsis ad tantam caliditatem aut frigiditatem, aut siccitatem, aut humiditatem, aut partium tenuitatem, aut earundem crassitudinem accedant. At uero ad quantam tandem accedant singula, enarrari nõ potest iuxta exactam sanè ueritatem. Sed nos tamen etiam hoc ipsum manifestis, & ad artis usum sufficientibus distinctionibus comprehendere tentauimus, unũ quidem genus esse demonstrando, quod ad simile corporibus nostris temperamentũ peruenias, ubi à caliditate quę ipsis corporibus inest, transmutationis & alterationis principium quoddam assumpsit. Alterum uero calidius fieri quàm pro nostro temperamento. Atq; huius quatuor ordines facere mihi usum est. Primum qui adhuc ad sensum obscurus est, ut ratione deprehendere oporteat. Alterũ ab eo secundum, qui tam ad sensum manifestus est. Tertiũ qui fortiter calfaciat, nondum tamen urat. Post hunc quartum & ultimum qui ustorius sit. Sic & frigefacientium primum ordinem eorum quæ ratione indigent ad demonstrandum quod frigefaciũt. Secundum eorum quæ sensibiliter frigefaciũt. Tertium fortiter frigefacientium, nondum tamen mortificantium. Quartũ mortificantium. Iuxta eandem proportionem etiam humectantium & siccantiũ. Fiat autem clarioris doctrinæ gratia harum distantiarum à temperamento ordo, ita ut frigidorum primus sit, in quo quis locauerit rosaceum oleum, aut ipsam rosam. Secundus ab eo sequens proximè, in quo rosæ succus. Deinde tertius & Quartus, donec ad frigidissima peruenias, cicutam, & papaueris succũ, & mandragoram, & hyoscyamum. Rursus in calidis anethum & fœnum græcum primo ordine ponamus. In secundo quæ se eunda apparent: ita & tertia & quarta, donec ad ustoria deueniamus. Iuxta eundem modum in humectantib ac siccantibus medicamentis, initio rursus à temperatis sumpto, ordines cõsequenter usq; ad summa faciemus, huiusmodi enim cognitio non parũ ad medendi methodum confert. Conuenit porrò præexercitatum esse in sensu gustus, & proprietatem uniciuiusq; qualitatis saporum in memoria habere, uelut uerbi causa: Quum corpus aliquod linguæ admotũ uehementer ũrat, & constringit, ipsamq; ad multam profunditatem exasperat, uelut pyra syluestria immatura, & corna, ac similia omne tale Acerbũ nominatur, hoc est intense Austerum. Quæcunq; uero in contactu linguæ, ipsum non constringunt,

a

Broad coverage of gynecology, reflecting the work of Soranus

AETIUS OF AMIDA (c. 200 - 250 CE)

Contractae ex veteribus medicinae tetrabiblos

Basel: Froben, 1549.

Aëtius is an encyclopedist and the *Tetrabiblos* is a compilation "contracted from the ancients," and it became a critical conduit for earlier authorities (notably Soranus and Philumenus) in gynecology and obstetrics, alongside Aëtius' own clinical material. Also covers Rufus of Ephesus and Leonides (who performed the first documented mastectomy) in surgery. J. B. Montanus and Janus Cornarius prepared the first edition of Aetius's collected works in Latin translation. That edition was the first to include Aetius's writings on obstetrics, which epitomized all previous knowledge of the subject.

Aëtius discussed various aspects of pregnancy and childbirth, offering advice on how to manage complications. He described normal pregnancy, delivery, and the care of both the mother and child postpartum. His work was particularly valuable because it synthesized earlier works by Soranus of Ephesus, the most famous and most progressive gynecologist of antiquity. Aëtius included guidelines on handling complications during childbirth, such as abnormal fetal presentations and labor difficulties.

Clinically, the *Tetrabiblos* is notable for its pragmatic attention to uterine pathology and reproductive management. Aëtius describes a wide range of gynecological conditions, including uterine prolapse, inflammation, abscesses, ulcerations, obstructive disorders, and complications of childbirth, often presenting symptom descriptions followed by graded therapeutic responses.

Book Notes: Second edition of the translation by Janus Cornarius. Folio (260 x 190 mm) stamped pigskin over wooden boards. 5 leaves, 1 blank leaf, 916 pages, 28 leaves of index. Vellum binding.

Provenance: Our copy previously owned by French bibliophile and psychiatrist Arthur Tatossian.

References: Durling 48, Leonardo 78; VD A 573, Wellcome I, 52.

TROTVLAE CVRANDARVM AEGRITVDINVM MVLIEBRIVM, ANTE, IN, ET POST PARTVM LIBER VNICVS, NVSQVAM ANTEA

editus, quo fœminei sexus accidentes morbi & passiones, infantum & puerorum à partu cura, nutricis delectus, ac reliqua ipsæ adnata, dispositiones utrique sexui contingentes, experimenta denique uariarum ægritudinum, cum quibusdam medicamētis decorationi corporis inseruientia, edocentur.

PROLOGVS.

CVM auctor uniuersitatis DEVS, in prima mundi constitutione, rerum naturas singulas, iuxta genus suum distingueret, naturam humanam supra cæteras creaturas singulari dignitate concidit. Huic enim, supra aliorum animalium conditionem, rationis & intellectus libertatem dedit. Propterea uolens eius generationem perpetuo subsistere, in sexu dispari, masculum & fœminam creauit, ut eorum fœcunda propagatione nunquam desineret emergere futura soboles. Quorum quidem cōplexiones grata quadam commixtione contemperans, naturam masculi calidam & siccā, fœmellæ uero frigidam & humidam constituit: qua cuiusque alterius complexionis excessus, mutua qualitatum cōtrariarum repugnantia coerceretur: adeo, ut uiri constitutio calida & sicca, mulieris frigiditatem & humiditatem: & econtra huius natura frigida & humida, illius complexionem calidam & siccam remulceret. Similiter ut masculus qualitate fortiori dignus, in mulierem tanquam in agrum semen effunderet, & mulier qualitate debiliore prædita, tanquam uiri officio subdita, semen effusum in gremium natura suscipe-ret. Quoniam ergo mulieres natura sunt uiris debiliores, hinc est quòd in eis sæpius abundant ægritudines, maxime circa membra operi naturæ debita. Quæ cum in loco secretiori accidant, ipsæ propter uerecundiam, & conditionis fragilitatem, non audent angustias suarum ægritudinum medico reuelare. Quapropter ego, miseranda illarum calamitate, præsertim cuiusdam matronæ instigatione, cōpulsa, incepi diligentius contemplari de ægritudinibus, quibus fœmininus sexus sæpissime molestatur. Cum itaque in mulieribus non tantus abundet calor, qui prauos & superfluos, qui in eis quotidie congregantur, sufficiat cōsumere humores, nec tantum laborem ualeat earum debilitas tolerare, ut sudorem possit ad exteriora illos natura expellere, sicut in uiris: ideo ipsa natura, propter defectum caloris, eis præcipuam quandam purgationem destinauit, scilicet menstrua, quæ uulgus flores appellat. Nam sicut arbores non producunt sine floribus fructus, sic mulieres sine proprijs floribus, conceptionis officio defraudantur. Hæc autē purgatio contingit mulieribus, sicut de nocte uiris pollutio. Semper enim natura grauata quibusdam humoribus, siue in uiris, siue in mulieribus, iugum suum nititur deponere, & laborem minuere. Solet præterea huiusmodi purgatio mulieribus contingere circa decimumtertium, uel quartumdecimum annū, uel paulo citius, uel paulo tardius, secundum quòd in eis magis, uel minus abundat caliditas uel frigiditas. Durat autem usque ad quinquagesimum annum, si est macra: quandoque usque ad sexagesimum, aut sexagesimumquintum, si est humida: in mediocriter pinguibus, usque ad quadragesimumquintum. Si autem debito tempore & ordine contigerit talis purgatio, exonerat se cōpetenter natura à superfluis humoribus. Si uero menstrua plus uel minus exierint, quàm debent, plures ægritudines inde emergunt. Quoniam inde minoratur appetitus tam cibi, quàm potus. Quandoque fit uomitus: & quandoque appetunt terram, carbones, cretam, & similia. Quandoque ex eadem causa dolor sentitur circa collum, dorsum, & in capite. Quandoque adest febris acuta, cordis morsus, hydropisis, uel dysenteria. Hæc autem contingunt, uel quia tempore longo deficiunt menstrua uel quia prorsus non habent: unde non solum hydropisis, uel dysenteria, uel morsus cordis accidunt, sed & alię peiores ægritudines. Aliquando enim accidit diarrhœa, propter nimiam frigiditatem matricis: uel quia uenæ eius sunt multum graciles, ut in extenuatis mulieribus: quia tunc humores spissi & superflui non habent liberos meatus, per quos possint erumpere: uel quia humores sunt spissi & uiscosi, ideo propter conglutinationem, eorum exitus impeditur: uel quia delicioſe comedunt: uel quia ex aliquo labore multum sudant. Sicut testatur Galenus. Mulier quæ se nō exercet multum, necesse est, quòd abundet in multis menstruis, ad hoc ut sana existat. Aliquando mulieribus deficiunt menstrua, quia in corpore earum coagulatus est sanguis: uel quia sanguis per alia loca emittitur, ut per os, aut per nares, per sputum, aut hæmorrhoides. Aliquando deficiunt menstrua ex nimio dolore, uel ira, uel motu, uel timore. Si autem diu cessauerint, suspicationē grauis ægritudinis futuræ arguūt. Nam urina eorum uertitur in ruborem, uel in colorem loturæ carnis recentis: quandoque in uiriditatē, uel liuiditatem, aut in colorem, qualis est color graminis, facies earum mutatur.

COMPILATION OF EARLY AUTHORS (TROTULA, THEODORUS PRISCIANUS, SORANUS)

Medici antiqui omnes

Venice: Sons of Aldus, 1547.

The Medici Antiqui Omnes ("All the Ancient Physicians") was a key compilation of significant Latin medical writers into a single definitive volume.

This book was influential in transmitting the gynecological and obstetrical knowledge of antiquity to the Renaissance. A cornerstone of the collection is the legacy of Soranus of Ephesus, whom historical texts identify as "the most famous gynecologist of antiquity".

Soranus took a rational approach to "uterine pathology and reproductive management" that avoided the supernatural explanations common in other eras. This lineage of knowledge provided Renaissance readers with foundational guidelines for handling complications during childbirth, such as "abnormal fetal presentations and labor difficulties," as well as protocols for the care of both mother and child postpartum.

Alongside these, the volume included the *Euporiston* of Theodorus Priscianus, whose section on women's diseases (Faemina) offered practical, accessible remedies for gynecological complaints, further cementing the text as a practical manual rather than just a theoretical one.

The volume is perhaps most notable for formally collecting the Trotula texts, which originated from the medical school at Salerno. These writings represent one of the rare historical instances where "important work in women's health" was produced by a woman (at least in part). See Green (2002).

The Trotula treatises offered a comprehensive account of female pathology that integrated "classical physiology... and humoral theory," covering essential topics ranging from menstrual disorders to the management of childbirth.

Book Notes: Folio (308 x 203 mm). Modern Vellum.

References: Durling 3050; GMN 54; Green (2002); Renouard I, page 251(9).

Incipiunt secreta mulierum
ꝗ secretorum ad Alberto mag
no cõposita.

Dilecto sibi in christo socio ꝗ amico. N. clerico
de tali loco. vere sapientie ꝗ augmentum conti
nuum. vite presentis.

Mirabilius cuius subiecti est ens mobile cõtractu ad materiam secre
tis multum. vtpote informatum possimus vere remedio. r ipsis con
tentibus fieri debere ex delicti. Et dicit dk primo ex duas res sapie
tibus fieri debere ex delicti. Et dicit dk primo ex duas res sapie
malle erectionis quo geratur. dicit ut scribit. Primo autem salutar gse
nis ex scribere dicis sci motis. Punitur. Dilecto sibi in xpo socio r amici
ex scribere dicis sci motis. Punitur. Dilecto sibi in xpo socio r amici
co. Ab vengit causa efficiens mouens r mota mouens fuit quidam secre
dos quo rogauit dum Albertus vt sibi scribere libri de secretis mulierum
Iocos quia mulieres sunt per mentem venenose. ita ꝗ intoxicent alium
pyrum r inficiant puteos in cuius. Et maculam speculi bene certum.
Et quod ꝗ fauere eorum ei ipsis leptosum fieri. quisq; cancrosus
r ꝗ multi ñ cuiusl nisi cognati ideo necesse est se velebibus abstinere r
cognatos. inundicis conuis. r multa alia que docent in isto libro. Et
Albertus videꝗ iste poterit cõiuncti. Et sic vengit causa efficiens
mota est dicit. Ligl. fordis r. Nota sapientia est cognitio dei r perpetuo
rum effectuũ. Et libro dicit philosophus in primo metaphysice. De
beogitie ñ est sola sed sapiẽtia. Ita nihil melius est vs bacvita. qi medi
ancipis sunt o felices. sette Bueno et in plogo phisicorũ. Idee autem
sentiu cõmõ augmentũ presentis vite. Et bene scribit sibi ita quis bo
ino medoke sapientia reddit homo dilio dei r hominibus.

Cum vestra fauorabilis ꝗ gratuita me rogauit socie
tas. et quedam dicuntur a nobis de his que apud mu
lieres naturam ꝗ conditionẽ sunt occulta ꝗ secreta. luci
dius manifestare. Vt sapientione vestra nulla pigricie
a compilatione breuis r compendiosi tractatuli de im
perata materia me retraxit. Sed pusilla ꝗ imbecilis
mea mens secũm eius possibilitatem ꝗ temporis im
portunitatem. que ad aliena detrahitur. nihilominus
vestro cupiens satisfacere appetit. hanc presentem epi
stolam in qua plurima de imperatis inuenietis vobis.

a ij

A medieval misogynist's manifesto portraying women's bodies as mysterious and inferior

PSEUDO ALBERTUS MAGNUS (c. 1200 - 1280)

De secretis mulierum et virorum

Augsburg: Johann Froschauer, c. 1500.

De secretis mulierum ("On the Secrets of Women"), traditionally attributed to Albertus Magnus but now widely regarded by scholars as pseudo-Albertine, is a medieval gynecological and sexual treatise composed in the mid-13th century that blends Aristotelian natural philosophy, Galenic medicine, and popular lore into a highly influential, if problematic, account of female physiology and reproduction.

Perhaps the most widely reprinted text in the history of women's health, the book presents itself as a compendium of "secret" knowledge about women's bodies, focusing on menstruation, conception, pregnancy, sexual difference, and perceived female pathologies. Its intellectual framework is fundamentally Aristotelian, portraying women as colder, wetter, and less perfected than men, with menstruation interpreted as the result of incomplete metabolic "cooking" of blood and as both a necessary physiological process and a source of danger or corruption.

Conception is explained through a hierarchical model in which male semen provides active power while the female supplies passive matter, while incorporating Galenic humoral theory and medieval Christian ideas about sexuality and sin. The text also speculates on fetal development, maternal imagination, and congenital anomalies, attributing outcomes to moral, emotional, or environmental influences on the mother.

Arguably the most misogynistic "mainstream book" of all time, the text shows no commitment to empirical observation and freely mixes medicine with folklore, astrology, and sexist tropes. Its enormous popularity in late medieval and early modern Europe made it one of the most influential sources shaping learned and popular ideas about women's health, reinforcing the notion that female bodies were mysterious, unstable, and in need of male control.

Book Notes: Our copy of *Secretis Mulierum* is, by our estimate, the 11th edition. Quarto, 34 unnumbered pages.

References: Cianfrani 106; Park p. 83; Prioreschi, *A History of Medicine* III, 182-211. Norman 424.

Practica Joānis anglici physici clarissimi ab opus prestantia Rosa medicine nuncupata.

Sicut dicit Galenus primo de ingenio sanitatis: non visites nimis curias et aulas principū: sicut nec ego feci quousque scriberem libros: quia dicit Gal. 7° de ingenio i phe°: non ē possibile aliquid fieri primi° deo q̄ p̄ scias. Ideo optaui hūlib° facere istū librū. Quia tū nullus liber ē sine vitupio: sicut dicit Gal. 2° de crisi: iō nec iste sine vitupio erit. Rogo tū vt istū librū vidētes nō dēte camino mordeāt sed humilr̄ ptractēt. quia quicquid hic dicet, erit vl auctēticū vel lōga experiētia approbatū. quia hęc audiuit ego Joānes ō gadeldē 7° āno lecturę meę 2pilaui. Circa quē librū talē volo obseruare ,pcessū. quia p° volo nomen inuestigare cuiuslibz morbi. 2° diffinitionez. 3° occasiōez eius et cāz. iuxta illud Isaac 4° febrium c. de icteritia. omne qd volum° inuestigare trib° modis intelligimus. aut suo nomie, qd ē ad placitū: aut diffinitiōe eius naturā ondēte: aut actione, et° effectū demiante. et ibi actio idez ē q occasio vel cā. 4° dicaz signa gnālia et spālia: quia accētia ifirmo sūt signa medico vt dicit Joānitio. c. de signis officialiū mēbrorum. 5° pnosticū 6° curā. et ibi sequēdo mesue dicā ,quę sūt facienda i cura cuiuscūqz morbi periculosi et curabil. Ante tū q̄ ista fiāt volo nomē isti libro ponere: vocādo ipm rosam medicinę, pp quiqz addi tamēta q̄ sunt i rosa: quasi quiqz digiti tenētes rosaz de quibus scribit: Tres sunt barbati sine barba sūt duo nati. i. tres articuli vel partes circūdātes rosā sūt cum pilositate et duę sūt sine: et iō erūt hic quiqz libri. Primi tres erūt barbati barba longa: quia ad multa se extēdent: quia erūt de morbis cōib°. et quot modis dicat morbus cōis vel vlis vide i phemio secūdi. Duo sequentes erūt de morbis pticularibus cuz declaratōe aliquoz omissorum i pcedētib° q̄si sine barba. Et sicut rosa excellit omēs flores: ita iste liber excellit omēs practicas medicinę: quia erit p pauperibus diuitib° cirurgicis et medicis. ō quo nō opus multū recurrere ad alios libros: quia hic videlicet fat de morbis curabilibus i spāli videbit et i gnāli.

Sūt ergo capla mlta primi libri. Primū est de fe. colerica tertiana simplici et duplici vera et nota et causone et accētibus. p° accis ē sitis. 1° vigilie. 3° dolor capitis. 4° frenesis. 5° sincopis. 6° fluxus ventris. 7° ostipatio ventris. 8° de icteritia. 9° de adustione et siccitate linguę. 10° de ulceratiōe linguę. 11° de vomitu. 12° de camino appetitu et eius defectu. 13° de sudore ad sistēdum et pouocādum. 14° de fluxu sanguis nariū. 15° de pfūditate somni et litargia nō vera. 16° de dieta febricitātiū i gnāli et spāli.

2° capl̄m principale ē de quotidiana diurna et nocturna et de emittritęis et de ēpiala et liparia.

3° capl̄z principale ē de ūrtana et ō eī spēbus

4° capl̄m ē de fe. sanguinea.

5° capl̄z de febre effimera et morbis ūnālib°

6° capl̄m principale ē de ethica febrili et senectuē. et sunt in istis capitulis dubia approbata ibi posita et c.

Quia ergo tres primi libri erunt de morbis cōibus et inter eos cōmunior est fe. et inter se. cōmunior est colerica: iō primo de ea tractandum ē. p° ergo ponenda est diffinitio febris absolute: 2° diffinitio febris colericę.

De febre quid sit. Cap. p°

Febris nihil aliud ē nisi calor nālis mutat° i igneū p° affo. et ſz Gal. 8° de igenio sanitat. i prin° ſz Auer. i 3° collz. c. 3°. Febris ē calor q totū corp° ledit: quia oēs actiōes et passiōes mēbrorz. et hoc dz intelligi sic: fe. hūorales sūt i hūoribus: effimerę i spiritib°: ethica i mēbris solidis. et calor q ē i trib° vicinis ē accis morbi et febril ñ febris. et ista cōtinet totū corp° fm diuersas ptes nisi impediat: vt dicit Auic. in 4°. vñ colerica ē circa colerā: flica i toto flegmate nisi impediat pp oppilatiōem vel pp aliqō tale. et hoc aptitudialr̄ ē per totū. et hoc sufficit ad diffōnē vt videbit in 5° li. vbi 2plebo deo dāte pma omissa p declatōez eorz. Dō ō colerica febre q̄ duplex ē, ptinua et interpolata Intpolata ē ttiana pura vl nota. 2ti° ē causon.

De tertiana et eius nomine.

Primo de tertiana sciendū q ē fe. ipsa ttiū diētenēs fm ethimologiā nois. et ideo 4° pticula ast. fe. i diatritis. i. in trib° dieb° ita hic. Vel dz ttiana q̄si ttiū tenēs vel 2m diē vel tertiā horā dici. quia ſz Gal. li° de vrinarum diis quasi i principio: Colera rubea ab hora diei tertia vsqz ad horā nonaz dñat, regnat et mouet. Ex his appet siue sint duę tertianę, siue vna simplex mouet de 3° i 3m vel de 3° die in tertiaz diem vel de 3ª hora i tertiā horā sequētis diei. et si sit continua tūc mouet fortius. et hoc si dereliquat naturę ,ppne et non ipediat.

De tertiana quid sit.

Secūdo videdū ē ō diffinitiōe ttianę fe. quę ē calor inālis de icē-

Discussed menstruation and the causes of female sterility in detail

JOHN OF GADDESDEN (c. 1280 - 1361)

Rosa anglica practica medicinae

F. Girardengus & J. A. Birreta, Padua, 1492.

First edition of the first printed medical book by an English writer. John of Gaddesden was court physician to Edward II and was supposedly the inspiration for Chaucer's "Doctour of Phisik" in The Canterbury Tales.

Gaddesden wrote the *Rosa Anglica* between 1305 and 1307. This compendium of practical medicine is organized by disease and covers fevers, illnesses, and injuries, and specifically diseases of the head (including the eyes, ears, and mouth – with interesting chapters on dentistry).

In sections such as *De Sterilitate* and De *passionibus mulierum*, Gaddesden offered detailed—if often derivative—protocols for treating infertility and managing childbirth. He viewed sterility through the lens of humoral theory, prescribing complex regimens of diet and herbal pessaries to balance bodily fluids, and he detailed various fetal presentations, distinguishing between "natural" head-first births and "unnatural" breech or transverse positions. Perhaps most notably, he propagated the ancient theory of "Suffocation of the Mother" (wandering womb), advising physicians to treat uterine displacement by using foul smells like burnt feathers near the nose to repel the womb downwards, and sweet smells near the vagina to attract it back into place. Ricci (p. 272): He prescribed a large number of drugs, especially for sterility… He differentiated five component parts of the menstrual blood.

Book Notes: With woodcut printer's device at end and red painted initials. 19th cent. half vellum. 29 x 20 cm. Extensive contemporary marginalia and in the lower margin with a pale illegible old stamp. Hand-painted rubrication throughout.

Provenance: Title with ownership entry of the American chemist and physician John Redman Coxe (1773-1864), dated 1826. - White endpaper with blind embossed stamp Peter Doyle, Bookseller, Philadelphia (later 19th cent.).

References: BSB I-394; GMN 2191; Goff J 326; GW M13622; Hain 1108; Hirsch II, 651; Waller 83; Wellcome I, 2485.

FELICIS
PLATERI
ARCHIATRI ET
PROFES. BASIL.
Obſeruationum,
In Hominis Affectibus pleriſq; corpori & animo, functionum læſione, dolore, aliáve moleſtiâ & vitio incommodantibus,
LIBRI TRES.
Ad Praxeos illius Tractatus tres, quorum primus Functionum læſiones, ſecundus Dolores, tertius Vitia continet, accommodati.
In quibus eo ordine, diuerſorum affectuum ſub generibus hiſce comprehenſorum, progreſſus, euentus, curationes, vti ab authore hæc obſeruata tractataq; fuerunt, Hiſtoricè deſcribuntur.

BASILEÆ,
Impenſis LVDOVICI KÖNIG,
Typis CONRADI WALDKIRCHII.
M DC XIIII.

Described a broad range of gynecologic disorders from clinical case studies

FELIX PLATTER (1536 - 1614)

Observationum in hominis affectibus plerisque, corpori & animo, functionum laesione, dolore, aliave molestia & vitio incommodantibus, libri tres

Basel: Ludwig König et Konrad von Waldkirch, 1614.

Felix Platter presents a series of clinical and anatomical case observations that include several concerning women's reproductive health, making the work one of the earliest systematic attempts to record gynecologic and obstetric pathology through bedside and postmortem experience. Platter discusses menstrual disorders, uterine hemorrhage, sterility, prolapse, tumors of the womb, and complications of childbirth, often describing them within the humoral and anatomical frameworks of late Renaissance medicine. He treats menstruation as a critical outlet for purgation and female equilibrium, noting that both excessive and suppressed menses could give rise to dangerous fevers, melancholia, or uterine swelling. His gynecologic observations are empirical and analytical: he records dissection findings of enlarged or indurated uteri, fibrous growths, and pelvic abscesses, interpreting them as "obstructions" or "scirrhous hardenings". He also refers to miscarriages and postpartum infections, linking them to retained lochia or corruption of the humors, and he describes the severe "suffocatio matricis" (hysterical suffocation) then believed to arise from uterine vapors affecting the brain. He recounts several pathological labors and maternal deaths that highlight the hazards of childbirth before modern antisepsis, including uterine rupture, hemorrhage, and retained placenta.

He approached diseases of women with the same observational rigor he applied to general pathology, transforming gynecology and obstetrics from speculative "diseases of women" into integrated medical pathology.

Book Notes: 8vo (175 x 105 mm). Contemporary vellum, spine hand-lettered, edges stained blue, minor loss along lower joint, some soiling.

Provenance: Our copy was previously owned by Jan Muhlbauer and the Earl of Roden.

References: GMN 3789, 4297.9, 4511.1; Krivatsy 9073; Norman 1716; Osler 3693; Waller 7505. Also, Long - *History of Pathology* p 41.

2.

DISSERTATIONES MEDICÆ, TRES.

I. De causis fluxus menstrui mulierum.
II. De sympathia variarum corporis partium cum utero.
III. De usu lactis ad tabidos reficiendos, & de immediato corporis alimento.

IN

QUIBUS RECEPTÆ COMMUNITER circa subjectam materiam, veterum ac recentiorum opiniones erroneæ refelluntur, & veræ morborum ac symptomatum causæ assignantur & demonstrantur.

AUCTORE

FRANCISCO BAYLE
Doctore Medico Tholosæ.

Seiagraphiam harū dissertationum vid. in Act. Anglic. ann. 1670. p. 415. et Ephem. Gallor. t. IV. ann. 1672. p. 734 seq.

HAGÆ-COMITIS.

Apud PETRUM HAGIUM Bibliopolam, anno 1678.

One of the first books to treat menstruation as a normal and healthy part of female anatomy – also described premenstrual syndrome

FRANCIS BAYLE (1622 - 1709)

Dissertationes Medicae Tres. I. De causis fluxus menstrui mulierum. II. De sympathia variarum corporis partium cum utero. III. De usu lactis ad tabidos reficiendos

The Hague: Petrus Hagius, 1678.

Francis Bayle

In his 1678 work *Dissertationes Medicae Tres*, François Bayle addresses the physiology of menstruation primarily through the lens of Cartesian mechanism. Moving away from purely teleological explanations, Bayle argues in the first dissertation (*De causis fluxus menstrui mulierum*) that the menstrual cycle is a result of fermentation and vascular pressure. He posits that a specific "ferment" accumulates in the blood, causing it to thin and expand until the uterine vessels can no longer contain the volume, leading to periodic discharge. This approach reflected the 17th-century shift toward viewing the human body as a hydraulic system governed by physical laws rather than mystical "purges."

When comparing Bayle to his predecessors, his work marks a significant departure from the Galenic model that dominated medical thought for centuries.

Before the mechanistic revolution, menstruation was largely viewed as a necessary "evacuation of superfluities." Galen and his followers believed women had a "colder" temperament and could not fully "cook" or concoct their nutrients, leading to an accumulation of excess blood that the body had to expel to maintain health.

While Bayle retains the idea of accumulation, he replaces Galen's "lack of heat" with the concept of chemical fermentation, aligning himself more closely with iatrochemical and mechanical peers like Thomas Willis.

Book Notes: 12°, (18), 98 pp, original boards.

EMMENOLOGIA:

IN QUA

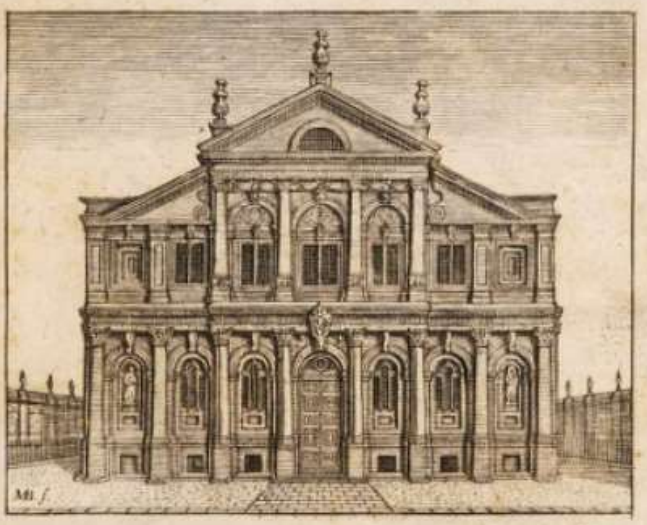
FLUXUS MULIEBRIS

MENSTRUI

Phænomena, Periodi, Vitia cum Medendi Methodo, ad Rationes Mechanicas exiguntur.

AUTHORE

JOH. FREIND M. B. *Æd. Christi* Alumn.



OXONIÆ,

E THEATRO SHELDONIANO,

Impensis *Thomæ Bennet* ad Insigne Lunæ Falcatæ in Cœmeterio S. Pauli LONDINI. A. D. 1703.

Described menstruation as a normal physiological discharge governed by the same principles as other bodily processes

JOHN FREIND (1675 - 1728)

Emmenologia in qua fluxus muliebris menstrui phænomena periodi vitia cum methodo ad rationes mechanicas

Oxford: Sheldonian Theatre for Thomas Bennet, 1703.

John Freind's *Emmenologia* (1703) was one of the first comprehensive attempts in the history of gynecology to explain menstruation through the "mechanical" or "Newtonian" philosophy. Freind, a distinguished Oxford-educated physician, rejected the Galenic view that menstruation was a mystical "purge" of impurities. Instead, he argued that the menstrual flow was a physical phenomenon governed by the laws of hydraulics and pressure. He posited that the upright posture of humans, combined with the specific resistance of uterine vessels and the force of blood circulation, led to a periodic "plethora" (excess) of blood.

Influenced by Archibald Pitcairne and the rising iatromechanical school, Freind treated the vascular system as a series of pipes and the blood as a fluid subject to momentum and friction. He utilized quantitative reasoning to discuss why periods occurred in specific cycles and why certain "vices" or illnesses (like amenorrhea) were essentially mechanical failures of the system—such as blood that was too thick to flow or vessels that were too rigid to expand. This shifted the medical focus from balancing "humors" to correcting physical obstructions and fluid dynamics.

John Freind
(Bodleian Libraries, University of Oxford)

Freind was an English classical scholar and subsequently became a doctor and accompanied the British army on expeditions to both Spain and Flanders. His career also involved a lectureship in Chemistry at Oxford University; being a member of the House of Commons which led to a sixth month spell in the Tower of London. Whilst imprisoned he conceived plans for his medical writings. He was a fellow of the College of Physicians, and he was the first English historian of medicine.

Book Notes: Octavo first edition in Latin. (12) 194 (14) Cased in 18th century but not original quarter calf and marbled boards. Hinges reinforced. First edition in Latin

References: Blake 161; Krivatsy 6003; Waller. 4924a; Wellcome III:66.

Loescher & Petsch
HOF-PHOTOGRAPHEN
S. M. D. KAISERS
Rudolf Virchow
BERLIN
Friedrichstadtstrasse
Fahrstuhl

RUDOLPH VIRCHOW (1821 - 1902)

Gesammelte Abhandlungen zur wissenschaftlichen Medicin

Frankfurt: Meidinger Sohn & Comp, 1856.

Virchow's 1856 text gathers essays that collectively argue a revolutionary proposition: all pathology is cellular pathology—*omnis cellula e cellula*. Disease, in Virchow's view, does not arise from imbalances of humors or vague constitutional states, but from specific, observable alterations in cells. This shift—from symptoms and organs to tissues and cells—reoriented 19th-century medicine and provided a new scientific foundation for obstetrics, gynecology, and women's health.

Applied to women's health, Virchow's cellular framework transformed understanding of uterine, cervical, and ovarian disease. Conditions long described impressionistically—"irritation," "congestion," or "inflammation of the womb"—were reconceived as distinct cellular processes: epithelial proliferation, stromal hyperplasia, degeneration, necrosis, and neoplasia. Fibroids (uterine leiomyomata), for example, could be understood as benign tumors arising from smooth muscle cells rather than as diffuse uterine swellings; cervical cancer as uncontrolled cellular growth rather than ulcerative decay. This shift sharpened diagnosis, clarified prognosis, and laid groundwork for rational medical management in gynecology.

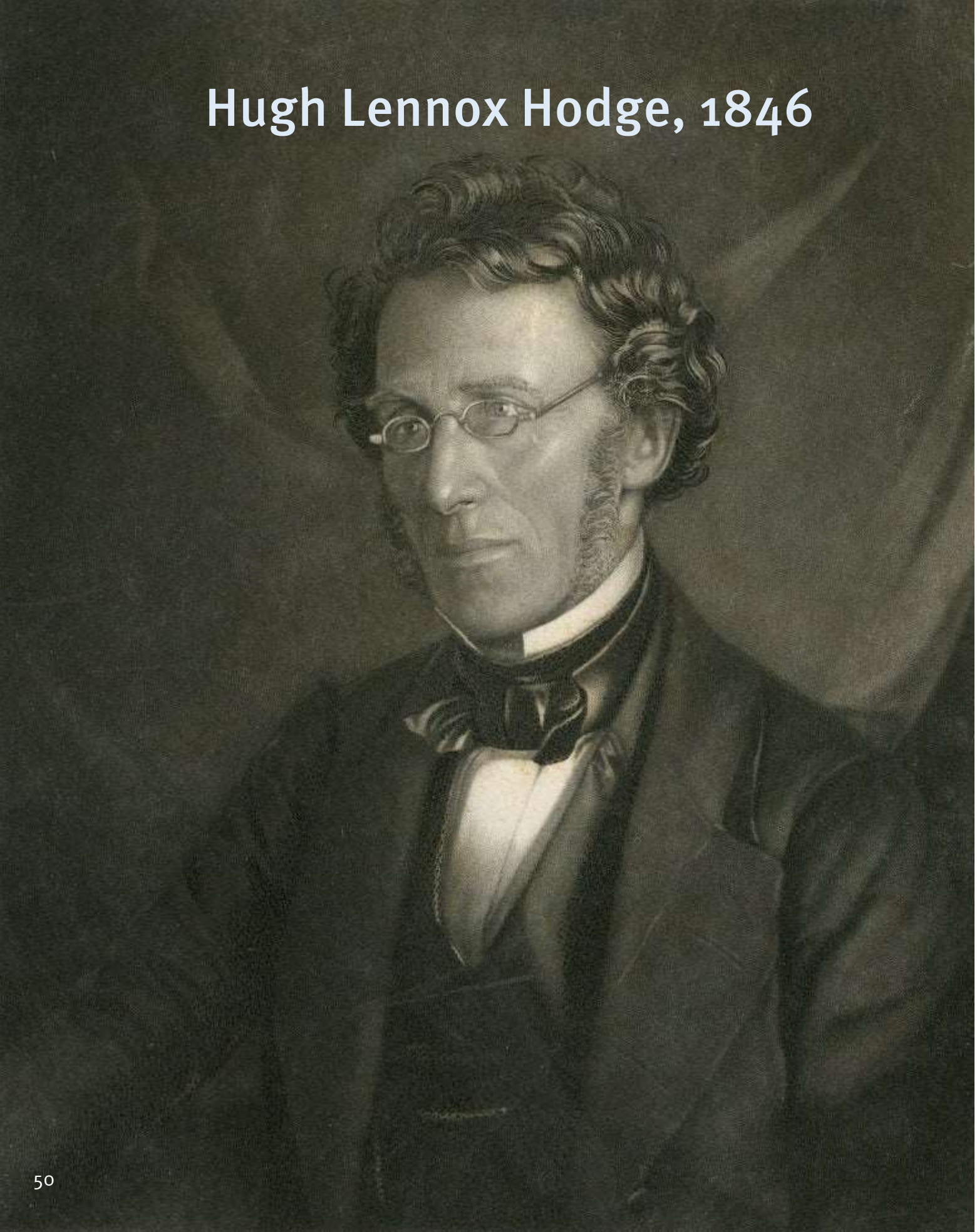
Virchow's essays also reshaped thinking about pregnancy-related pathology. By insisting that placental, decidual, and uterine changes be studied histologically, he encouraged precise differentiation between normal gestational adaptations and disease states such as placental infarction, puerperal inflammation, and hemorrhagic lesions. Crucially, his cellular pathology undermined moralized or constitutional explanations of female illness—particularly those tied to menstruation, hysteria, or "female weakness".

Book Notes: 8vo (225 x 157 mm). 3 engraved plates (2 hand-colored, 1 folding), wood-engraved illustrations in text. Contemporary black boards, paper lettering piece on spine.

Provenance: Our copy (and signed photo) was previously owned by Dr. William von Valtier. Book also formerly owned by Dr. Henry Gans.

References: GMN 3006 & 3064; Heirs of Hippocrates 1891; Norman 2155; Osler 1629; Waller 10005.

Hugh Lennox Hodge, 1846



Arguably, the most important text on gynecology of the 1800s

HUGH HODGE (1796 - 1873)

On Diseases Peculiar to Women

Philadelphia: Blanchard and Lea, 1860.

After his graduation from Princeton in 1814, Hodge began his study of medicine under Dr. Caspar Wistar. Hodge received his M.D. from the University of Pennsylvania in 1818.

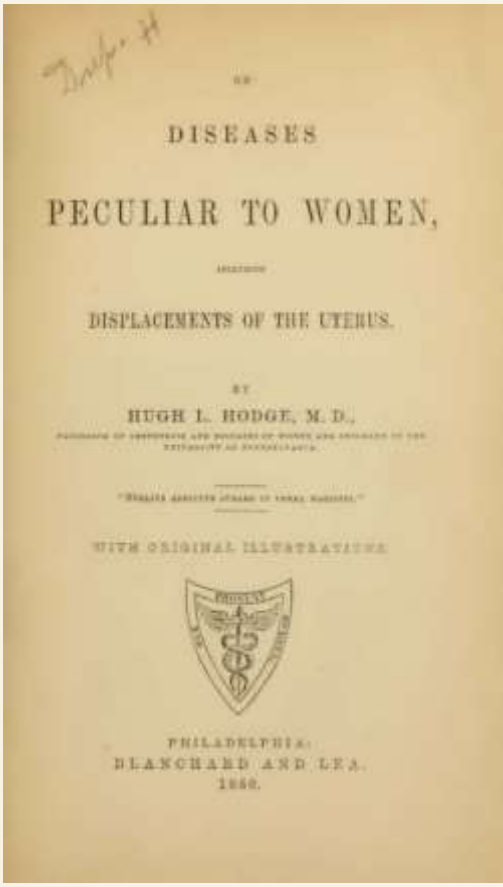
Hodge first taught at the University of Pennsylvania in 1821 and in 1834 became the principal Professor of Obstetrics at the University of Pennsylvania – which had the leading medical school in America at the time.

Hodge's 1860 book *On Diseases Peculiar to Women: Including Displacements of the Uterus* became the best-known 19th-century text in the field of gynecology. Hodge shifted gynecology toward the mechanical and physiological causes of uterine ailments, arguing that many "nervous" symptoms in women, such as hysteria and neuralgia, were actually secondary effects of "Irritable Uterus" or physical displacements.

His work was highly regarded for its systematic approach, moving beyond vague Victorian diagnostic categories to emphasize tangible, treatable anatomical issues.

His text is most famous for introducing the Hodge Lever Pessary, a device designed to support a retroverted or displaced uterus. In Part II of the book, Hodge meticulously describes the "natural position and supports of the uterus" and provides detailed instructions on the application of his S-shaped lever pessary, which was revolutionary for its time (Hodge, 1860, p. 330).

By using the principles of a lever, Hodge's design utilized the movement of the pelvic floor and the patient's own breathing to maintain the organ's position, a significant improvement over the static and often harmful circular or stem pessaries used by his contemporaries.


DISEASES

PECULIAR TO WOMEN,

DISPLACEMENTS OF THE UTERUS.

BY

HUGH L. HODGE, M. D.,

WITH ORIGINAL ILLUSTRATIONS.

PHILADELPHIA:
BLANCHARD AND LEA.
1860.

References: GMN 6043.1; Classic pages in obstetrics and gynecology: Hugh Lennox Hodge. *American Journal of Obstetrics and Gynecology*, 112(8), 1129.

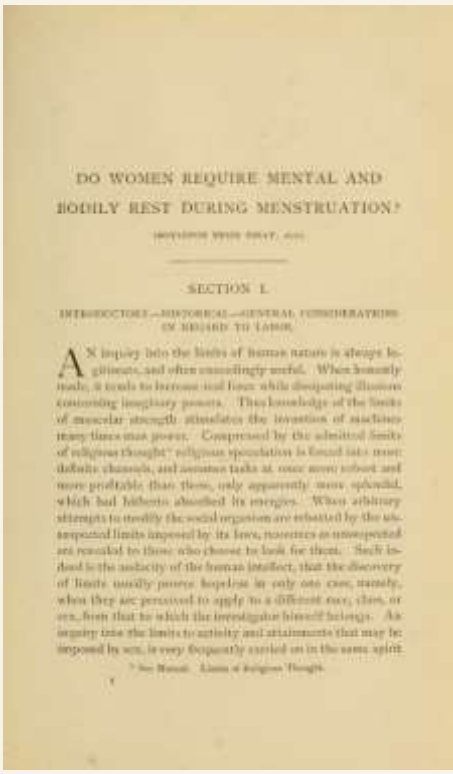
Mary Putnam Jacobi

Showed that menstruation was not a barrier to active participation of women in work life

MARY PUTNAM JACOBI (1829 to 1919)

The Question of Rest for Women During Menstruation

New York: G.P. Putnam's Sons. 1876.



DO WOMEN REQUIRE MENTAL AND BODILY REST DURING MENSTRUATION?

SECTION I.

INTRODUCTORY.—HISTORICAL.—GENERAL CONSIDERATIONS IN REGARD TO LABOR.

AN inquiry into the limits of human nature is always legitimate, and often exceedingly useful. When honestly made, it tends to increase real force while dissipating illusions concerning imaginary powers. Thus knowledge of the limits of muscular strength stimulates the invention of machines many times our power. Compressed by the admitted limits of religious thought[1] religious speculation is found into more definite channels, and assumes tasks at once more robust and more profitable than those, only apparently more splendid, which had hitherto absorbed its energies. When arbitrary attempts to modify the social organism are rebutted by the unsuspected limits imposed by its laws, resources as unsuspected are revealed to those who choose to look for them. Such indeed is the audacity of the human intellect, that the discovery of limits usually proves hopeless in only one case, namely, when they are perceived to apply to a different race, class, or sex, from that to which the investigator himself belongs. An inquiry into the limits to activity and attainments that may be imposed by sex, is very frequently carried on in the same spirit.

[1] See Manuel. Limits of Religious Thought.

Mary Putnam Jacobi's 1876 book, *The Question of Rest for Women During Menstruation*, was a landmark scientific rebuttal to the prevailing Victorian belief that women were biologically incapacitated by their reproductive cycles. The work was an expanded version of her essay that won the prestigious Boylston Prize at Harvard University, making Jacobi the first woman to receive the honor. Her research was a direct response to Dr. Edward H. Clarke's influential book, *Sex in Education*, which argued that higher education for women was dangerous because the "vital energy" required for menstruation would be diverted to the brain, leading to infertility, hysteria, or physical collapse.

Unlike the anecdotal claims of her contemporaries, Jacobi utilized a rigorous, data-driven methodology. She surveyed 268 women regarding their menstrual experiences and conducted extensive physiological experiments, including blood and urine analysis, strength tests, and measurements of pulse pressure using a sphygmograph. Her data revealed that 65% of the women surveyed experienced no significant pain or diminished capacity during their periods. She successfully demonstrated that "there is nothing in the nature of menstruation to imply the necessity, or even the desirability, of rest," and that any observed weakness was more likely a result of poor nutrition or a sedentary lifestyle rather than a biological imperative.

The significance of Jacobi's monograph extended far beyond the medical field, providing the scientific foundation for the women's suffrage and educational rights movements. By proving that menstruation was a normal physiological process rather than a monthly disability, she dismantled the "biological excuse" used to exclude women from universities and the professional workforce. Furthermore, her study led to the discovery that body temperature fluctuations could indicate the timing of ovulation, an early contribution to reproductive science.

References: GMN 11912, Speert p. 280; Reeder (2024).

AMENORRHEA ASSOCIATED WITH BILATERAL POLYCYSTIC OVARIES*

IRVING F. STEIN, M.D., AND MICHAEL L. LEVENTHAL, M.D.,
CHICAGO, ILL.
(From Michael Reese Hospital and Northwestern University Medical School)

ACCORDING to leading authoritative works on gynecology, the bilateral polycystic ovary is most commonly found in association with *uterine bleeding* (Fig. 1). This association has been recognized by the medical profession and is not infrequent in occurrence. Endometrial hyperplasia, multiple follicle cysts with granulosa cell lining, and a notable absence of corpora lutea in the ovary are the significant pathologic findings in such cases. The bleeding in these patients is readily explained by the fact that the increase in number of follicles lined by granulosa cells produces an excess of secretion of estrogenic hormone.

According to the same authoritative works, little or no mention is made of bilateral polycystic ovaries accompanied by *amenorrhea,* and inasmuch as we have encountered a series of cases exemplifying the latter conditions, we desire to present the results of our study of them.

Cyst formation in the follicular apparatus of the ovary is very common and is regarded to some extent as a physiologic process. When these structures are visible to the naked eye, they are regarded as cysts; when not, they are called follicles. When this process becomes excessive, persistent or progressive, the ovary becomes enlarged, tense, tender and painful, and produces what has been termed "cystic degen-

*Read at a meeting of the Central Association of Obstetricians and Gynecologists, November 1 to 3, 1934, New Orleans, La.

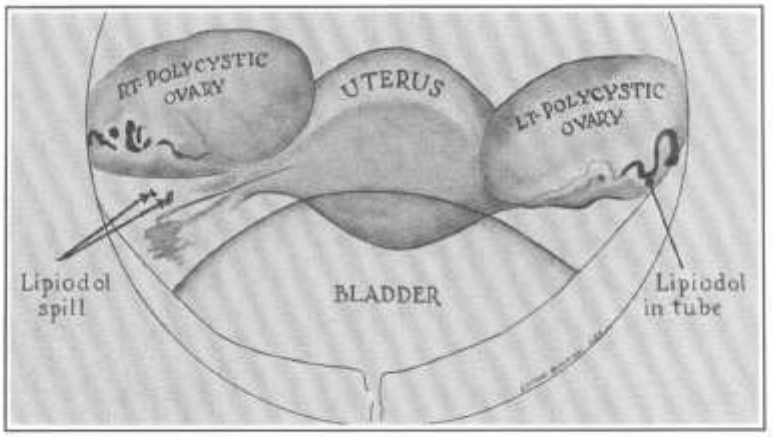


Fig. 1.

First paper to describe the constellation of symptoms later known as Polycystic Ovary Syndrome (PCOS)

IRVING F. STEIN (1887 - 1976) AND MICHAEL L. LEVENTHAL (1901 – 1971)

Amenorrhea associated with bilateral polycystic ovaries

American Journal of Obstetrics and Gynecology, 29:181–191, February 1935

Irving F. Stein

Michael L. Leventhal

Stein and Leventhal's paper is considered the classic that first described what we now know as Polycystic Ovary Syndrome (PCOS). The first description of "pigeon eggs" cysts in ovaries had been made by Achille Chéreau in 1844. Today, PCOS is the most common endocrine disorder in women's health and there are more than 10,000 medical publications on the topic.

Stein and Leventhal were the first report to describe a series of patients, rather than isolated cases, who demonstrated the triad of polycystic ovaries, hirsutism, and oligo/amenorrhea, connecting what had previously been disparate features. The study moved beyond merely describing the physical appearance of the ovaries to establishing a functional correlation between ovarian pathology and systemic endocrine symptoms. Stein and Leventhal observed that the thick, fibrotic outer layer of the ovary (the tunica albuginea) appeared to act as a physical barrier that prevented ovulation. This led them to hypothesize that mechanical obstruction rather than a primary defect in the eggs themselves, was the cause of the patients' infertility and irregular cycles.

The paper introduced the "bilateral wedge resection," a surgical procedure where a pie-shaped piece of each ovary was removed. The authors reported remarkable success with this method, noting that the reduction of ovarian mass and the "opening" of the thickened capsule led to the restoration of regular menses.

While the modern understanding of PCOS has shifted toward a focus on insulin resistance and complex hormonal signaling (such as LH and androgen levels), the 1935 Stein-Leventhal paper remains the definitive starting point for the clinical study of the most common endocrine disorder in women today.

References: Eskes and Longo p. 253; GMN 6132.1; O'Dowd and Phillipp p. 265; Speert 419; Adashi EY, et al., "The polycystic ovary syndrome: the first 150 years of study," *F S Rep.* Dec 22, 2022; 4(1):2-18.; John Powell, "Powell's Pearls: Irving Freiler Stein, MD (1887–1976) and Michael Leo Leventhal, MD (1901–1971)," *Journal of Pelvic Medicine and Surgery* 14(5):p 413-414, September 2008.

3

The Female Body

If the last section shows that it has only been recently that many female-predominant diseases have come into focus, this section discusses an even more basic issue – humankind's rather slow apprehension of the mechanics of female anatomy.

For much of recorded history, the female body was treated as mysterious, dangerous, or derivative, its inner workings obscured by cultural taboo and male-centered medical theory.

As discussed in detail by Katharine Park in her 2006 book *Secrets of Women*, female reproductive organs were literally hidden from view—rarely dissected, poorly illustrated, and often explained through analogy, superstition, or moral judgment.

The scientific understanding of female anatomy lagged far behind that of the male body, not because it was inherently more complex, but because it was less observed, less questioned, and less permitted to be known. The gradual unveiling of the uterus, vagina, cervix, ovaries, breasts, and fallopian tubes is therefore not just a medical story, but a cultural one—about secrecy, authority, and who was allowed to look.

Early Misconceptions: The Wandering Uterus and the Passive Female Body

Ancient and medieval medicine inherited deeply flawed ideas about female anatomy. Greek authors, especially Hippocrates, viewed the uterus as an independent, mobile organ—the infamous "wandering womb"—capable of roaming the body and causing disease at whim.

Opposite page: The Venus de Milo or Aphrodite of Melos statue, 2nd century BCE, Louvre Museum, Paris.

These ideas persisted because systematic dissection of female bodies was rare. Religious prohibitions, modesty norms, and legal restrictions meant that most anatomical investigation relied on male cadavers. When women's bodies were discussed, it was often through the lens of reproduction alone.

Renaissance Anatomy: Seeing the Female Body, Incompletely

The Renaissance marked the first serious attempt to correct ancient anatomical errors. Andreas Vesalius's sixteenth-century dissections dismantled many Galenic myths, yet female anatomy remained underrepresented even in his revolutionary anatomical treatise.

Gabriele Falloppio

Progress came from figures such as Gabriele Falloppio, who described the uterine tubes—later called fallopian tubes—clarifying the pathway between ovary and uterus and decisively rejecting the idea that conception occurred in the uterus alone.

The Seventeenth and Eighteenth Centuries: Structure Without Physiology

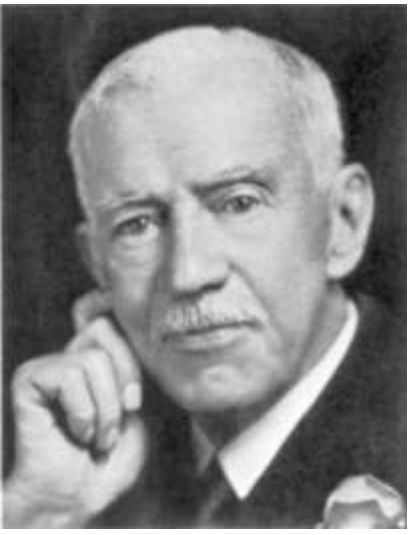
By the seventeenth century, anatomists such as Hieronymus Fabricius and Adriaan van de Spiegel refined descriptions of the uterus, cervix, fetal membranes, and ovaries through careful dissection and illustration.

Yet anatomy remained largely static. Physicians knew what organs looked like but had little idea how they functioned across time. Menstruation, ovulation, lactation, and menopause were poorly understood; the ovaries' role in cyclic change was unknown; and the cervix was not yet recognized as a frequent site of cancer.

The Nineteenth Century: Attention on Anatomic Pathology

The nineteenth century brought a decisive transformation: female anatomy became pathologic anatomy. With the rise of hospital medicine, microscopy, and surgery, women's organs were no longer merely described—they were examined in disease. Uterine fibroids, once lumped together as vague "hard swellings," were recognized as smooth-muscle tumors. Cervical cancer emerged as a distinct clinical entity.

However, much of this newfound knowledge of anatomy was omitted from medical textbooks for years, creating an "anatomical gap" that would not be closed until the late 20th century.



Howard Kelly

Surgical anatomy—mapped by figures like Howard A. Kelly—integrated ureters, pelvic fascia, and vascular planes, making complex operations survivable. Beyond the pelvis, the nineteenth century also established sex differences in skeletal anatomy and bone remodeling. Yet bone density and fracture risk in women would not be fully appreciated until the endocrine era.

The 20th Century

In the 20th century John A. Sampson identified endometriosis as ectopic endometrial tissue, shifting chronic pelvic pain from psychosomatic explanations to anatomical pathology.

The last 125 years witnessed the most rapid progress, driven by the discovery of the endocrine system. The work of Pincus and Chang in 1953 on the effects of progesterone provided the first chemical map of the hypothalamic-pituitary-ovarian axis. This milestone transformed the ovaries and uterus from static "vessels" into dynamic endocrine organs that regulate not just fertility, but bone density and cardiovascular health.

John Sampson

As life expectancy increased, the anatomy of aging females became a focal point. Research into the mechanisms of osteoporosis revealed that female bone anatomy is uniquely dependent on estrogen levels. In the last three decades, the focus has shifted to the nervous system and the integrated "functional" anatomy of the female body.

One area where recent progress has been notable is the female sexual response. Helen O'Connell's 1998 and 2005 MRI studies "rediscovered" the clitoris as a massive, triplanar complex that wraps around the urethra and vagina. This discovery led to the modern concept of the Clitourethrovaginal (CUV) Complex, a unified anatomical zone where erectile tissue, the urethra, and the anterior vaginal wall function in concert.

Helen O'Connell

Concepts of the "G-Spot" identified by Ernst von Graefenberg in his 1950 article "The Role of Urethra in Female Orgasm" have become antiquated as it is increasingly clear that the clitoris and anterior vaginal wall function as a single organ. Recent work from David Ginty's lab at Harvard has been quite informative. In his 2024 paper "Krause corpuscles are genital vibrotactile sensors for sexual behaviours" Ginty and colleagues showed that a specific cell type in this CUV, the Krause corpuscle, is responsible for the sexual response – in both females and males.

Advanced imaging and molecular tools have further refined anatomy. MRI and ultrasound reveal living pelvic anatomy in motion; histology and genomics show tissue-specific responses to hormones and injury.

From Secrets to Systems

Across these centuries, the history of female anatomy reflects a slow movement from secrecy to scrutiny. Early medicine treated the uterus as a capricious creature, the vagina as an afterthought, the ovaries as passive, and the breasts as utilitarian. Scientific progress depended not only on better tools, but on the willingness to see women's bodies as worthy of full investigation. The nineteenth century's embrace of pathology marked a turning point: women's diseases became visible, nameable, and eventually treatable.

ARETAEI CAP-
padocis medici lib. VIII.

RVFFI EPHESII
de hominis partib. li. III.

IVNIO PAVLO CRASSO
Patauino interprete.

ACCESSERE quę Craſſus nõ vertit
Aretæi aliquot Capita.
Ruffi liber de Veſicæ ac renum affectib.
Eiuſdem de Medicamentis purgãtibus.
Adnotationes locorum in quibus ab interprete Græca diſcrepant.

Lectio cauta prodest: varia delectat
Senec. ep. 45.

PARISIIS, M. D. LIIII.
Apud Guilielmum Morelium, & Iacobum Puteanum.

RUFUS OF EPHESUS (c. 70 - 150 CE)

Aretaei Capadocis Medici Libri VIII. / Ruffi Ephesi de Hominis Partibus Libri III

Paris: Guilielmum Morelium & Iacobum Puteanum, 1554.

Rufus of Ephesus also known as Rufus Menius, was a Greek physician, anatomist, pharmacologist, and medical writer. He lived during the Roman Imperial period, around the time of Emperor Trajan (98–117 AD).

In his views, Rufus largely followed Hippocrates, despite some reservations about Hippocratic ideas and treatment methods, adapting the teachings of Hippocrates and his successors to his own understanding. He became famous for his precise observations and clinical work. His treatise *De corporis humani partium appellationibus* (O*n the Name of the Parts of the Human Body)* conveys the anatomical nomenclature of the time and represents the oldest surviving anatomical textbook.

Written as a comprehensive glossary for medical students, the text identified the organ as a "fleshy muscle" located centrally within the vulva. In this same passage, Rufus explicitly linked the anatomical name to the Greek verb *kleitoriazein*—meaning to touch lasciviously—thereby linguistically anchoring the organ to its specific function in sexual pleasure. This description was the first known in the literature, although others have subsequently taken credit for the discovery of the clitoris including Matteo Realdo. An entertaining description of this history is given in Helen King's recently released book *Immaculate Forms*. Also see Katharine Park's informative 1997 article entitled "The Rediscovery of the Clitoris" in *The Body in Parts* (Routledge).

Book Notes: Our 1554 copy of Rufus anatomy treatise is co-published with a book written by his contemporary Aretaeus the Cappadocian. This copy is bound in full contemporary calf with gilt-tooled spine compartments and red morocco title label ("Aretaei et Ruffi"), marbled endpapers, and decorative initials throughout. The pages feature extensive marginalia from an early scholar.

Provenance: Previously the property of Arthur Tatossian, a French bibliophile and psychiatrist.

References: Adams A1548; Durling 257; King p. 110; Wellcome 394.

Incipit Anothomia Mundini

Via vt ait. G. vij. terapentice methodi auctoritate Platonis: opus in aliqua scientia vel arte traditur tribus de causis Primo vt quis satisfaciat amicis. secundo vt quis exercitetur vtilissimo exercitio quod est per intellectuz. tercio vero vt illo remedietur obliuioni que est ex senectute Hinc est q̃ his tribus de causis promotus. proposui meis scholaribus quoddam opus in medicina componere: et quia cognitio partiũ subiecti in medicina quod ē corpus humanũ: que loca dispositionũ appellantur est vna partium scientie medicine vt dicit Auerrois primo sui colliget capitulo de diffinitione medicine: Hinc est q̃ inter cetera vobis cognitionem partiuz corpis humani que ex anothomia insurgit ꝓposui tradere. non hic obseruans stilum altuz sed magis secundum manualem operationem vobis tradam noticiam.

Capitulum primum

Jtuato itaq̃ corpore vel hom̃ie mortuo per decollationē vel suspensionem supino: primo notitiaz tocis debemus habere: secundario ptiũ Nam cũ om̃is nostra cognitio incipiat a notioribus nobis et que sunt confusa notiora sunt: et totum confusus sit suis partibus: maxime a cognitione tocius incipiemus Circa totum autez: q̃ primũ debemus cognoscere est in quo homo habet differentiã ab animalibus alijs. habet autē differētiaz in tribus. s. in figura vt situ partiũ in moribus siue artibus et in partibus quibusdam In figura: nam stature est recte ⁊ hanc habuit propter quatuor suas causas. nam corpus humanũ primo habz inter cetera animalia materiã leuissimã spirituosã ⁊ aeream: ⁊ ideo ad superiora eleuabilez. Secũdo inter cetera eiusdē quãtitatis calorez habz ampliorē cuius est semp ad supiora eleuare. tercio formam habet pfectissimaz que cũ angelis ⁊ intelligētijs q̃ regunt vniuersum cõmunicat. et ideo sursum eius secundum sursum

Described the vagina, uterus, ovaries and placenta based on observations from dissection

MUNDINUS (Mondino de Luzzi, c. 1270 - 1326)

Anatomia

Edited by Martinus Polichius de Mellerstadt. Leipzig: Martin Landsberg, [c. 1493].

In his book *Anatomia*, Mundinus set a new standard for dissection that defined anatomical knowledge across Europe for the next two centuries.

Written in 1316, *Anatomia* in manuscript form was widely popular and effective in reintroducing surgery as a vital part of anatomical training and medical knowledge more broadly. From the 1470s onwards, the work proved to be successful among Italian presses, receiving many incunable editions and solidifying its status as an essential contribution to understandings of the human body.

While his aim was general anatomy, Mundinus included sections on the female reproductive organs, the uterus (matrix), vagina (via genitalis), ovaries ("testes mulieris"), and placenta — subjects that directly shaped medieval and Renaissance gynecologic thought.

Remarkably, despite having dissected two women cadavers, Mondino got it wrong on the uterus. He described the uterus as having seven compartments rather than one – a conclusion in keeping with Galenic thought. Despite having empirical data, Mondino was not able to shake Galenistic tradition.

Book Notes: Our 1493 edition was edited by Martinus Polichius de Mellerstadt, who served as personal physician to Frederick the Wise of Saxony and was a professor at Leipzig, where this edition was printed, until 1502 and one of the founding members of the University of Wittenberg. Chancery quarto (211 x 144mm). 39 leaves of 40. 19th-century vellum.

Provenance: Early marginal annotations. Previously the property of the Royal Society of Medicine.

References: Cianfrani 106; Eccles p. 27; Goff M-874; Hain 11633*; GW M25670; Klebs 688.6; Park p. 89; Radcliffe p. 11. Waller 105. Also see Castiglioni, *A History of Medicine*, 1975, pp. 342-4;

Lucrezia Borgia, the Duchess of Ferrara sponsored Ludovico Bonnacioli's effort to write one of history's first printed books on female anatomy and gynecology.

LUDOVICO BONACCIOLI (1475-1536)

De uteri partiumque eius consectione [Enneas Muliebris]

Strasbourg: Heinrich Sybold, 1530.

Bonaccioli, who taught philosophy and medicine at the University of Ferrara, was one of the first to write about the clitoris and the hymen, which he described accurately. However, he did not name the clitoris and was not fully aware that Rufus had described and named the organ fourteen centuries before.

Bonaccioli followed Galen and Mondino's error regarding the anatomy of the uterus, describing it as seven-celled.

Bonaccioli cites the leading Arabic medieval authors on occasion, but the text overall is a humanistic *tour de force* —literally a revival of the views of the ancients (everyone from Herodotus to Pliny) on the nature of generation and sexual reproduction. The humanism that characterized Bonaccioli's work had been spreading throughout medical writing since the 1460s.

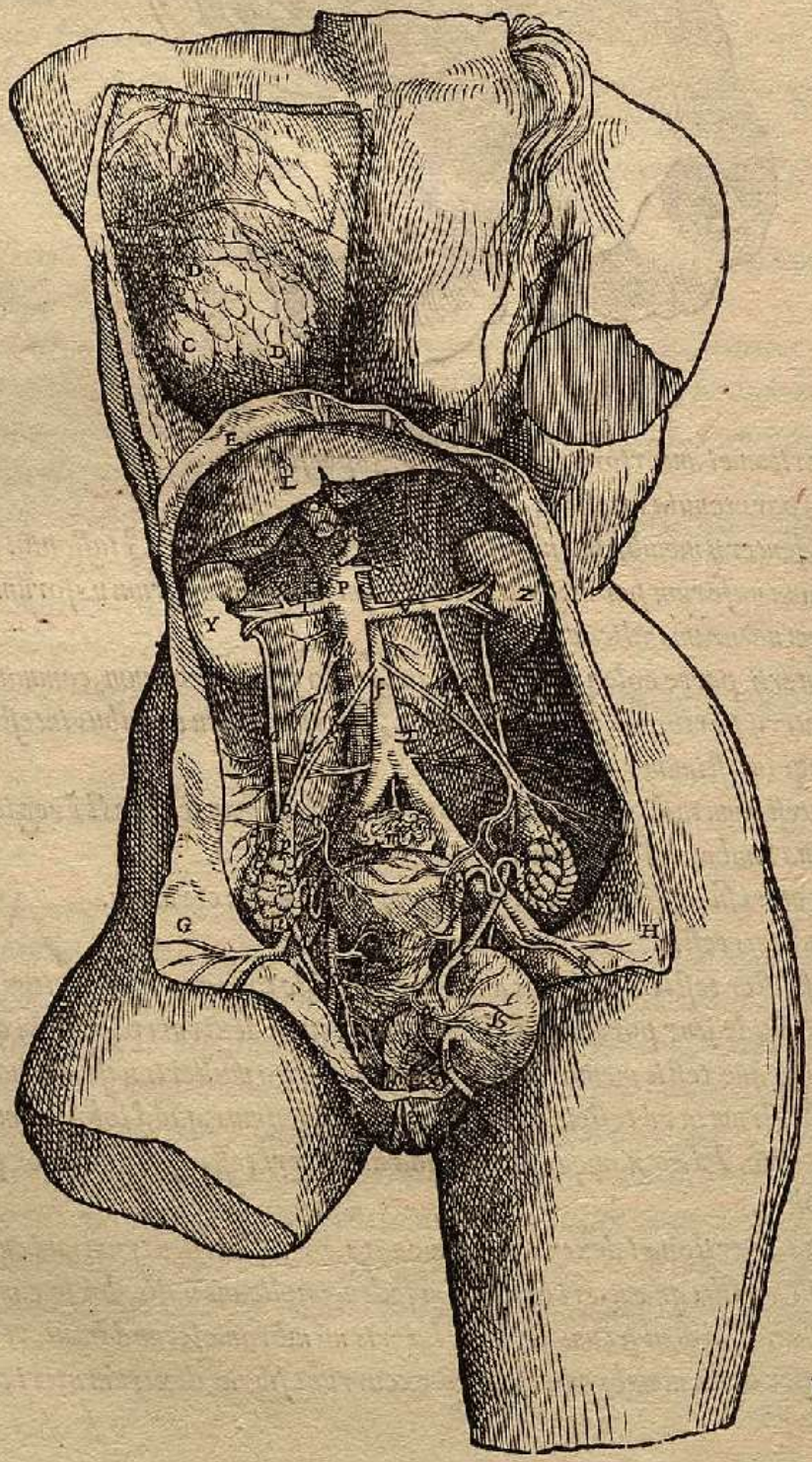
Bonaccioli was Lucrezia Borgia's personal physician, and he dedicated this work to her. "An entirely new composition, [Bonaccioli's work] was unusual not so much in being dedicated to a woman . . . but in eschewing a therapeutic focus for a more discursive, compendious survey of scientific opinion on generation" [Green (2008)].

This edition of *De uteri partiumque* also contains another tract on reproduction, Aristoteles "De signis quae puerorum seminis emissionem, puellarumque viripotentiam preveniunt".

Book Notes: Our 1530 edition contains the first three chapters of Bonaccioli's *Enneas muliebris,* first published in 1502. 8vo. (156 x 98 mm). Contemporary vellum.

References: Cianfrani p. 116; Leonardo, p. 189; VD16- ZV 22963. Also see Gionata Liboni's essay "Theories and practices on the female body at the court of Lucrezia Borgia: the Enneas muliebris of Ludovico Bonaccioli among philosophy, medicine, and erudition," *Itinerari* (2023, LXI, 1), pp. 183-217.

VIGESIMAQVINTA QVINTI LIBRI FIGVRA.



VIGE

Identified the uterus as having a single chamber and accurately defines the pelvis for the first time

ANDREAS VESALIUS (1514-1564)

De humani Corporis Fabrica libri septem

Venice, Franciscum Franciscium Senensem & Joan. Criegher, 1568.

Andreas Vesalius revolutionized medicine by establishing anatomy as a discipline based on direct observation rather than the unquestioned authority of ancient texts. Educated in Paris and Louvain, he flourished at the University of Padua, where he performed dissections himself. His defining work, *De Humani Corporis Fabrica* (1543), published when he was just 28, is widely regarded as the foundational text of modern human biology. The volume is as much an artistic masterpiece as a scientific one; produced in collaboration with Titian's studio.

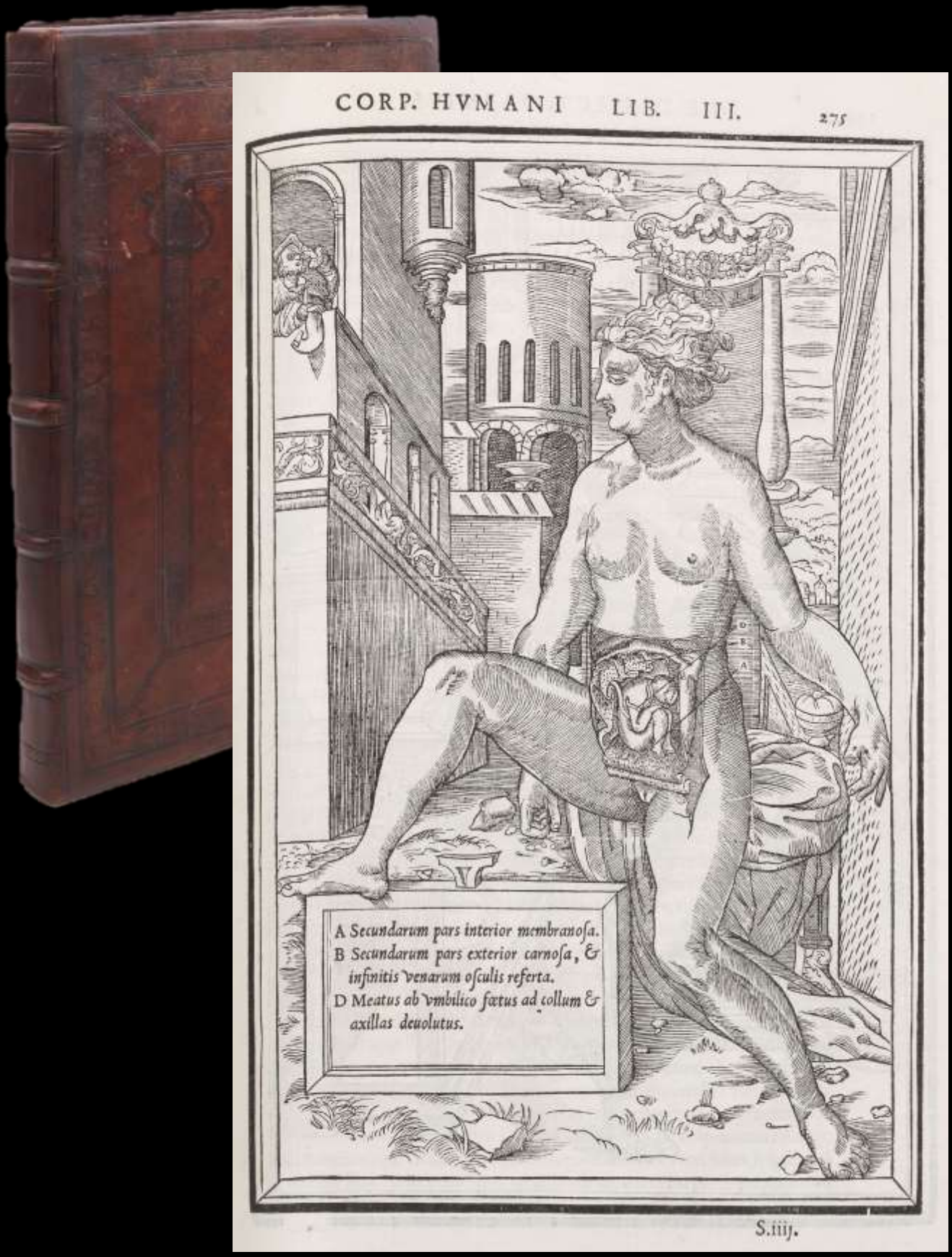
Regarding female anatomy, Vesalius successfully debunked Galen's notion of a multi-chambered uterus, correctly identifying the human uterus as having a single cavity, although Berengario da Carpi was the first to correct the Galenic error in print (Leonardo Da Vinci preceded him but his drawings were not printed). Vesalius's female figures are often referred to as "torsos" which are truncated focusing on the reproductive tract. He was among the first to identify and draw the pelvis.

Vesalius also improved anatomical understanding of the cervix and vagina, presenting them with unprecedented visual accuracy. His illustrations clearly differentiated the uterus from the bladder and rectum, correcting frequent confusions in earlier texts. In his 1555 second edition he was the first to show the ovaries and follicles correctly.

Book Notes: Our copy is the fourth edition, the first Italian edition. Folio, contemporary vellum, Illustrated with woodcuts in the text, 19 full-page illustrations, numerous vignettes and initial letters. It has superb illustrations engraved for this edition by Joannes Criegher.

Provenance: 18th-century manuscript ex-libris on the endpaper of Captain Pascal Leblanc, commander of the Le Cardinal S. Raymond. Previously the property of the French bibliophile Arthur Tatossian.

References: Adams V 606; Cianfrani p. 120; Cushing VI.A-4 p. 92-93; Durling 4580; Eskes and Longo xiii; Goldschmid S. 37; King p. 341; Leonardo p. 185; Nutton (2024 p. 185); O'Dowd and Phillipp p. 256; Radcliffe p. 11; Wombs p. 28.


CORP. HVMANI LIB. III. 275
A Secundarum pars interior membranosa.
B Secundarum pars exterior carnosa, & infinitis venarum osculis referta.
D Meatus ab vmbilico fœtus ad collum & axillas deuolutus.
S.iiij.

First visuals of the uterine membranes and the vascularity of the female reproductive system

CHARLES ESTIENNE (1504 - 1564)

De dissectione partium corporis humani libri tres

Paris, Simon de Colines, 1545

First edition of one of the principal treatises on anatomy of the Renaissance. Although published two years after Vesalius's *Fabrica*, Estienne's work is believed to have influenced Vesalius. Charles Estienne, son of Henri, had studied medicine at the University of Paris. He had the work printed on his father's presses by his stepfather, S. de Colines, who had succeeded him. We know from the signatures on Jollat's plates that he had begun on the illustrations for the volume in the early 1530s.

F. Schreiber suggests that Vesalius may have become acquainted with Estienne's work, as they were fellow students in J. Sylvius's class, during his stay in Paris in 1533-36.

"One of the finest woodcut books of the French Renaissance," says Fred Schreiber, an enthusiasm shared by Haskell Norman.

The female figures, including the pregnant women are famously adapted from a series of erotic prints (the Loves of the Gods) by Jacopo Caraglio and Rosso Fiorentino. Estienne repurposed these sensual poses by surgically "opening" the abdomen to reveal the reproductive organs. Despite this bizarre juxtaposition of erotica and dissection, the book provided groundbreaking depictions of the uterus and the fetus. Estienne offered detailed descriptions of the uterine membranes (the amnion and chorion) and the placement of the fetus, and he was one of the first to emphasize the rich vascularity of the female reproductive system, tracing the veins and arteries of the uterus with a precision that advanced the field beyond the simple schematics of the Middle Ages.

Book Notes: Our copy is a folio size, brown calf, central floral motif and double border of blind-stamped friezes and fillets, spine with raised bands and blind-stamped fillets. Contemporary binding) 12 unnumbered leaves (title, preface, index), 379 pp. (incorrectly numbered 375), woodcut illustrations in the text. Previously owned by Arthur Tatossian.

References: Adams S1725; Choulant, pp. 152-155; Durling 1391; GMN 378; Heirs of Hippocrates 256; Lilly p 38; Norman 728; Stillwell 626; Waller 2819; Wellcome 6076; Wombs p. 32.

HABES LECTOR STVDIOSE HOC VOLVMINE

ALEXANDRI

Benedicti veronensis physici præstantissimi, singulis corporum morbis a capite ad pedes, generatim membratimq; remedia, causas, corũq; signa. xxxi. libris complexa, præterea

Historiæ corporis humani libros quinq;,
De pestilentia librum vnum, &
Collectionum medicinalium libellum.

Omnia summa diligentia excusa, atq; nunc primum in lucem edita, quorum clenchũ indicemq; sequens liber demonstrabit.

VENETIIS IN OFFICINA LVCAE ANTONII IVNTAE MENSE AVGVSTO.

ANNO. M. D. XXXIII.

The first to use the word cervix and perineum

ALESSANDRO BENEDETTI (1460 - 1525)

Singulis corporum morbis a capite ad pedes, generatim membratimque remedy

Venice: Giunta, 1533.

Alessandro Benedetti (c. 1460–1525) was an Italian Renaissance physician, anatomist, and humanist best known for helping reframe anatomy as a disciplined, observational science at the University of Padua during the crucial transitional period just before Vesalius.

Benedetti's anatomical treatise included 31 books on diseases "a capita ad pedes" (from head to toe), followed by the five books of Historia corporis humani. Benedetti was physician to the Emperor Maximilian, and Surgeon General of the Venetian army.

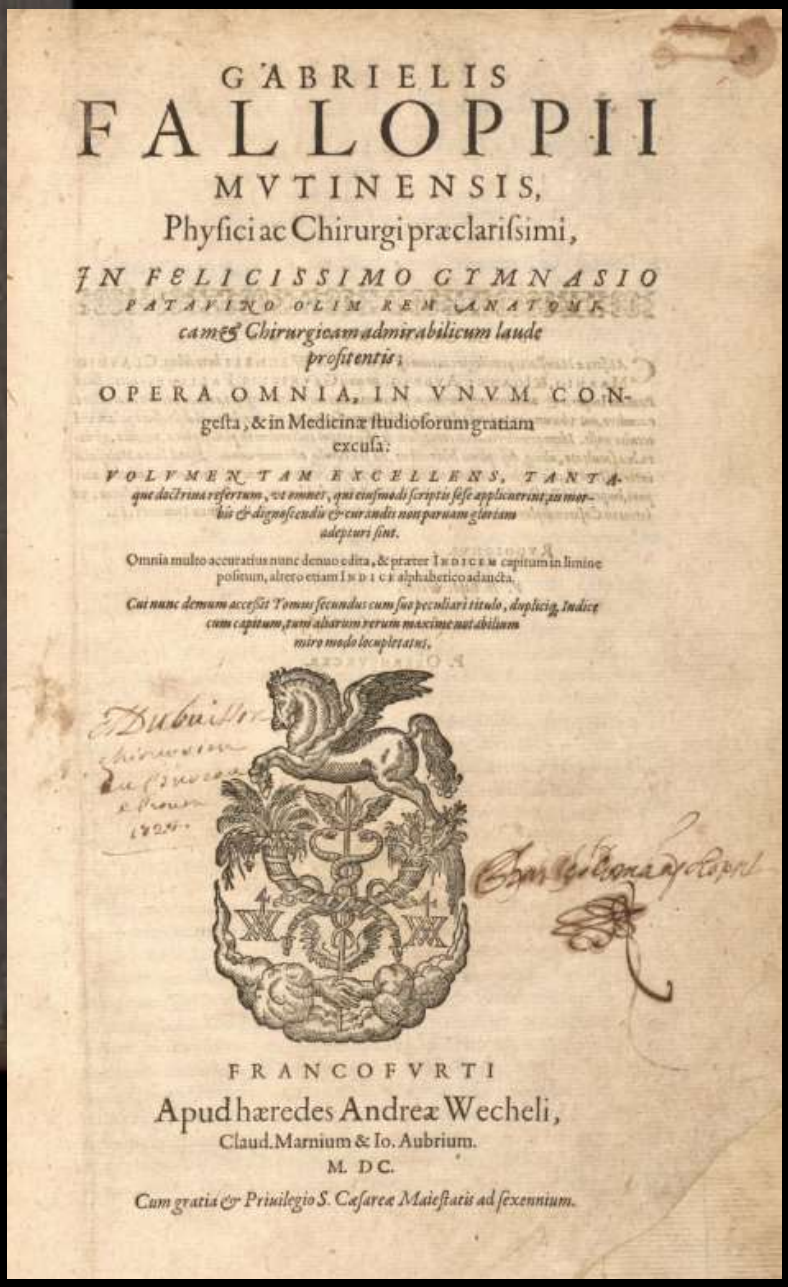
He argued for the teaching of anatomy through direct observation, leading the establishment of the Anatomical Theatre of Padua, where Vesalius and Harvey would later study. He was the first to publish detailed instructions for the reconstruction of the nose.

Ricci p. 285: "He was one of the earliest anatomists to use the words perineum, cervix and procidentia. His medical treatise contains a number of chapters on gynaecological subjects, ulcers of the matrix, on the seed (impregnation), sterility, superfoetation and the signs of abortion," all derived from Paul of Aegina, Galen and Aristotle.

He also wrote on ectopic pregnancy.

Book Notes: Folio (305 x 211 mm). Title page with historiated woodcut border, numerous woodcut initials, woodcut printer's device on colophon. Contemporary vellum over boards with title inked to spine with 3 raised bands.

References: Cianfrani 116; Durling 517; EDIT16 CNCE 5157; Hirsch I, 389; Ricci p. 285.



GABRIELIS
FALLOPPII
MVTINENSIS,
Physici ac Chirurgi præclarissimi,
IN FELICISSIMO GYMNASIO
PATAVINO OLIM REM ANATOMICAM & Chirurgicam admirabilicum laude profitentis;
OPERA OMNIA, IN VNVM CONgesta, & in Medicinæ studiosorum gratiam excusa:
VOLVMEN TAM EXCELLENS, TANTAque doctrina refertum, vt omnes, qui eusmodi scriptis sese applicuerint, summoris & dignoscendis & curandis non parvam gloriam adepturi sint.

Omnia multo accuratius nunc denuo edita, & præter INDICEM capitum in limine positum, altero etiam INDICE alphabetico adaucta.

Cui nunc demum accessit Tomus secundus cum suo peculiari titulo, duplicis Indice cum capitum, tum aliarum rerum maxime notabilium miro modo locupletatus.

FRANCOFVRTI
Apud hæredes Andreæ Wecheli,
Claud. Marnium & Io. Aubrium.
M. DC.
Cum gratia & Priuilegio S. Cæsareæ Maiestatis ad sexennium.

Discovered fallopian tubes and was the first to use the word vagina

GABRIELE FALLOPPIO (1523 - 1562)

Opera omnia...denuo edita...Cui nunc demum accessit tomus secundus...

Frankfurt: Andreas Wechel (heirs of), Claude de Marne et Johann Aubry, 1600 to 1606.

Gabriele Falloppio is best remembered for his precise description of the oviducts, which he likened to the shape of a brass trumpet (tuba), earning them the enduring name "Fallopian tubes." Beyond this famous eponym, Falloppio corrected many errors found in the works of his predecessors, such as Vesalius and Galen, by providing some of the first accurate anatomical accounts of the clitoris and the hymen, proving the existence of the latter against contemporary skepticism.

He also coined the term "vagina" (Latin for "sheath") to describe the muscular canal and distinguished the ovaries—which he still referred to as "female testes"—as distinct organs separate from the uterus, helping to dismantle the ancient "one-sex" model that viewed female organs merely as inverted male ones.

Falloppio is remembered as an anatomist – e.g., *tubae Falloppii* – but he was also a first-rate surgeon. During the last years of his short life he occupied the combined chairs of anatomy, surgery and botany at the renowned university of Padua.

Book Notes: Two works and appendix in 1 volume. Folio (350 x 218 mm). Rebacked contemporary calf decorated in gilt and blind, original spine laid down, vellum lettering piece on spine. Hagelin: "Weschel's Frankfurt edition of Falloppio's Collected Works is considered the best, containing much more than the first edition published by Valgrini in Venice in 1584. In 1606 Weschel issued an appendix of 100 pages."

Provenance: Claude-Nicolas Le Cat (French surgeon, 1700-1768, bookplate); Joseph Claude Anthelme Recamier (French gynecologist and pathologist, 1774-1852, bookplate); and Jan Muhlbauer, American physician and book collector.

References: Cianfrani p. 120; Durling 1427 and 1428; GMN 1537; Hagelin p. 17; Radcliffe p. 14; Waller 2939; Wellcome I, 2167 (for 1606 reprint). Also Michael Stolberg, *Gabrielle Falloppia, 1522/23-1562: The Life and Works of a Renaissance Anatomist*, New York: Routledge, 2023.

Plate V.

JACQUES FABIEN GAUTIER D'AGOTY (1711 - 1786)

Anatomie des parties de la génération, et de ce qui concerne la grossesse et l'accouchement

Paris: J. B. Brunet et Demonville, 1778.

Jacques-Fabien Gautier d'Agoty's large folio book on generation—issued in the 1770s with ten color mezzotint plates—is one of the most visually ambitious anatomical works of the Enlightenment.

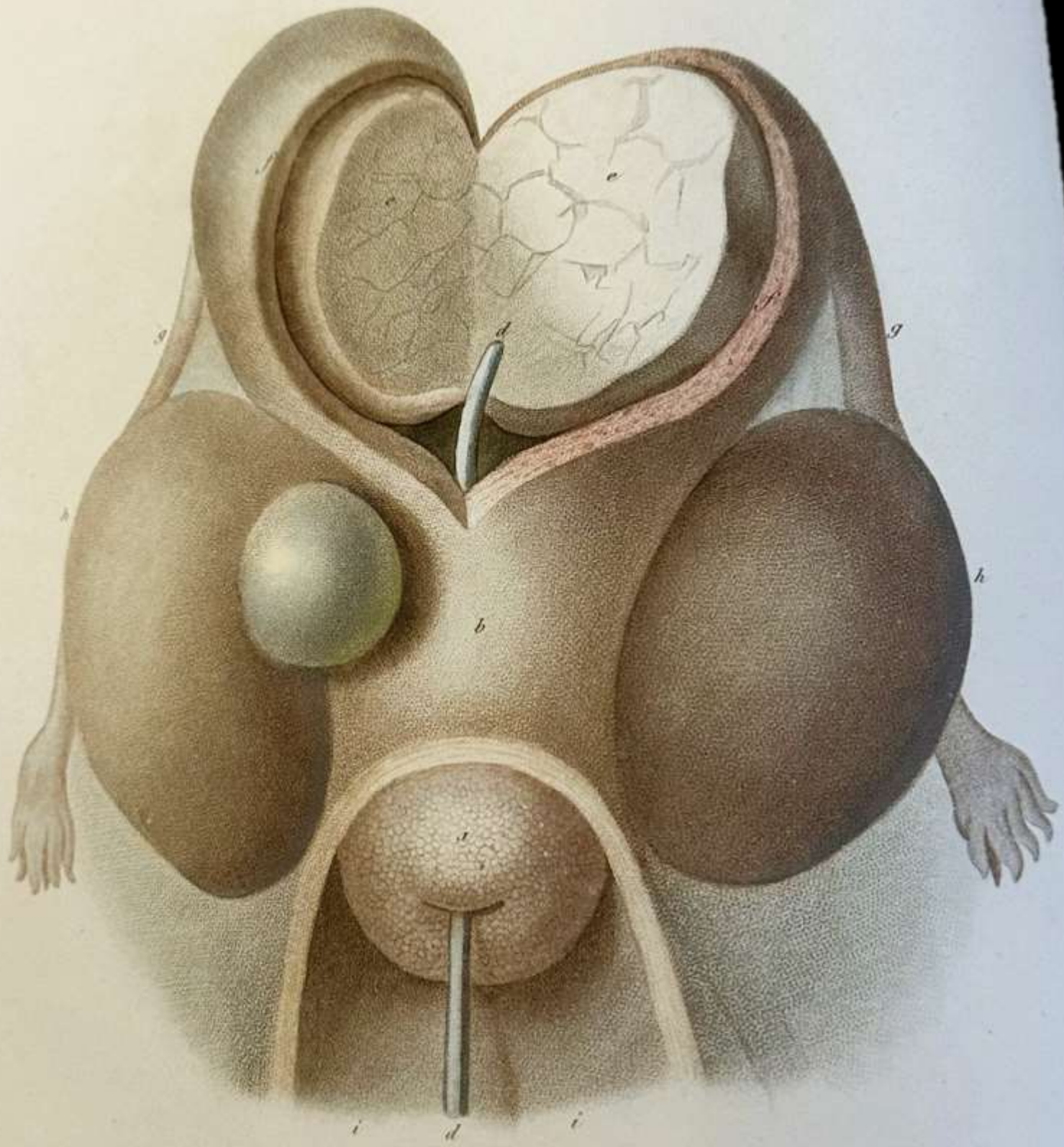
The true originality of the book lies in Gautier d'Agoty's approach to color printing, specifically his mastery of polychrome mezzotint. Trained in the Le Blon color-printing tradition, he employed multiple plates—typically yellow, red, blue, and black—to build images with unprecedented tonal depth and anatomical realism. Artistically, it marks one of the high points of hand-crafted color anatomical printing before cheaper methods displaced it.

This book "begins with tall plates of man and of woman, each formed from two sheets and folding out from the book . . . These first plates showing muscles, arteries and the nervous system are worked out and tabulated in detail. The female figure is a typical Gautier plate, stripped and dissected but with healthy head and throat, charming classical face and hair in perfect order, standing poised as a dancer. In the next folding illustration, we find a fair instance of his semi-erotic treatment of a scientific theme - one woman standing in profile, her living head looking back to us above a naked breast; the womb open, with folded figure of a foetus. At her feet and knees is a nude figure finely modeled sits to show the 'parties de la generation', and from the front her dissected womb. The final folding illustration is of a similar sort, two figures of which the lower seems a curiously relaxed classical nude with impeccable hair, her child just born and resting on her lap, the umbilical cord still uncut. Womb and child are in the open dissection. At the mother's feet is a debris of placenta and cords as if they have not yet been cleared from last night's party" (Franklin, Early Colour Printing, pp. 47-48).

Book Notes: Large Folio (410 x 283 mm). [6], 34, [2] pp. and 10 color mezzotint plates, signed Gautier d'Agoty père, plates I to VIII dated 1773, two plates on the "cup of the symphise" added in this edition: plate IX dated 1773 and Plate X (engraved), dated 1779.

References: Blake 169; Choulant p.272; Wellcome III, p.97 (first ed.); Wombs p. 152.

Fig. 3.



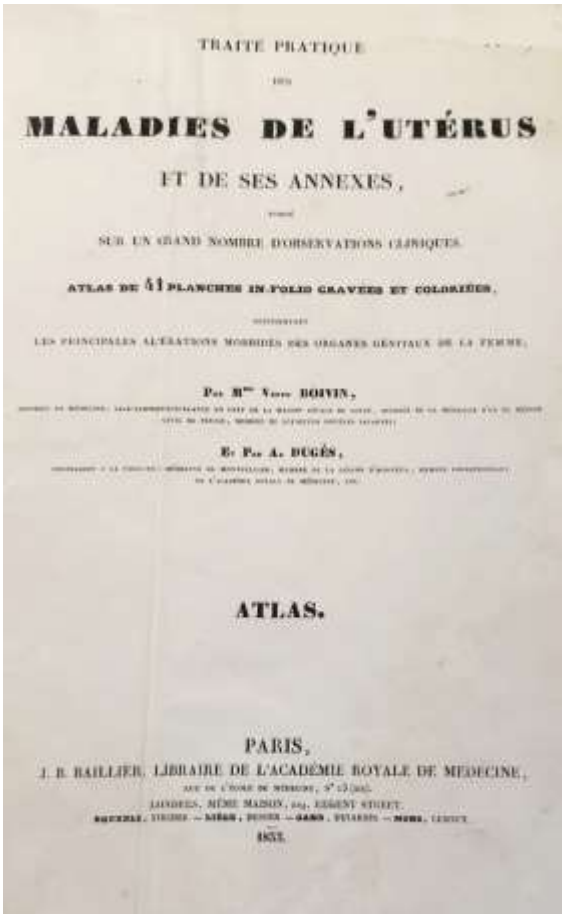
MARIE ANNE VICTOIRE BOIVIN (1773 - 1841)

Traité des maladies de l'utérus... Atlas

Paris: J. B. Bailliere, 1833.

As a highly skilled midwife and researcher at the Maison Royale de Santé, Boivin combined her vast clinical experience with rigorous anatomical study to produce a two-volume treatise that systematically categorized diseases of the uterus, ovaries, and fallopian tubes. Unlike many of her contemporaries who relied on theoretical speculation, Boivin based her work on meticulous post-mortem dissections and thousands of clinical cases, providing some of the earliest and most accurate descriptions of conditions like uterine cancer, fibro-cartilaginous tumors (fibroids), and tubal pregnancies.

The Atlas is known for its hand-colored lithographs, which were praised for their clinical realism and anatomical fidelity. These plates allowed practitioners to visualize the progression of various pathologies—such as the "cauliflower" excrescence of the cervix or the internal structure of hydatid cysts—with a level of detail previously unavailable. Boivin's work was so influential that it was quickly translated into several languages and earned her an honorary doctorate from the University of Marburg, a rare feat for a woman at the time.


TRAITÉ PRATIQUE

MALADIES DE L'UTÉRUS

ET DE SES ANNEXES,

SUR UN GRAND NOMBRE D'OBSERVATIONS CLINIQUES.

ATLAS DE 41 PLANCHES IN-FOLIO GRAVÉES ET COLORIÉES,

LES PRINCIPALES ALTÉRATIONS MORBIDES DES ORGANES GÉNITAUX DE LA FEMME.

Par Mme Vve BOIVIN,

Et Par A. DUGÈS,

ATLAS.

PARIS,

J. B. BAILLIÈRE, LIBRAIRE DE L'ACADÉMIE ROYALE DE MÉDECINE,

LONDRES, MÊME MAISON, 219, REGENT STREET.

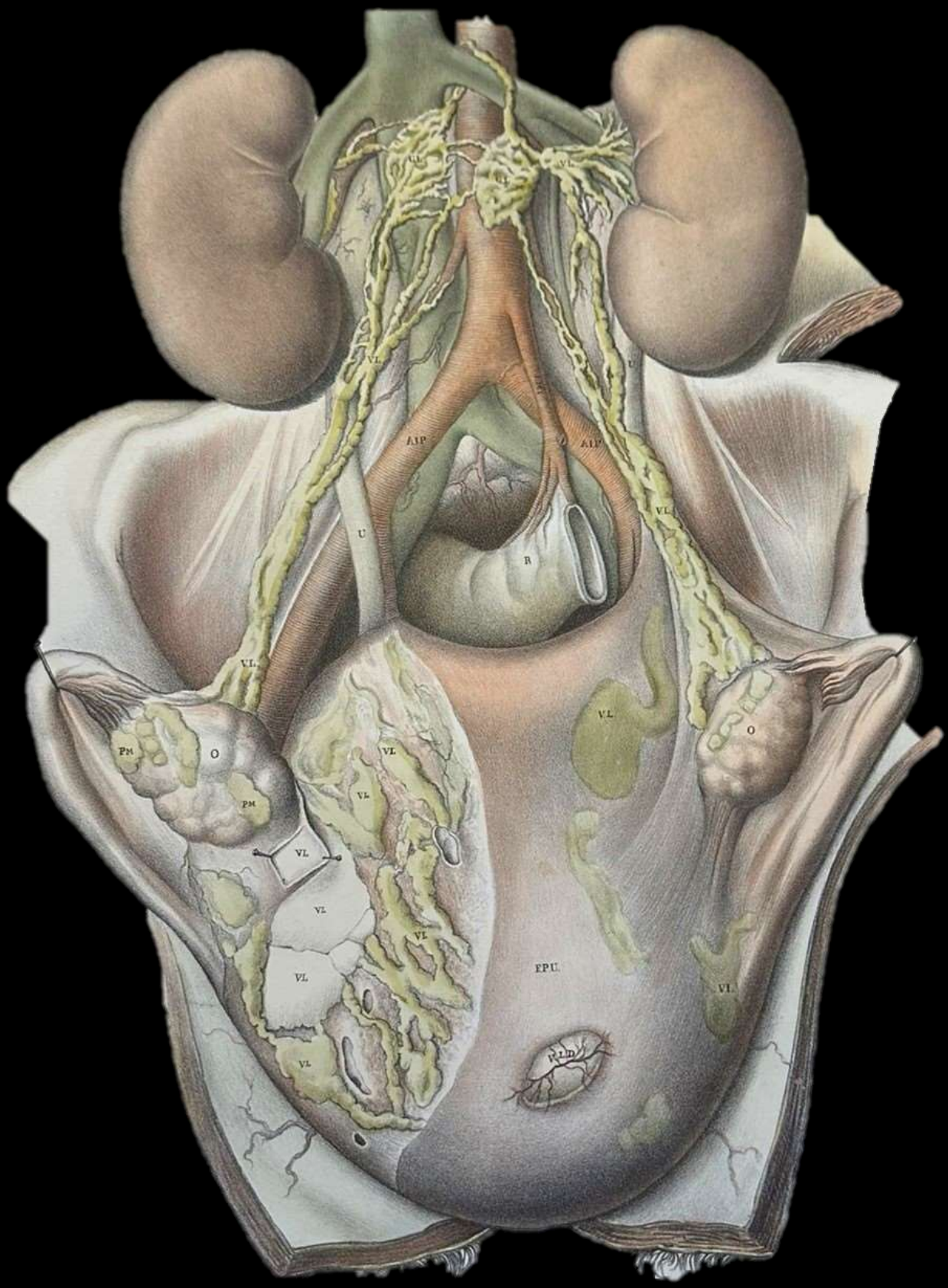
1833.

Book Notes: Atlas only. folio, 39 pages + 41 numbered plates. Bound in original boards covered in red paper.

Provenance: Previously owned by Dr. Arthur Tatossian.

References: Cutter & Viets p. 200; GMN 6028 ; Heirs of Hippocrates, 1282; Hirsch 1, 613; Wellcome II, 195.

Opposite Page: Fig 3. Benign Uterine Fibroid
[e,e: A multi-lobed tumor occupying the proper cavity of the uterus and not adhering to it except by a very fine lamellar tissue, which allowed for easy enucleation]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JEAN CRUVEILHIER (1791 - 1874)

Atlante generale della Anatomia patologica

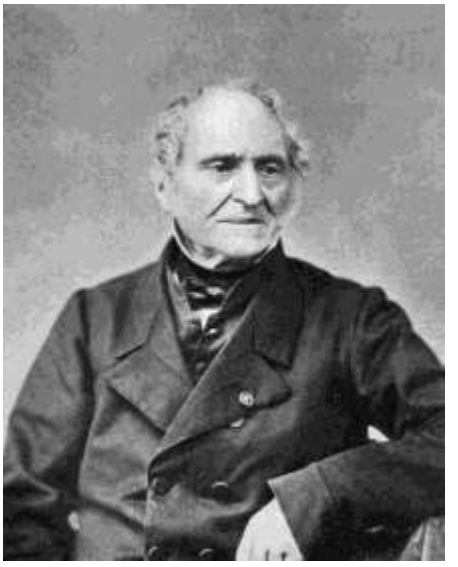
Florence: Vincenco Batelli, 1843.

The two-volume anatomical atlas of pathology contains 233 beautifully illustrated and colored lithographic plates by Antoine Chazal, a renowned painter and illustrator of the 19th century. Cruveilhier was an accomplished pathologist possessing a comprehensive knowledge of morbid anatomy. He was the first to describe the lesions which are associated with multiple sclerosis, one example among many contained within *Anatomie pathologique* (the first ed of this work).

Jean Cruveilhier's work was revolutionary because it was one of the first to use color lithography to show the "living" appearance of diseased tissue rather than just dry anatomical sketches.

Anatomie pathologique was originally issued in 40 livraisons (i.e. issues or parts) from 1829 to 1842. Each livraison contains three to five descriptions of various pathologies with accompanying plates.

The hand-painted lithographs of female anatomy are stunning and, occasionally gruesome, illustrating the effects of uterine gangrene, among other pathologies.



Jean Cruveilhier

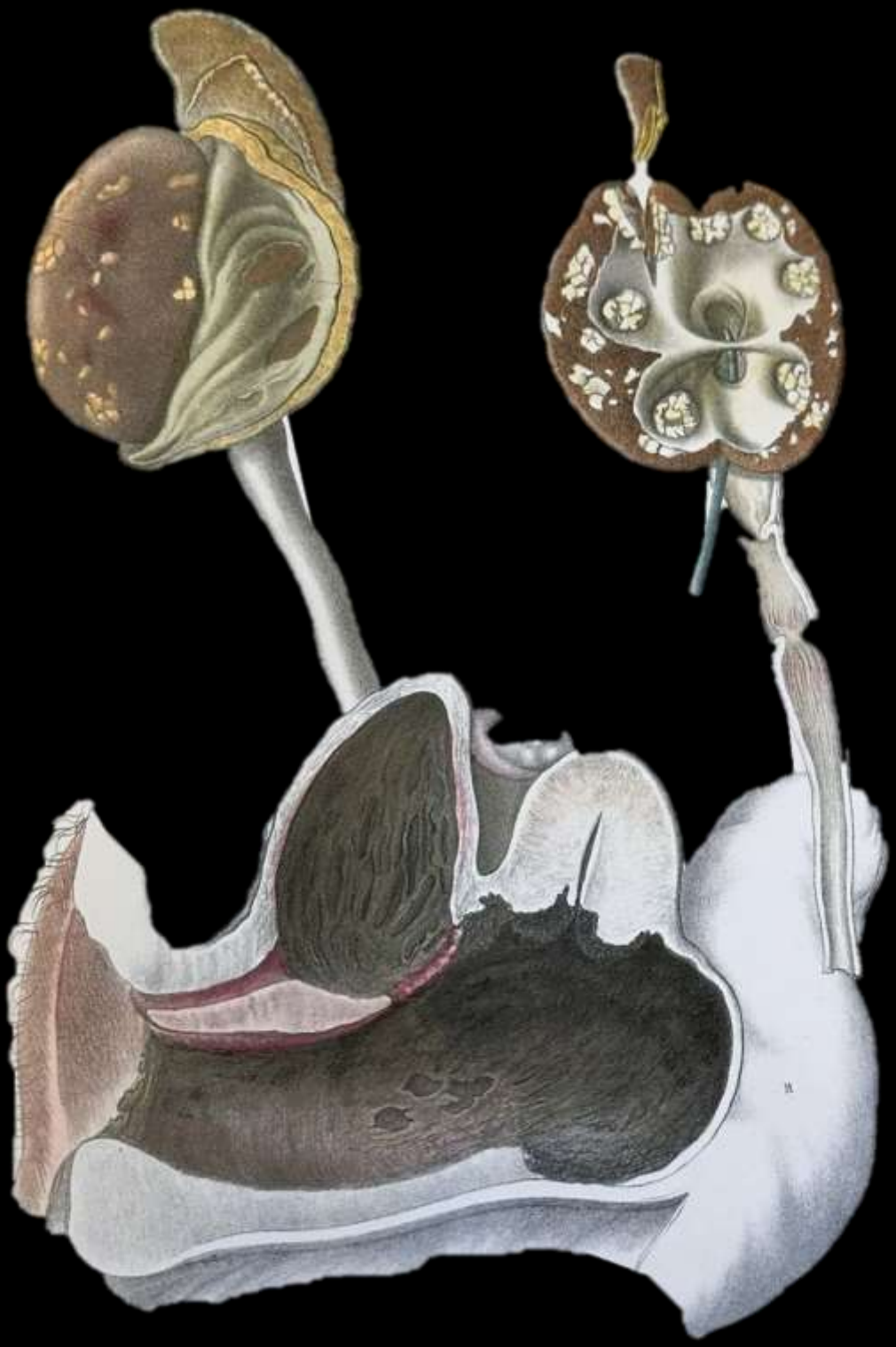
Book Notes: This is the Italian translation of Cruveihier's *Anatomie pathologique du corps humain*.

Provenance: Previously owned by Dr. Arthur Tatossian.

References: GMN 2286 (French ed.); Hirsch II, 150-151; Walleriana I, 2230; Wellcome II, 412.

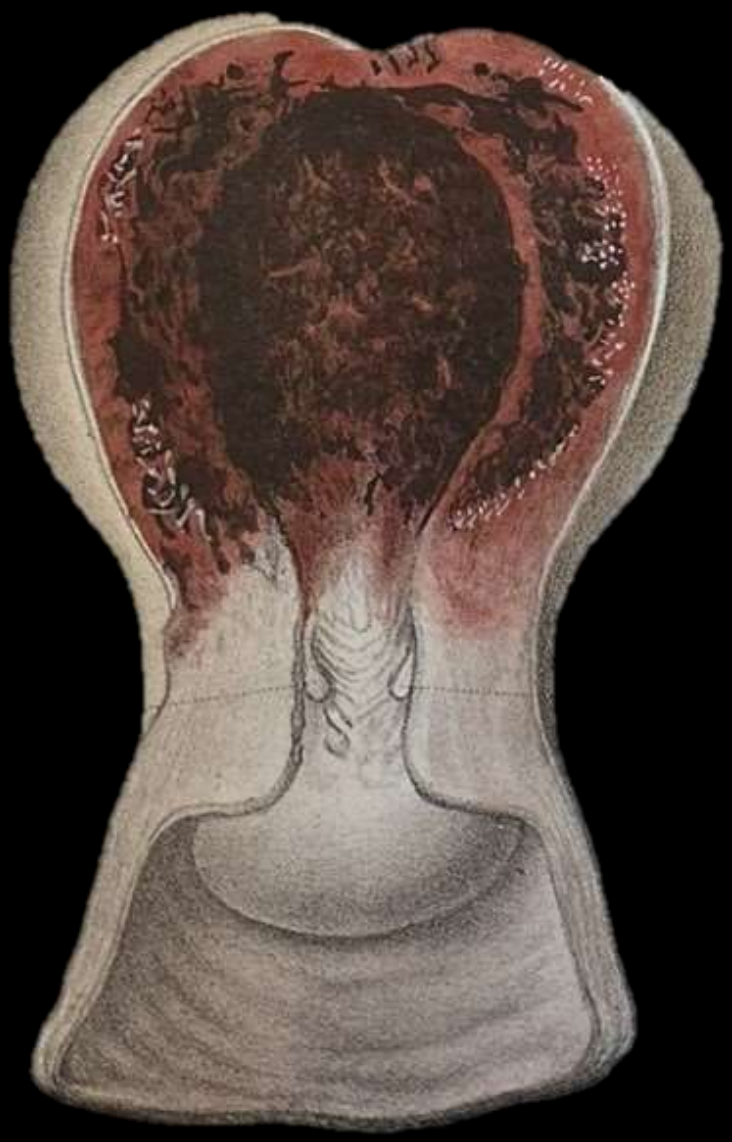
Opposite Page: Severely infected uterus
The uterus of a woman who died of puerperal typhus on the 4th day of the onset of the disease and the 5th day after delivery.

Severe infection of the uterus and ovaries
(as a result of puerperal fever)



From Jean Cruveihier, *Atlante generale della Anatomia patologica*

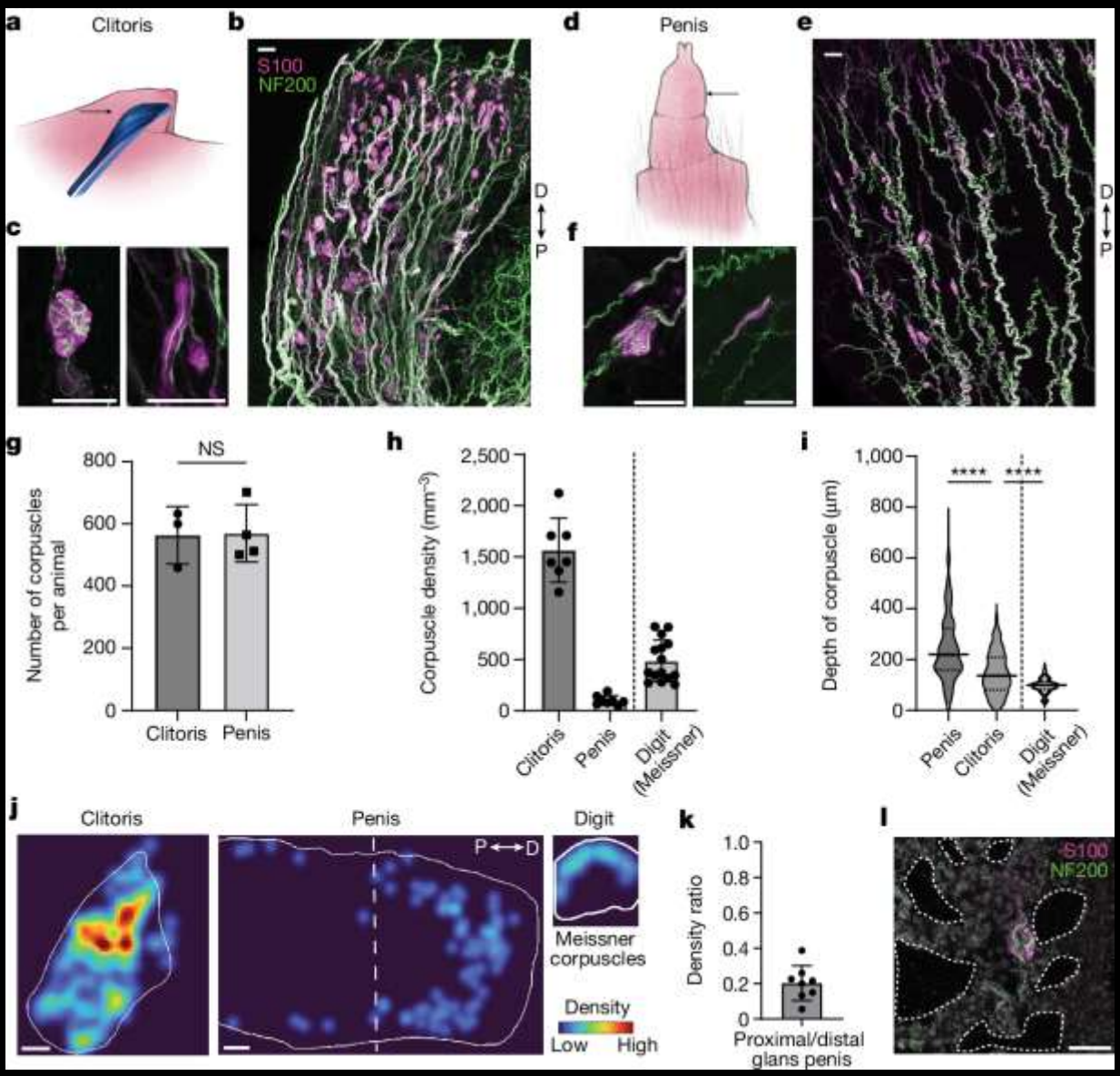
Advanced uterine cancer



The dark, brownish-black central mass represents a cancerous tumor that has become necrotic (dead tissue). Cruveilhier used these dark tones to show "gangrenous" or "putrid" changes within a tumor.The "Cauliflower" Growth: The red, irregular fringes surrounding the dark center are characteristic of what early pathologists called a "fungoid" or "cauliflower" excrescence. This is a classic visual description of an aggressive cervical or endometrial carcinoma that is actively invading and destroying the surrounding healthy tissue.

From Jean Cruveihier, *Atlante generale della Anatomia patologica*

Fig. 1: Krause corpuscles are distributed across female and male mouse genitalia.



a, Illustration of the mouse clitoris (blue, black arrow) within the genital protrusion. **b**, Sagittal section (200 µm) of the clitoris stained for S100 and NF200. **c**, Examples of complex (left) and simple (right) Krause corpuscles in the clitoris. **d**, Illustration of the glans penis (arrow) externalized from the retracted prepuce. **e**, Sagittal section (200 µm) of the adult glans penis stained as in **b**. **f**, Examples of complex (left) and simple (right) Krause corpuscles in the penis. **g**, The total number of corpuscles summed across all sections of the clitoris or penis from each animal. Statistical analysis was performed using unpaired *t*-tests; $P = 0.94$; NS, not significant. $n = 3$ (female) and 4 (male) mice. **h**, The density of Krause corpuscles in the mouse clitoris and penis, compared with that of Meissner corpuscles in the digit (7 sections from 4 female mice; 8 sections from 2 male mice; and 15 sections from digits of 2 mice). **i**, Violin plot of the depth of corpuscles from the nearest tissue surface ($n = 365$ (penis), 554 (clitoris) and 130 (digit) corpuscles). Data are median ± quartiles. Analysis using one-way analysis of variance (ANOVA) with post hoc multiple-comparison test showed an effect of tissue type ($F_{2,1,046} = 151.2$, $P < 0.0001$); ****$P < 0.0001$. **j**, Example heat map of corpuscle density across a clitoris, penis and digit. Heat maps are normalized equally across the tissue types to the densest region of the clitoris. **k**, The ratio of the number of corpuscles located in the proximal half of the glans penis to that in the distal half. **l**, Example of a Krause corpuscle adjacent to expanded cavernous space (dotted lines) in a penis fixed in the erect state and stained as in **b**. Scale bars, 200 µm (**j**) and 50 µm (**b**, **c**, **e**, **f** and **l**). D, distal; P, proximal. For **g**, **h** and **k**, data are mean ± s.d. The diagrams in **a** and **d** were created by G. Park.

LIJUN QI, MICHAEL ISKOLS, RACHEL GREENBERG, JIA YIN XIAO, ANNIE HANDLER, STEPHEN LIBERLES AND DAVID GINTY

Krause corpuscles are genital vibrotactile sensors for sexual behaviours

Nature, June 19, 2024.

Krause corpuscles, which were discovered in the 1850s, are specialized sensory structures found within the genitalia and other mucocutaneous tissues. The physiological properties and functions of Krause corpuscles have remained unclear since their discovery. Here we report the anatomical and physiological properties of Krause corpuscles of the mouse clitoris and penis and their roles in sexual behaviour.

We observed a high density of Krause corpuscles in the clitoris compared with the penis.

Using mouse genetic tools, we identified two distinct somatosensory neuron subtypes that innervate Krause corpuscles of both the clitoris and penis and project to a unique sensory terminal region of the spinal cord. *In vivo* electrophysiology and calcium imaging experiments showed that both Krause corpuscle afferent types are A-fibre rapid-adapting low-threshold mechanoreceptors, optimally tuned to dynamic, light-touch and mechanical vibrations (40–80 Hz) applied to the clitoris or penis.

Functionally, selective optogenetic activation of Krause corpuscle afferent terminals evoked penile erection in male mice and vaginal contraction in female mice, while genetic ablation of Krause corpuscles impaired intromission and ejaculation of males and reduced sexual receptivity of females. Thus, Krause corpuscles of the clitoris and penis are highly sensitive mechanical vibration detectors that mediate sexually dimorphic mating behaviors.

Annette Fenner (*Nature*, July 16, 2024) discussed the paper and wrote: “These data solve a centuries-old mystery about the physiology and function of genital Krause corpuscles, showing that they are highly sensitive mechanical vibration detectors mediating sexually dimorphic mating behaviours.”

After hundreds of years of watching others fail to explain why sex feels so good, Harvard neurobiologist David Ginty’s lab in 2024 publishes a paper that explains the cells that account for the tactile and sensory response associated with sex.

4

Endometriosis

Endometriosis is a chronic gynecological condition, characterized by abnormal presence of endometrial glands and stroma outside the uterus accompanied by chronic inflammation. Most commonly it affects organs of the pelvic cavity: ovaries, fallopian tubes, urinary bladder, intestines or peritoneum.

Rarely, it is localized in other organs outside the pelvis—diaphragm, pleura, abdominal wall, central or peripheral nervous system. Endometriosis is mainly found in girls and women of reproductive age.

Approximately 10% of reproductive-aged women (190 million) globally are diagnosed with this condition. Usually, it takes up to 8 to 10 years to diagnose this disease.

Endometriosis has a variable range of manifestations—from accidentally found asymptomatic lesions to severe condition which does not depend on the size of the lesion.

The main symptoms caused by endometriosis are chronic pelvic pain, severely painful menstrual periods, dyspareunia, dysuria and/or painful defecation, abdominal bloating and constipation. It may also increase the risk of mental health issues, such as anxiety and depression. The other manifestation of endometriosis is infertility without any other symptoms: 40–50% of infertile women are diagnosed with endometriosis.

The Long History of Endometriosis

In their paper “Endometriosis: Ancient Disease, Ancient Treatments”, Nezhat et al., (2012) note that diseases that sound like endometriosis have been in the literature since the Hippocratic era. The ancient condition called “uterine suffocation” bears remarkable resemblance to endometriosis.

Hildegard von Bingen

Our reading of Hildegard’s *Causae et Curae* (from the 1200s) also gives us the distinct sense that endometriosis has been with us the entire time. Hildegard describes problems associated with heavy menstruation – in a manner that sounds remarkably like endometriosis.

Ever more precise definitions of this condition were given over time.

Notably, a number of French physicians began to describe a type of monthly hysteria as a psychological problem in the 1840s. Nezhat et al. (2012) believe that this was almost certainly endometriosis.

Thomas Addison, better known for his work in endocrinology, described endometriosis rather well in 1830. Addison observed that many women suffered from chronic pelvic pain, severe menstrual cramps, and "irritation" that seemed to worsen cyclically. He noted that this was not necessarily confined to the uterine region.

However, real progress in classifying this disease would require the microscope, access to gynecologic tissue and pathological skill. Johannes Peter Müller (see our female cancers section for his work) built up a significant laboratory in Vienna for tissue pathology work in the early 1830s and brought in Rokitansky.

Ronald Batt’s well-researched and wonderful 2011 book *A History of Endometriosis* argues quite convincingly that Carl Freiherr von Rokitansky described the scientific and histological aspects of endometriosis rather well in 1860. Most other observers also credit Rokitansky as the key pioneer.

Nonetheless, others such as Benagiano and Brosens (2010) disagree indicating that the lesions identified by Rokitansky were neoplastic.

From here, late-19th-century gynecology and pathology began to differentiate uterine wall disease (what we now call adenomyosis) from extrauterine implants.

That distinction would remain contested for decades, but it laid the groundwork for later classification and treatment. Retrospectively, this era also illustrates a persistent theme: the disease was present, but medicine's interpretive lens was often inadequate—leading to misattribution and long delays in diagnosis, a problem that remains clinically salient even today.

Freud, for example, misdiagnosed the individuals with the disorder as hysteric and tried to treat them by hypnosis in the last decades of 19th and the first decades of the 20th centuries.

The term "endometriosis" was first used by Sampson in 1925, and Cullen described it strikingly well in a 1908 paper. Sampson's theory that retrograde menstruation is the cause remains the main explanation accepted today, although most experts believe that this disease has more than one cause.

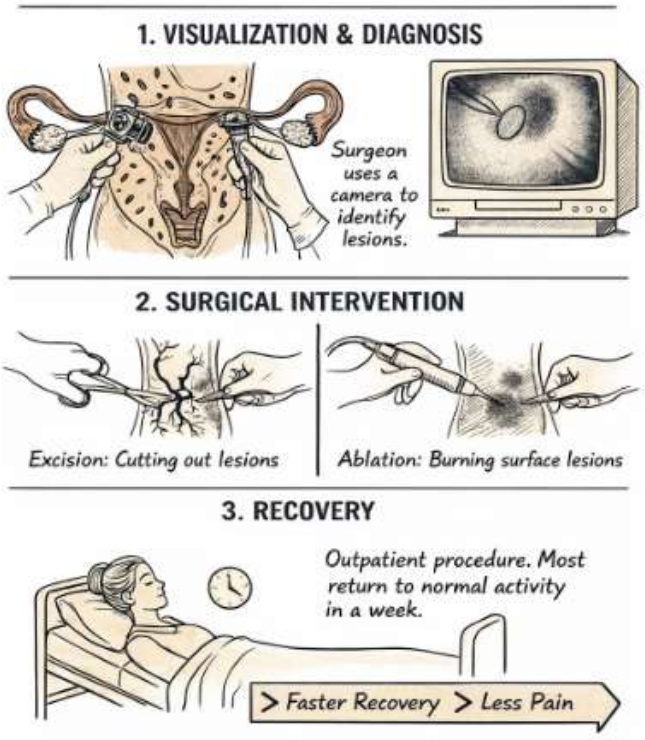
Sampson's retrograde menstruation theory remains influential, but modern biology has reframed it as necessary-but-not-sufficient: retrograde menstruation is common, while endometriosis is not inevitable. Contemporary models therefore integrate immune dysfunction, inflammatory signaling, stem/progenitor cell contributions, coelomic metaplasia, and genetic susceptibility alongside mechanical reflux. Still, Sampson's contribution was foundational: he provided an explanatory "first draft" that made the condition investigable.

Emil Novak in 1948 noted that endometriosis fluctuated with hormonal levels, providing the insight that triggered the development of the first hormonal therapies in the 1960s. Big progress has come in the last half century with ever improving hormonal therapies, including GnRH agonists.

Laparoscopy has also been a game changer for many women. Laparoscopy was first developed in France in the 1940s (particularly Raoul Palmer) and began to be used effectively for endometriosis in the United States in the late 1970s, particularly by Harry Reich.

Historically, endometriosis was frequently diagnosed late, at laparotomy, or inferred indirectly. Laparoscopy changed the disease from a pathological curiosity to a common operative finding—and enabled a surgical discipline around lesion recognition, excision/ablation, and adhesiolysis.

As reproductive endocrinology advanced, endometriosis came to be framed as an estrogen-dependent condition with inflammatory and neuroangiogenic features. This enabled medical strategies aimed at ovarian suppression and lesion quiescence—often effective for symptom control, but historically limited by side effects, recurrence after discontinuation, and incomplete disease eradication.



Laparoscopy has been a game changer for many endometriosis patients

Karl Freiherr von Rokitansky 1860

Described endometriosis quite well for the first time in modernity without using the word

KARL FREIHERR VON ROKITANSKY (1804 - 1878)

Ueber Uterusdrüsen-Neubildung in Uterus- und Ovarial-Sarcomen

Ueber
Uterusdrüsen-Neubildung
in Uterus- und Ovarial-Sarcomen.
Von
Hofrath Prof. Dr. C. Rokitansky.

Vienna: Druck von Carl Ueberreuter, September 10, 1860.

During the nineteenth century, Karl Freiherr von Rokitansky conducted research on the causes of disease by performing approximately 30,000 autopsies, a practice that many people opposed at the time. Rokitansky performed his research in pathology, or the study of disease, and morbid anatomy, in a morgue in Vienna.

Rokitansky's 1860 article, "Ueber Uterusdrüsen-Neubildung in Uterus- und Ovarial-Sarcomen" (New Growth of Uterine Glands in Sarcomas of the Uterus and Ovaries), is a key early text in the modern study of endometriosis and adenomyosis.

Using a Brunner microscope and his unparalleled experience from thousands of barehand autopsies, Rokitansky was the first to provide a detailed histological description of ectopic endometrial glands and stroma. His work was pathbreaking insofar as it moved the study of these conditions beyond naked-eye observations to objective diagnostic criteria—specifically, whether endometrial tissue is in abnormal locations—a criterion that physicians still use more than 150 years later.

Rokitansky identified three distinct phenotypes of the disease, providing them with descriptive Latin names based on the medical terminology of the mid-nineteenth century. It is important to note that Rokitansky used the term sarcoma to designate "benign growths" and not malignancies, clearly specifying that these invasions were non-neoplastic in nature.

By demonstrating that this tissue could "flow" into and inhabit areas outside the uterine cavity, he prepared the medical community for a century of research into pathogenesis and treatment, a lineage of ideas that stretches from his station in the Vienna General Hospital morgue to the later work of Thomas Cullen and John Sampson.

References: Batt p. 27; Radcliffe p. 75.

Source: Wellcome Collection.

THOMAS ADDISON (1795 - 1860)

Observations on the Disorders of Females Connected with Uterine Irritation

Glasgow: S. Highley, 1830.

Thomas Addison's 1830 monograph, *Observations on the Disorders of Females Connected with Uterine Irritation*, is an important gynecology text that explored the profound systemic effects of reproductive health issues. This book is a reprint of a lecture on what he learned treating women patients at Guy's Hospital in London.

While Addison is most famous for "Addison's Disease" (adrenal insufficiency), this earlier publication focused on the clinical manifestations of what he called "uterine irritation"—a term used to describe a cluster of painful symptoms that he believed originated from the uterus but affected the entire nervous system.

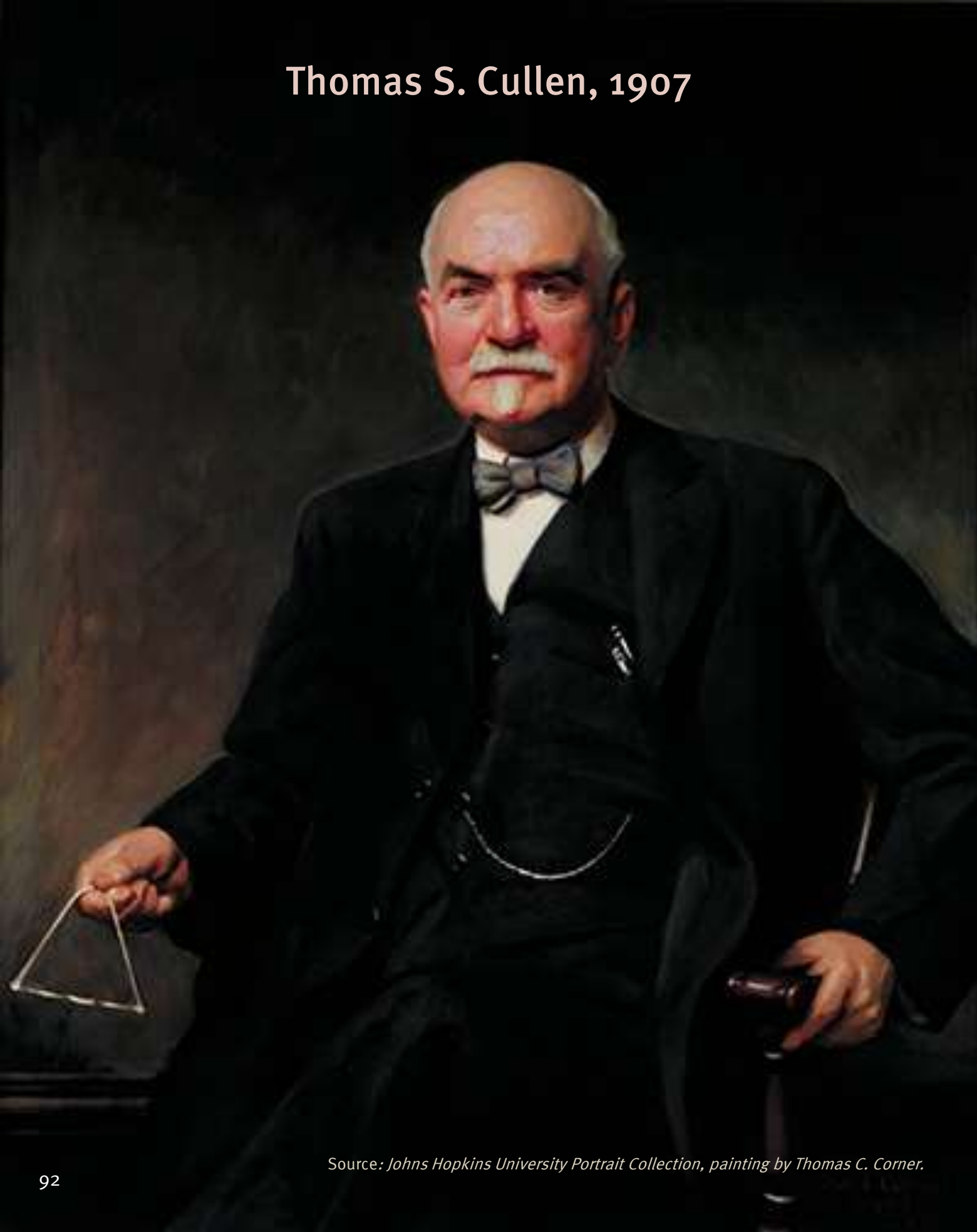
Modern medical historians often point to this work as a significant, though indirect, early description of endometriosis.

Addison observed that many women suffered from chronic pelvic pain, severe menstrual cramps (dysmenorrhea), and "irritation" that seemed to worsen cyclically.

Crucially, he noted that this irritation could lead to painful symptoms in parts of the body far removed from the uterus. Although he lacked the laparoscopic tools to visualize endometrial implants outside the uterine cavity, his descriptions of the cyclical nature of the pain and the progressive "thickening" or "morbid sensibility" of the pelvic tissues align closely with the clinical presentation of endometriosis.

Addison was particularly interested in how uterine problems could manifest not only as localized pain but also in more general disorders, such as changes in mood, fatigue, and disturbances that affected the overall health of women. Its core concepts—that uterine irritation can cause various disorders and systemic symptoms—remain relevant today in understanding conditions like endometriosis, pelvic inflammatory disease, and uterine fibroids.

Thomas S. Cullen, 1907



Source*: Johns Hopkins University Portrait Collection, painting by Thomas C. Corner.*

An early clinical report that clearly described the pathology of adenomyosis, the sister condition of endometriosis

THOMAS STEPHEN CULLEN (1868 - 1953)

Adeno-myoma Uteri Diffusum Benignum

Johns Hopkins Hospital reports, 1896

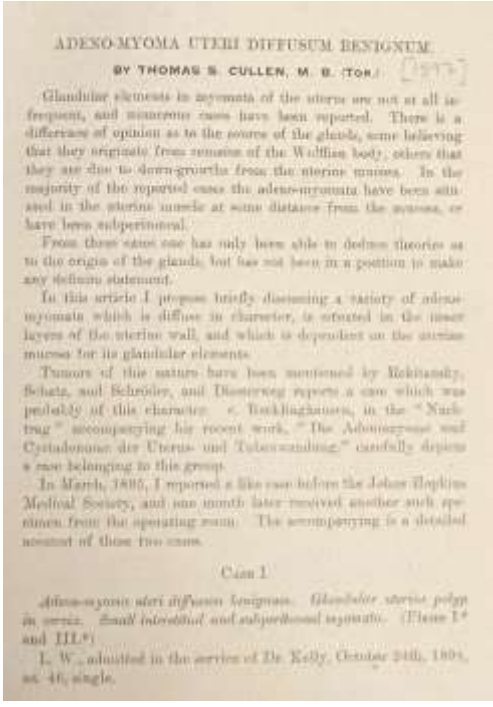
Thomas Cullen's 1896 monograph, titled *Adeno-myoma Uteri Diffusum Benignum*, was an important landmark in gynecological pathology.

In this article, Cullen provided a meticulous description of what is now known as adenomyosis, though at the time he categorized it under the broader umbrella of "adenomyoma." He described the condition as a benign but diffuse invasion of the uterine muscle (myometrium) by the lining of the uterus (endometrium).

Crucially, Cullen was among the first to demonstrate that this "mucosal invasion" was not a malignancy but rather a migration of normal uterine mucosa into the underlying muscular wall, often observing the direct physical connection between the surface lining and the deep muscular pockets.

Importantly, adenomyosis and endometriosis are "sister conditions" because both involve endometrial tissue growing where it shouldn't, causing pain and heavy bleeding during menses, with the key difference being location: adenomyosis is tissue growing inside the uterine muscle wall, while endometriosis is tissue growing outside the uterus (e.g., on ovaries, bowels).

Cullen's 1896 paper is recognized as an accurate pathological description of endometriosis. During the late 19th century, physicians were still struggling to differentiate between various forms of ectopic endometrial tissue. Cullen's work was pathbreaking because he identified both the morphological structure (endometrial glands and stroma) and the clinical picture associated with the disease, specifically noting the hallmark symptoms of severe pelvic pain and prolonged, heavy menstrual bleeding. Importantly, he argued that adenomyosis has a mucosal origin, an idea that was highly controversial at the time. See Hudelist, Keckstein and Wright (2009).



ADENO-MYOMA UTERI DIFFUSUM BENIGNUM.

BY THOMAS S. CULLEN, M. B. (TOR.)

Glandular elements in myomata of the uterus are not at all infrequent, and numerous cases have been reported. There is a difference of opinion as to the source of the glands, some believing that they originate from remains of the Wolffian body; others that they are due to down-growths from the uterine mucosa. In the majority of the reported cases the adeno-myomata have been situated in the uterine muscle at some distance from the mucosa, or have been subperitoneal.

From these cases one has only been able to deduce theories as to the origin of the glands, but has not been in a position to make any definite statement.

In this article I propose briefly discussing a variety of adeno-myomata which is diffuse in character, is situated in the inner layers of the uterine wall, and which is dependent on the uterine mucosa for its glandular elements.

Tumors of this nature have been mentioned by Rokitansky, Schatz, and Schröder, and Doderlein reports a case which was probably of this character. v. Recklinghausen, in the "Nachtrag" accompanying his recent work, "Die Adenomyome und Cystadenome der Uterus- und Tubenwandung," carefully depicts a case belonging to this group.

In March, 1895, I reported a like case before the Johns Hopkins Medical Society, and one month later received another such specimen from the operating room. The accompanying is a detailed account of these two cases.

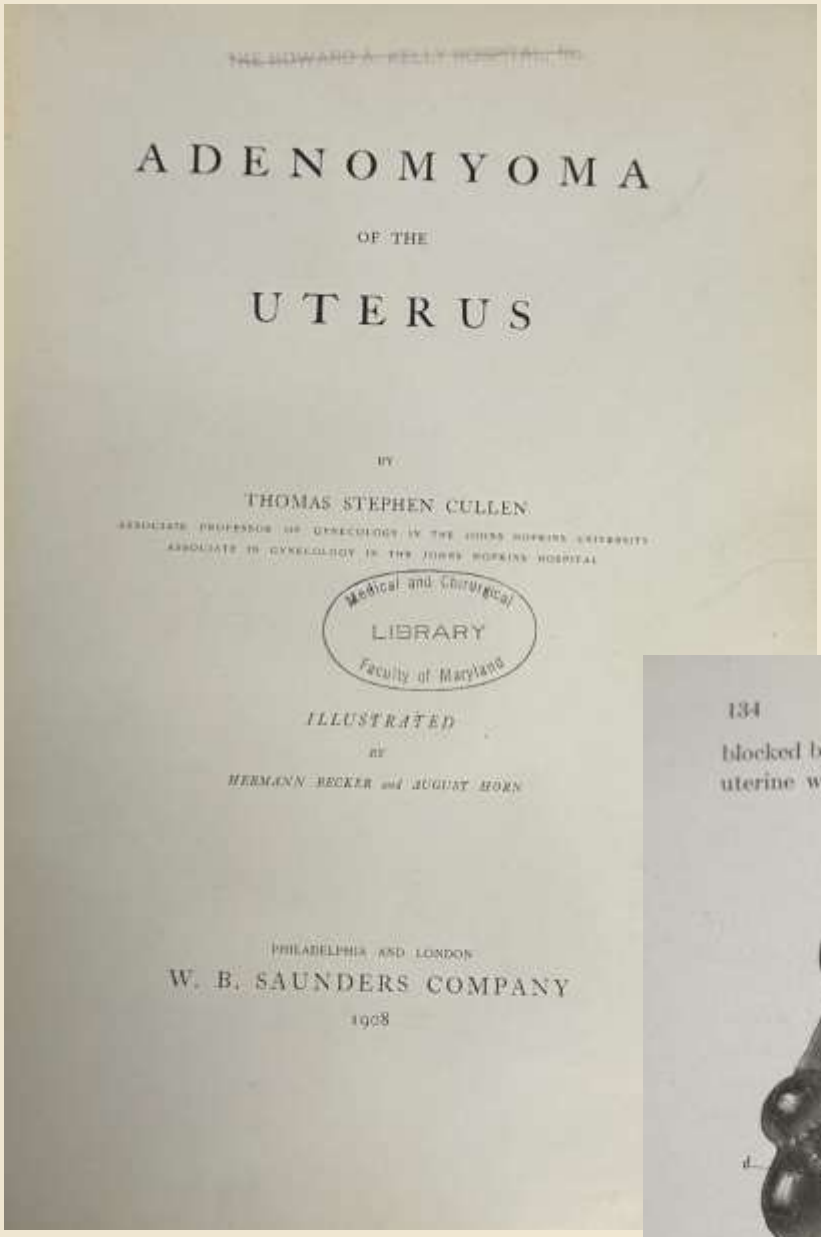
Case I.

Adeno-myoma uteri diffusum benignum. Glandular uterine polyp in cervix. Small interstitial and subperitoneal myomata. (Figs. I* and III.*)

L. W., admitted to the service of Dr. Kelly, October 24th, 1894, æt. 46, single.

Thomas S. Cullen established Johns Hopkins' gynecologic pathology laboratory. He came to Johns Hopkins in 1891 to study under William Welch in the pathology laboratory. He wrote a pathbreaking set of reports on cancer of the uterus, adenomyoma of the uterus, hyperplasia of the endometrium, diseases of the umbilicus, fibroid tumors of the uterus, and extrauterine pregnancy. Cullen's sign, a discoloration of the skin about the navel that is regarded as a sign of a ruptured ectopic pregnancy, is named for him.

References: Batt p. 123; Leonardo p. 365; Nezhat et al. (2012), Gernot Hudelist, Joerg Keckstein, Jeremy T. Wright, "The migrating adenomyoma: past views on the etiology of adenomyosis and endometriosis," *Fertility and Sterility*, Nov 2009;92(5):1536-43.



ADENOMYOMA

OF THE

UTERUS

BY

THOMAS STEPHEN CULLEN

ASSOCIATE PROFESSOR OF GYNECOLOGY IN THE JOHNS HOPKINS UNIVERSITY
ASSOCIATE IN GYNECOLOGY IN THE JOHNS HOPKINS HOSPITAL

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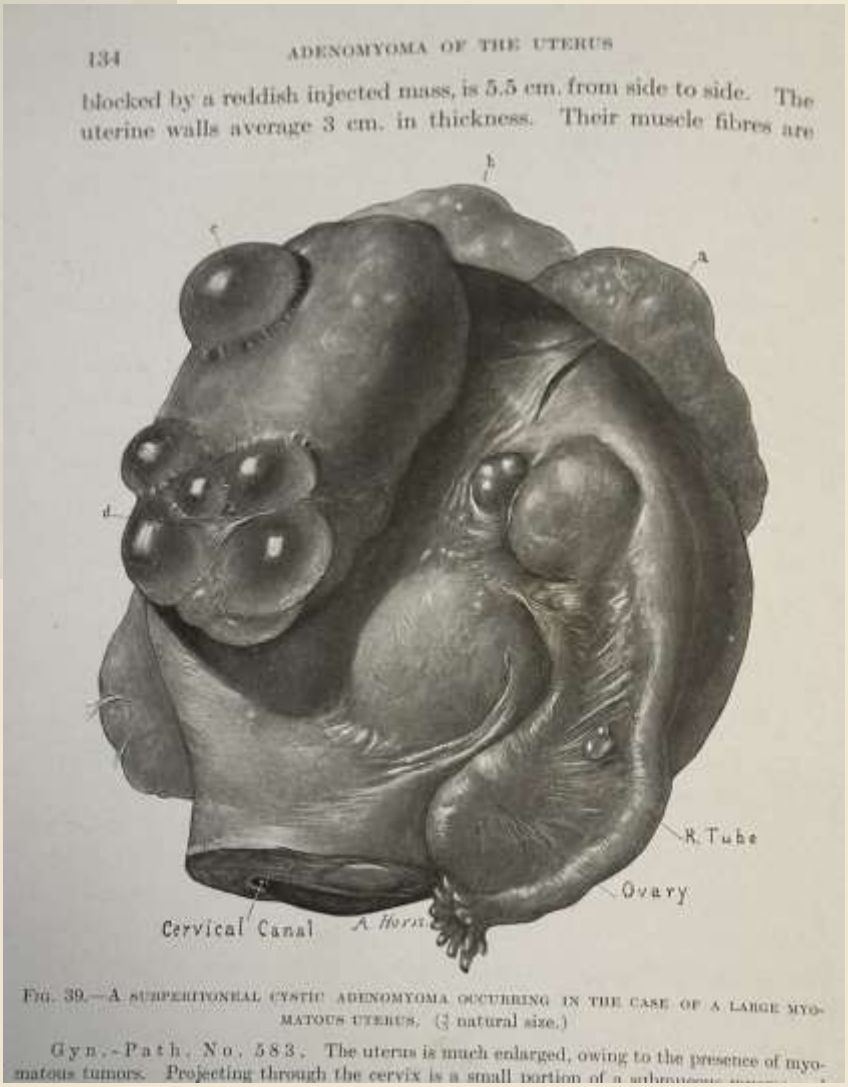


134 ADENOMYOMA OF THE UTERUS

blocked by a reddish injected mass, is 5.5 cm. from side to side. The uterine walls average 3 cm. in thickness. Their muscle fibres are

FIG. 39.—A SUBPERITONEAL CYSTIC ADENOMYOMA OCCURRING IN THE CASE OF A LARGE MYOMATOUS UTERUS. (⅓ natural size.)

Gyn.-Path. No. 583. The uterus is much enlarged, owing to the presence of myomatous tumors. Projecting through the cervix is a small portion of a submucous

Endometriosis lesion with chocolate cysts identified by Cullen in 1908 (without naming it using contemporary language.

The first clear description of endometriosis that combined relevant pathological observations with clinical signs

THOMAS STEPHEN CULLEN (1868 - 1953)

Adenomyoma of the Uterus

Chicago: American Medical Association, 1908.

Reprinted from *The Journal of the American Medical Association*. Cullen carefully documented cases of endometrial tissue outside the uterus, including in the rectovaginal septum. He argued these lesions originated from the uterine mucosa — establishing the foundation for the concept of endometriosis.

Benagiano and Brosens (2011) carried out a careful review of the many claims in the medical history literature as to who was the first to identify endometriosis. They conclude that Cullen was first (followed by Sampson):

> "Reconstructing the paths that led to the identification of the diseases we today call adenomyosis and endometriosis is a complex undertaking. A number of investigators contributed to the creation of the overall picture of what constitutes the essential features of these conditions. Nonetheless, we believe that the first investigator to assemble all the essential pieces of the puzzle was Thomas Cullen, followed by John A. Sampson."

We include both the 1896 paper and this 1908 book. The 1896 paper provides a very clear pathological discussion of adenomyosis while this 1908 book is the first to clearly describe clear identification of endometriosis (uterine tissue outside of the uterus), which he referred to as an "adenomyoma".

Benagiano and Brosens (2011) discuss a number of other researchers who either carried out pathology work on ectopic tissue or clinical work but conclude that it was only Cullen who combined meticulous pathology work with clinical signs – and argued that he was observing a distinct disease state. Specifically, Cullen was the first to associate morphological finding of ectopic uterine tissue with the patient's lived experience, identifying menorrhagia (heavy bleeding) and dysmenorrhea (severe pain) as the hallmark clinical signs.

References: Batt p. 130; Benagiano and Brosens (2011); Leonardo p. 365; Nezhat et al. (2012); Speert America p. 200.

JOHN A. SAMPSON (1873 - 1946)

Perforating hemorrhagic (chocolate) cysts of the ovary

***American Journal of Obstetrics and Gynecology*, 1921.**

Sampson's 1921 seminal article defined the modern understanding of ovarian endometriomas. Through meticulous clinical and histopathologic observation of 14 patients, Sampson described cysts filled with a "chocolate-like" fluid—the result of accumulated hemorrhagic blood—and noted that these cysts were lined with tissue functionally identical to the uterine endometrium.

He hypothesized that these cysts formed when endometrial tissue was "spilled" through the fallopian tubes and implanted on the ovary, a concept that later evolved into his famous "theory of retrograde menstruation". This theory is mentioned in the 1921 paper.

While the association between refluxed menstrual blood and hemorrhagic cysts had been suggested as early as the 17th century, Sampson's paper was novel for its systematic study and its proposal of a mechanical origin.

He further argued that the rupture or "perforation" of these cysts released endometrial cells into the peritoneal cavity, seeding secondary adhesions and lesions throughout the pelvis.

This article established endometriosis as a distinct clinical entity, although Sampson didn't use the term until 1925. By shifting the focus from "adenomyoma" (which emphasized uterine tumors) to "endometriosis" (emphasizing ectopic tissue), Sampson created the framework that has dominated gynecological research for the last century.

In a subsequent 1927 article, Sampson continued the studies from here, describing 293 cases over five years. He theorized that retrograde flow of menstrual contents could explain how uterine contents reached the ovary and surrounding tissue.

References: Batt p. 156; Eskes and Longo p. 277; GMN 6128; Leonardo p. 366; Speert America p. 201.

EXPERIMENTAL ENDOMETRIOSIS IN THE HUMAN*

JOHN H. RIDLEY, M.D., AND I. KEITH EDWARDS, M.D., ATLANTA, GA.

(From the Grady Memorial Hospital)

SAMPSON'S[1] theory of the histogenesis of endometriosis, although not the first, was the primary one of wide acceptance. Russell,[2] in 1899, having found endometrial glands in the ovary, suggested a theory of growth from cell rests of the Müllerian duct. Sampson, in 1921, surmised that the actual implantation of fragments of the shed endometrium that had been regurgitated from the fimbriated ends of the tubes explained the origin of the phenomenon. This seemd logical because "retrograde" menstruation can be observed at the time of laparotomy and the sites of implantation most frequently seen are in the cul-de-sac of Douglas or on the ovary closely adjacent to the tubal fimbria. Then these fragments would be expected to gravitate to these new sites of growth.

This theory was challenged, however, because of the rather frequent occurrence of endometriosis at sites where direct implantation would be impossible, viz., the umbilicus, inguinal lymph nodes, etc.; thus the theory of celomic metaplasia described by Iwanoff and Meyer, and championed by Emil Novak[3] gained popularity. Furthermore, Halban[4] demonstrated the "benign metastasis" of endometrial fragments through the lymphatics, as into the inguinal nodes.

Sampson,[5] thus challenged, eloquently stated, "If bits of Müllerian mucosa carried by the menstrual blood escaping into the peritoneal cavity are always dead, the implantation theory, as presented by me, also is dead and should be buried and forgotten. If some of these bits are even occasionally alive, the implantation theory also is alive." Therefore, the fundamental weakness in the Sampson theory, admittedly, was the inability to demonstrate that menstrually shed fragments are viable.

As the incidence of endometriosis has so amazingly increased, so has the interest in the enigma of its origin and behavior increased. There now seems to be a spirit of compromise between the protagonists of the various theories on the understanding that no one theory could explain all cases.

The viability of the shed endometrium of the human has never been proved in vivo although tissue cultures by Keettel and Stein[5] in 1951 showed that both epithelial and stromal elements could be grown artificially for a short period in the laboratory. Cron and Gey[6] had done previous pilot work and in 1927 reported growth by tissue culture but the results were mitigated by the fact that the uterine cavity had been invaded by "a small curette" in procuring the specimen. Te Linde and Scott[7] in 1950 reported their experiment on the rhesus

*Presented at the Twentieth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Hollywood, Florida, Feb. 1 to 5, 1958.

Ran experiments to support the retrograde menstruation theory of endometriosis

JOHN H. RIDLEY (c. 1921 - 2005)

Experimental endometriosis in the human

American Journal of Obstetrics and Gynecology, 76(4):783-9 (with JK Edwards), October 1958.

John H. Ridley's 1958 paper is one of the most important experimental studies in the history of endometriosis research because it provided direct human evidence supporting Sampson's theory of retrograde menstruation and implantation.

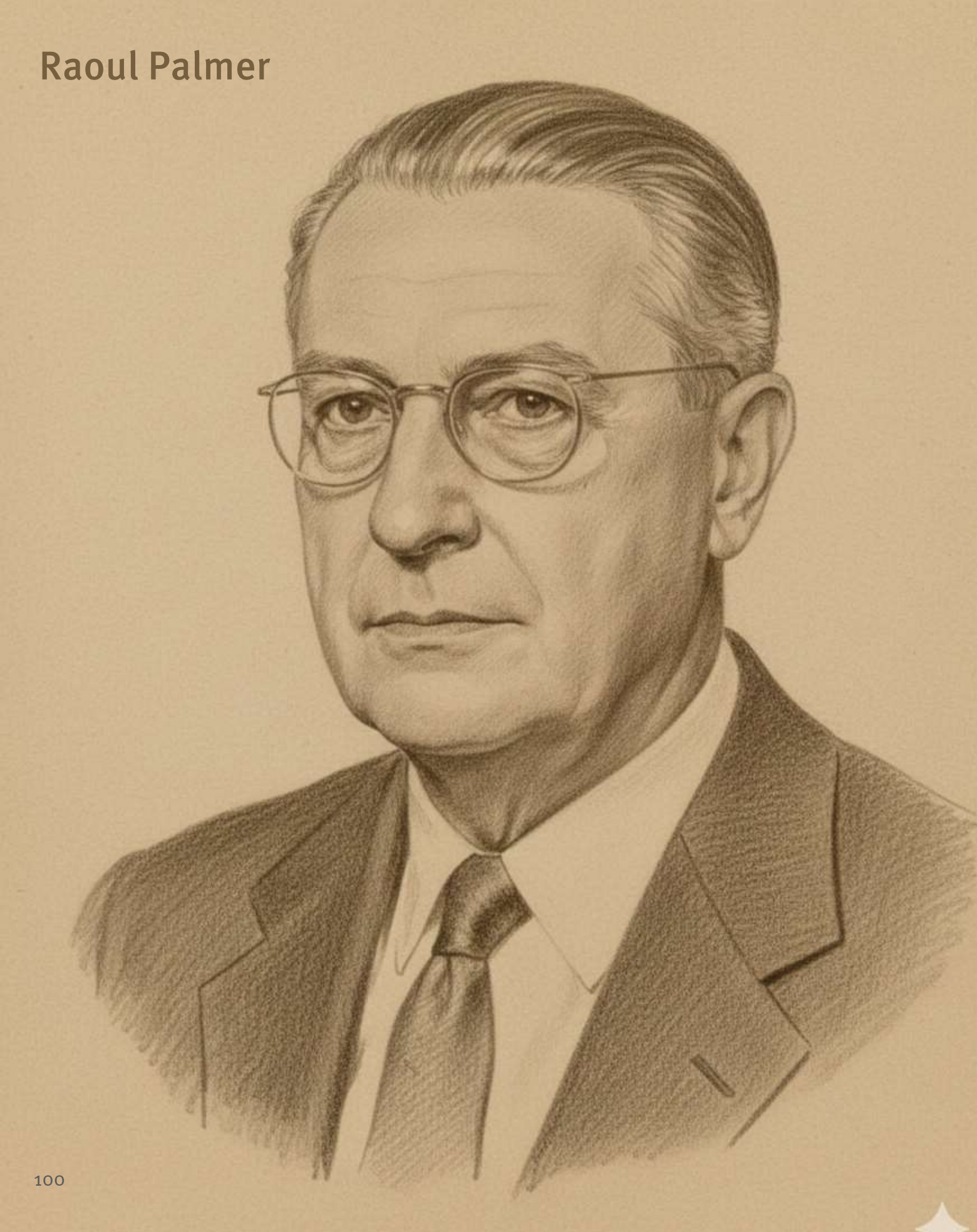
Ridley reported a unique set of observations in which viable endometrial tissue was deliberately implanted into ectopic sites in women undergoing abdominal surgery. He demonstrated that transplanted endometrial fragments could survive, vascularize, proliferate, and develop histologic features indistinguishable from spontaneous endometriosis. The implants responded to hormonal cycling, showing glandular and stromal organization consistent with functional endometrium. Importantly, Ridley documented that implantation could occur on peritoneal surfaces without any congenital anomaly or preexisting disease, directly replicating the proposed mechanism of lesion formation.

The paper was the first controlled human "proof-of-principle" that endometriosis could arise from iatrogenic or mechanically displaced endometrial tissue, rather than requiring embryologic remnants or metaplasia alone.

While Sampson's retrograde menstruation theory had strong circumstantial and anatomical support, Ridley's work supplied experimental causality in humans, something animal models alone could not fully establish.

Ridley's findings cemented implantation theory as a biologically plausible mechanism, shaping surgical thinking for decades—particularly the emphasis on minimizing endometrial spillage during gynecologic procedures. At the same time, later research revealed the limitations of a purely implantation-based model: retrograde menstruation occurs in most women, yet only a subset develop disease.

Raoul Palmer



Early pioneer in gynecologic endoscopy and, later, laparoscopy. He was the first to apply endoscopy for endometriosis operations

RAOUL PALMER (1904 - 1985)

La stérilité involontaire. Evaluation des méthodes de diagnostic et de traitement

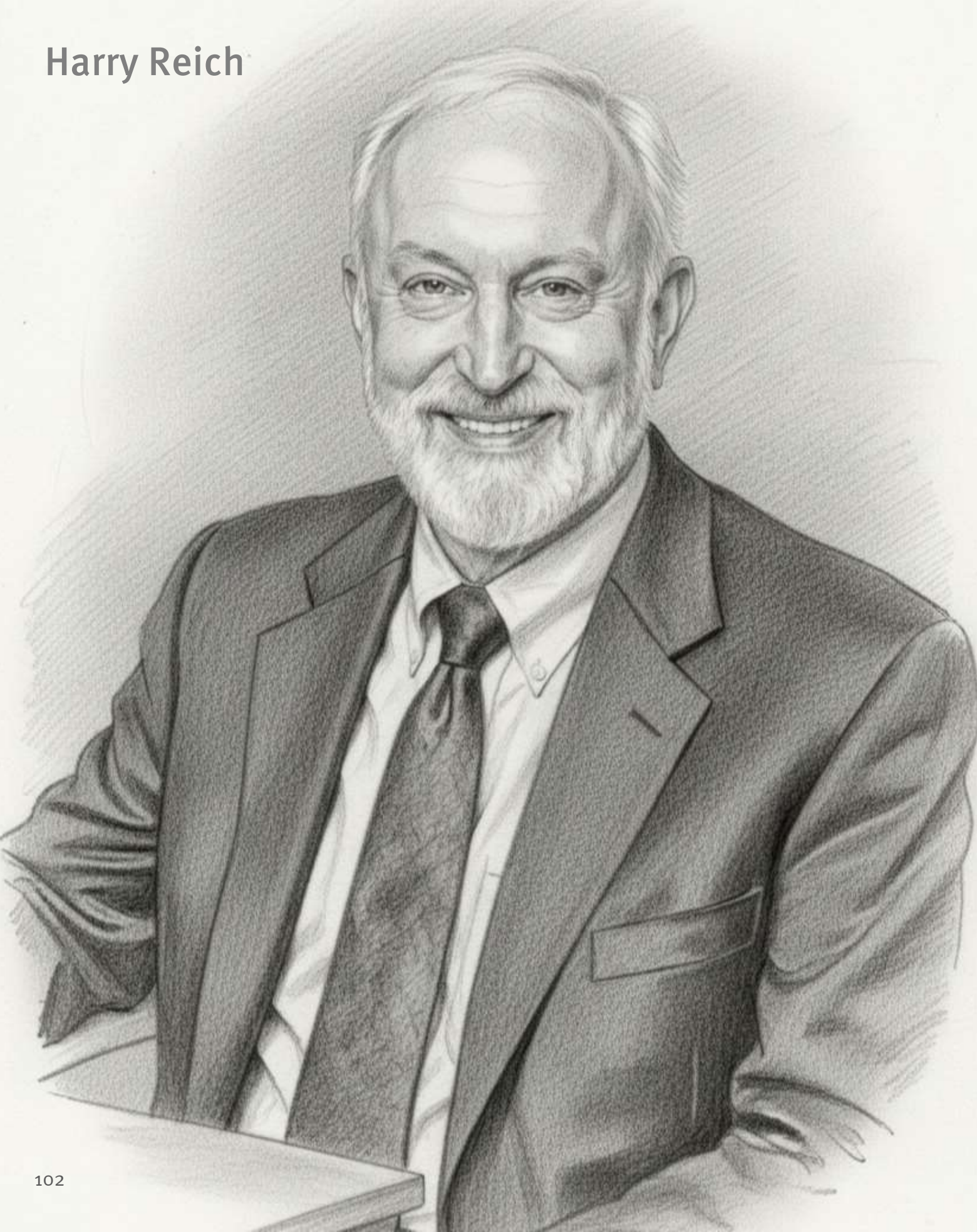
Paris: Masson et Cie., 1950.

Raoul Palmer was a key early figure in gynecological surgery who transformed the diagnosis and treatment of endometriosis by pioneering modern laparoscopy, which he termed "coelioscopy." Trained as a gynecologist, he became the head of gynecological research at the Faculty of Medicine in Paris in 1934 and began his experiments with intra-abdominal endoscopy during World War II with the support of his wife, Elisabeth. In his seminal 1950 book, *La stérilité involontaire*, Palmer focused on coelioscopy as a critical tool for evaluating involuntary sterility, maintaining that no test of ovulation was as certain as the direct discovery of an ovum or pregnancy during an operation. By using coelioscopy to visualize the pelvic cavity, he moved beyond speculative diagnosis, allowing for the direct identification of the "chocolate fluid" and "miniature uterine cavities" characteristic of the disease.

Palmer's mechanical and safety innovations made endoscopic endometriosis surgery viable and repeatable. He established safe criteria for creating a controlled pneumoperitoneum using the Veress needle to insufflate CO_2 instead of oxygen, which significantly reduced the risk of gas embolism. To optimize the surgical field, he introduced the use of the Trendelenburg position and developed a transvaginal cannula to mobilize the uterus, allowing surgeons to inspect the retrocervical area and the rectovaginal pouch where endometriosis often hides. Although his first 250 procedures at Hospital Broca were performed under local anesthesia, he shifted to general anesthesia in 1952, the same year he adopted quartz rod illumination to provide a clearer, more detailed laparoscopic image. Therapeutically, he used coelioscopy to cut pelvic adhesions, including those in endometriosis, and by 1962, he was performing laparoscopic tubal coagulations and other complex interventions.

References: Nezhat et al. (2012). Also see Jean Cohen, 2007, “Raoul Palmer: A Maker of Fate,” Reproductive BioMedicine Online 14(1): 125-126 and G. Schogel, “Raoul Palmer and the coelio-surgical adventure from 1940 to 1995,” *Hist Sci Med* 30(2), p. 281.

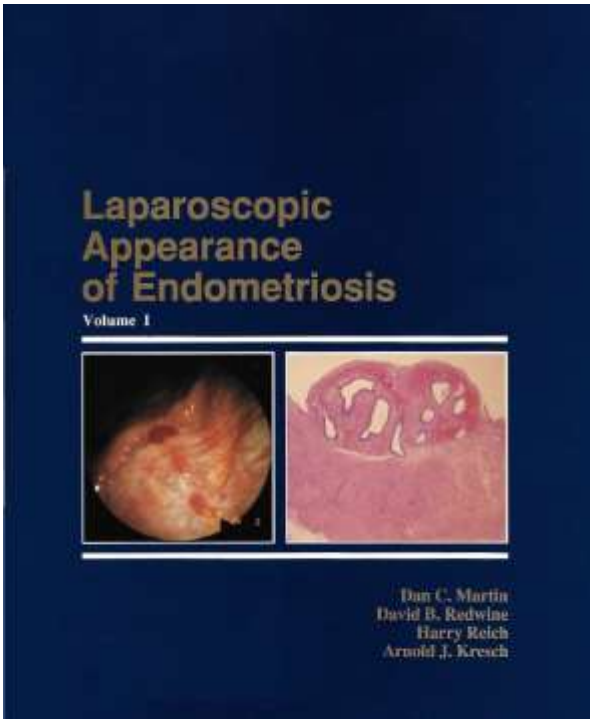
Harry Reich



HARRY REICH (1941 - Present)

Laparoscopic Appearance of Endometriosis

By Dan Martin, David Redwine, Harry Reich and Arnold Kresch, Memphis: The Resurge Press, 1990



Harry Reich is the pioneer of modern laparoscopic surgery, having performed the world's first laparoscopic hysterectomy in 1988. He performed the world's first laparoscopic excision surgery for endometriosis in the late 1970s.

At a time when many of his peers were skeptical that complex procedures could be safely performed through small ports, Reich's technical proficiency and innovative use of equipment—including early electrosurgery and specialized "aqua-dissection"—proved that even advanced disease could be managed without major abdominal trauma.

Published in 1990, this book *Laparoscopic Appearance of Endometriosis* served as a critical visual and clinical guide for a new generation of surgeons and reflected Reich's teachings. This was the first publication we are aware in which Reich details the laparoscopy procedure for endometriosis – which has a substantial diagnostic component.

Recognition of endometriosis is necessary for diagnosis and treatment, and as this volume demonstrates the diagnosis of endometriosis and differentiation from other diseases of similar appearances can be difficult. The pathbreaking content provided detailed photographic documentation of the "chameleon" nature of endometriosis. The book provided a systematic atlas for identifying these varied manifestations, which was essential for ensuring that surgeons did not leave behind occult or "atypical" lesions that could cause persistent pain.

References: Sutton (1997).

5

Operative Gynecology

The history of operative gynecology reflects the slow, often painful transition from speculative ancient practices to the technology-driven interventions of the 21st century.

For much of history, gynecologic surgery was constrained by limited anatomic knowledge, prohibitive mortality from hemorrhage and infection, and deep cultural unease about operating on the female reproductive organs. Yet necessity—obstructed labor, fistula, prolapse, tumors, and ectopic pregnancy—forced innovation. Over centuries, operative gynecology evolved from rare, often desperate interventions into a highly specialized surgical discipline grounded in anesthesia, antisepsis, imaging, and minimally invasive technology.

For millennia, surgical interference with the female reproductive system was considered a desperate measure of last resort, often resulting in fatal infections or hemorrhages.

Foundations in Antiquity and the Middle Ages

In ancient Egypt, Mesopotamia, and Greece, gynecological "operations" were largely non-invasive, focusing on the application of materia medica via pessaries, fumigations, and manual maneuvers. Hippocrates (5th century BCE) described uterine prolapse, vaginal ulceration, and gynecologic abscesses, recommending mechanical repositioning, pessaries, cautery, and drainage rather than excision. Soranus of Ephesus (2nd century CE), often cited as the zenith of ancient gynecology, provided the first detailed surgical descriptions for conditions like uterine prolapse and the delivery of a dead fetus.

Despite this, major abdominal surgery remained elusive. During the Byzantine and Islamic periods, compilers like Aetius of Amida and Albucasis preserved these techniques, with Albucasis introducing specialized surgical instruments for the training of midwives in complex cases.

The Renaissance transformed operative gynecology indirectly through anatomy. Andreas Vesalius's dissections corrected long-standing errors about female pelvic anatomy, enabling surgeons to conceptualize uterine and adnexal operations with greater precision.

Early cesarean sections—almost exclusively post-mortem—were described by François Rousset (1581), while rare survivals following live cesarean delivery appeared sporadically in the seventeenth century.

Ephraim McDowell performing America's first ovariotomy.

The 19th Century: The Surgical Revolution

Ovariectomy (removal of the ovaries) and hysterectomy (removal of the uterus) were the first successes in this era.

Ephraim McDowell performed the first successful elective ovariotomy in 1809 on Jane Todd Crawford, proving that the abdominal cavity could be safely opened. Early hysterectomies were often performed for "mother fits" or severe prolapse, but the mortality rate remained staggering until later innovations in ligation techniques and antisepsis became standard.

The modern era of operative gynecology began in earnest with the successful treatment of the vesico-vaginal fistula (VVF), a debilitating condition typically caused by prolonged obstructed labor. James Marion Sims is famously credited with the first successful surgical repair of VVF in 1849, utilizing silver wire sutures and a specialized position (Sims' position) to provide visualization. While historically lauded, Sims' work is now viewed through a critical lens due to his use of enslaved women as experimental subjects.

Hysterectomy evolved in parallel. Early abdominal hysterectomies carried extreme mortality, but refinements by surgeons such as Wilhelm Freund and Ernst Wertheim enabled radical hysterectomy for cervical cancer, integrating lymphadenectomy and oncologic principles. Meanwhile, ectopic pregnancy—uniformly fatal if untreated—became surgically manageable through salpingectomy, transforming maternal survival.

The 20th Century to Present: Minimally Invasive Surgery Advances

The twentieth century witnessed explosive growth in operative gynecology as a scientific specialty.

Advances in blood transfusion, antibiotics, and anesthesia dramatically reduced mortality.

Gynecologic oncology emerged as a defined field, refining radical pelvic surgery and cytoreductive techniques. Vaginal and abdominal approaches to hysterectomy were standardized, while pelvic floor surgery for prolapse incorporated fascial repair, suspension procedures, and later mesh-based techniques.

The excision of endometriosis, once requiring radical pelvic surgery, was revolutionized by the development of laparoscopy. Pioneers like Raoul Palmer and later Harry Reich (who performed the first laparoscopic hysterectomy in 1988) moved gynecology into the endoscopic era.

This allowed for the precise removal of endometrial lesions while preserving fertility, a sharp departure from the Galenic model of merely treating "naughty humors" of the womb.

Today, the field continues to evolve with robotic-assisted surgery. Modern operative gynecology now balances technical precision with a holistic understanding of women's physiology, moving beyond the "heroic chronicles" of early male practitioners to include the voices and innovations of female physicians and specialized surgeons.

Today, operative gynecology is characterized by minimally invasive approaches, subspecialization, and patient-centered outcomes.

Laparoscopic and robotic hysterectomy, nerve-sparing endometriosis excision, fertility-preserving ectopic pregnancy surgery, and sophisticated pelvic reconstructive procedures dominate modern practice. Imaging, energy devices, and enhanced recovery protocols have reduced morbidity while expanding surgical indications.

Robotic surgery has transformed today's practice of operative gynecology.

colligitur Varro tradit. Ab ana uero quo Iusitaniã a betica discreuimus.cxxvi.mil.passuum. A gadibus.cii.mil.pas.additis gentes celticæ turduli:& circa tagum uetones. Ab ana ad sacrum Iusitani oppida memorabilia a tago in ora:olysippo equarum & fauonio uẽto conceptu nobile salatia cognomiata. Vrbs imperatoria merobrica:promontoriũ sacrũ:& alterum cuneus. Oppida ossonoba bassa myrtili. Vniuersa prouintia diuiditur in conuentus tres emericensem:pacẽsem:scolabitanum. Tota populorum xlvi.in quibus cõloniæ sunt quinq;:municipiũ ciuium romanorum latii antiqui quattuor. Stipendiaria xxxvi.Colonia augusta emerita anæ fluuio apposita : mertallinensis:pacensis : norbensis cæsariana cognomine.Contributa sunt in eam castra iulia:castra:cæcilia.Quinta est scalabis:quæ præsidium iulium uocatur.Municipium ciuium romanorum olysippo fœlicitas iulia cognominatum. Oppida ueteris latii ebora: quod idẽ liberalitas iulia'& myrtilis & salatia quæ diximus stipendiariog;.quos nominare non pigeat.Præter iam dictos in betica cognominibus:augustobrigenses:ãmienses:aranitani: taxabritenses blaxenses:cæsarobricenses:caperenses:caurenses:colarni Cibilitani:concordienses.Qui & bocori:interausenses:lãcienses:mirobrigẽses:qui celtici cognominanẽ:madrubricẽses:qui plũbarii:ocelẽses: lancienses:turduli qui barduli:& tapori.Lusitaniam cum asturia & galecia patere longitudine.xl.m.p.Latitudine.d.xxxvi.m.Agripda prodidit:omnes autem hispaniæ a duobus pyrenei promontoriis p maria totius oræ circuitu.xxxix.m.xii.colligere existimantur ab aliis.xxvi.mil.Ex aduerso celtiberiæ complures sunt insulæ cassiterides dictæ a græcis a fertilitate plumbi:& e regione arrotrebarum promontorio deorum sex:quas aliqui fortunatas appellauere.In ipso uero capite mox beticæ ab hostio freti passus.lxxv. mil.gadis longa & (ut Polibyus scripsit).xii.mil.lata.iii.mil.passuum abest a continente.Proxima parte minus pedes.d.cc.Reliqua plus septẽ mil.ipsius spatiũ.xv.mil.pas.est.Habet oppidum ciuiũ romanoq; qd' appellat' augustana urbs iulia.Gaditani ab eo latere quo hispaniã spectat passibus fere.c.Altera insula ẽ in longũ.cc.miliũ passuũ.xl.mil.lata. In qua prius oppidũ gadiũ fuit. Vocat' ab Epboro & philistide: erythia a Timæo & Syleo ophrodisias:ab indigenis Iunonis. Maiorẽ Timæus continusam apud eos uocitatã ait.Nostri tarteron appellant:pœni gadiritam gadiruta punica lingua sepem significante.Erythia dicta est:quoniã tyrii ab origine eoꝝ orti ab erythreo mari ferebantur. In hac Geriones habitasse a quibusdã existimantur:quoꝝ armenta Hercules abduxerit.Sunt qui aliam esse eam:& cõtra Iusitaniam arbitrarentur:eodemq; nomine quondam ibi appellant.

Vniuersæ europæ mensura. Cap.xxiii.

Eracto ambitu europæ reddenda consumatio est:ne quid in expedito non sit noscere uolenti-
P bus.Longitudinẽ eius Artemidorus atq; Isidorus a tanai usq; gades.lxxxiiii.mil.xiiii.passuum prodiderunt.Polybius latitudinem europæ ab italia ad oceanum scribit.xi.mil.l.esse etiã tum ĩ comperta magnitudine huius.Est autem'ipsius italiæ(ut diximus).xii.mil.xx.ad alpes.Vnde lugdunũ ad portum morinorum britannicum:qua uidetur mensuram agere Polybius.xiii.mil.xviii. Sed certior mensura ac longior ad occasum solis æstiui hostiumq; rheni per castra legionum germaniæ ab iisdem dirigitur alpibus.xii.mil.xliii.pas.Hinc deinde africa atq; asia dicentur.

CAII PLINII SECVNDI NATVRALIS HISTORIAE LIBER.V.

Africæ Descriptio.

FRICAM GRAECI LIBYAM APPELLAVERE QVA MARE
a ante eam libycum incipiens ægypto finitur. Nec alia pars terrarum pauciores recipit sinus longe ab occidente littorum obliquo spatio. Populorum eius oppidorumq; nomina uel maxime sunt ineffabilia: præterq; ipsorum linguis & alias castella ferme inhabitant.

Mauritania. Cap.i.

P Rincipio terrarum mauritaniæ appellantur usq; ad.C.Cæsarem Germanici filium regna. Seuitia eius in duas diuisa est' prouincias. Promontorium oceani extimum ãpelusia nominatur a græcis.Oppida fuere lissa:cotte:ultra columnas Herculis:nunc est tingi quondam ab Anteo conditum:postea a Claudio Cæsare cum coloniam faceret appellatum traducta iulia.Abest a belone oppido beticæ proximo traiectu.xxx.mil.pas. Ab eo.xxv.mil.in ora oceani colonia Augusti iulia constantia zili regum ditioni exempta: & iura in bericam petere iussa:& ab eo.xxxii.mil.passuum colonia a Claudio Cæsare facta lixos:uel fabulosissime ab antiquis narrata.Ibi regia Antei:certamenq; cum Hercule:& hasperidum horti. Affunditur autem huic æstuarium e mari flexuoso meatu:in quo draconis custodiæ instar fuisse nunc interpretantur. Amplectitur intra se insulam:quam solam e uicino tractu aliquanto excelsiore non tamen æstus ma-

Cotes

Ampelusia
Lyxa
Tingi

Antei regia
Hesperidum

f

PLINY THE ELDER (23 - 79 CE)

Plinii Secundi naturae historiarum libri XXXVII

Venice: Bernardinus Benalius, 1497.

Pliny's encyclopedic work became the reference scientific book for the entire early modern period and went through countless editions.

Pliny's writings provide a rich snapshot of ancient Roman beliefs about women's bodies. His work shows a world where women's health was governed by powerful natural forces, and where treatment involved a complex mix of observation, herbal knowledge and magical thinking.

Pliny describes a menstruating woman as a destructive force of nature. Her touch could turn new wine sour, dull mirrors, kill bees, cause fruit to fall from trees, and even make mares miscarry just by looking at them. Despite its destructive potential, Pliny also saw menstruation as a necessary natural purgation for women.

Pliny lists countless remedies to promote fertility. These involved plant and animal products, such as the consumption of certain herbs or the wearing of amulets made from animal parts (like the right testicle of a donkey wrapped in a bracelet).

Pliny notes the phenomenon of strange cravings during pregnancy, such as the desire to eat earth. He also mentions remedies for pregnancy nausea. Pliny famously mentions that children born by cutting open the mother's womb (*a caeso matris utero*) were called Caesones or Caesares. He cites Scipio Africanus as an example.

Book Notes: Edited with the utmost care from the corrections of Hermolaus Barbarus. Folio. 370x245 mm. Later binding in full rigid parchment, manuscript title on the spine. 268 unnumbered leaves. Numerous marginalia in an old hand.

Provenance: This copy previously was the property of Roberto Almagià, 1884-1962, professor at the universities of Padua and Rome and historian of cartography.

References: BMC V 377; BSB-Ink P-609; Bod-inc P-370; Hain *13101; Goff P-799; GW M34321; Klebs 786.14; Radcliffe p. 98.

Liber Primus

¶ Incipit liber primus Cirugie magistri petri de Largelata de bononia artium ⁊ medicine doctoris.

Rogauerunt me socij mei vt ꝓn q̃ legerẽ eis tertiam ⁊ quartam fen. quarti canonis auicenne receptas ordinarem: que satis sepius ordinate sunt. ¶ Et quia amicus ẽ alter ego cõpellor ⁊ cogor eis cõplacere in ꝗ. amicitia enim fit propter honestum ⁊ non propter aliud. qua propter ad eum qui est omnis boni possessor: ⁊ omnis boni liberalis largitor: recurro gratiam postulans ⁊ exquirens vt cor meum ⁊ mentem meam illuminare dignetur vt sit recta regula ⁊ mensura in hoc. Et vna cum aureoi in libello quem fecit de commendatione intellectus naturalis cum extracto loquar. Laudatus sit inquit deus ⁊ perducat nos ad id quod sit voluntas eius vt simus fortunati primo. Et postea. ¶ Et hic est vt virginis ad hoc mihi auxilium innocem vt ipsa ad filium. filius ad patrem porrigat preces meas securum accessum habet omnis homo ad ipsum: vbi ⁊ quis est habens filium ⁊ patrem. filius autem patri ostendit latus ⁊ vlcera. mater pectus ⁊ vbera certe nulla potest cẽ repulsa vbi tor ⁊ tanta sint caritatis insignia. ¶ Precor igitur filium deum patrem vt omnibus nobis gratias munera ⁊ benemerita largiri dignetur in hoc ⁊ in aliis peragendis.

¶ In hoc autem opere sic procedam: quia in hoc opere erunt ser libri. ¶ In primo libro pro se quar de capitulo in capitulum. vt Auice. procedit ipsius ordinando rubricas ⁊ alias aliorum antiquorum ponam: dimittens tamen empirica vameri rose angliceane ⁊ aliorum empiricorum: ⁊ semper ad simplicia aliqua me extendam: penes etiam theoricam cuz signis: vt me sepe rogauerunt. ¶ In secundo libro ego mentionem faciam de omnibus apostematibus a capite vsqz ad pedes de quibus Auicen. in 4. non fecit mentionem. ⁊ ponam semper signa. ¶ In tertio libro ponam de vulneribus a capite vsqz ad pedes vnus modum vobis curandi ⁊ accidentibus succurrendi. ¶ In quarto ego faciam mentionem de omnibus vlceribus particularibus a capite vsqz ad pedes: quia omnium membrorum de quibus Auice. non fecit mentionem. ¶ In quinto ego aliquid loqui volo de decoriatione incipiens a capite vsqz ad pedes. ¶ In sexto aliquid loquar de dislocatione ⁊ fracturis ossium q̃z breuius potero adiungens aliquid anothomie. ¶ Et ego ista faciam solum ad memoriam mei ⁊ meorum sociorum: ⁊ non propter aliud quia loquar vt alij magistri mei locuti sunt ⁊ si non complete locutus fuero imputetur ignorantie mee ⁊ non alteri cause: stans semp correctioni in isto ⁊ in omnibus aliis magistrorum maiorum meorum.

¶ De flegmone. CA. I.

Flegmon duob⁹ modis capit̃. vno modo comuniter pro omni inflãmatione pticulari: ⁊ hoc voluit Auic. cũ dixit. Et scias q̃ nomẽ flõnis in ligua greco ẽ absolutũ sup oẽ q̃ ẽ inflãmatum. ⁊ hoc vult ẽt Ga. in primo de sinthomate ⁊ egritudine. ⁊ alio mõ capit̃ proprie pro apate ex sanguine. vero ⁊ puro generato vel ex alio currẽte cursu ei⁹ ẽt sic causat̃. Hec aũt flegmõ. 2. mõ accepta ẽ duplex. s. vera ⁊ nõ vera. Vera flõn est ex sanguine benigno q̃ est multo plus q̃z indigeat illo membr: est ergo talis sanguis peccãs solo quãto. Non vere flõn fit ex sanguine non naturali ⁊ malo. peccat ergo in q̃li ⁊ q̃z ro. i qualitãt̃ peccare solũ. ¶ Et p notitia horũ apatum nota q̃ sanguis ẽ humor calus ⁊ humidus in substãtia temptatus ex temptatione parte chili generatus. Est ãt duplex. s. nãlis ⁊ ñ nãlis. nãlis humor ẽ calus ⁊ humidus. in substãtia temptatus. in colore rubeus. in odore ⁊ sapore amicabilis. ¶ Sanguis vero nõ naturalis est ille q̃ deuiat ab isto vltra terminos sue latitudinis quos si transiit nõ est sanguis naturalis. Egredit̃ aũt illos terminos vno mõ q̃n eius substantia efficitur magis grossa vel minus q̃z debeat. Alto modo erit ꝓprios terminos quãdo subtile aduritur. ⁊ grossum remanet absqz remotione vel separatione istarum partium. Tertio modo erit proprios terminos quando aliquid adueniet ei defectus quod multipliciter potest fieri secundum q̃ multe sunt species colẽ flãtis ⁊ melancolie que cuz eo commisceri p̃nt. ¶ Ex quibus dictis apparet q̃ ex sanguine generantur quatuor species apostematum. primo ex sanguine benigno generatur flõn vera. ¶ Secũdo ex sanguine illaudabili per admittionem tripler generatur apostema secũdus q̃ tres humores possunt secum permisceri. vnde si miscetur colera cum sanguine vincente vocatur flõn crisipilaides. ⁊ si flegma flõn vndimiades. ⁊ si melãcolia flõn sephiroides. ¶ Tertio ex sanguine illaudabili ratione sui modi substãtie: q̃ sanguis est nimis subtilis vel grossus potest generari flõn que potest dici vera. ⁊ licet Auic. dixerit ⁊ sanguis illaudabilis est subtilis vel grossus: quia ex ꝗ videtur vel le sanguinem subtilem ⁊ grossum esse laudabilem. tamen dico ego q̃ iste sanguis non est laudabilis proprie ⁊ simpliciter: est tamen laudabilis secundum quid. ⁊ ꝗ voluit auic. quomodo est laudabilis secũdum quid. isto modo: quia illi cui inest naturaliter vt sanguis grossus inest melancolico sibi sano naturaliter: ⁊ sanguis colicus inest colerico sibi sano: non tamen absolute q̃ in comparatione ad sanguinẽ temptatũ innaturalis ⁊ illaudabilis est. Iste ergo sunt species apatis: ⁊ q̃ sit innaturalis patet: q̃ erit ꝓprios terminos sanguinis naturalis. ¶ Quarto ex sanguine illaudabili p adustionẽ ꝑn subtilitatem ⁊ grossiciez sui gñantur oes pustule ⁊ crustose vsqz ad estiomenum. vt sunt carbunculi pruna ignis plicus aut sacer ignis.

¶ Cause autem flõnis sunt tres scilicet primitiua vt est in cisio aut fractura aut vlceratio: aut vlcera que sunt in mẽbro ⁊ propter dolorem declinat materia ad locum ⁊ retinetur in vijs vacuis ⁊ fit flegmon. est ergo causa extrinseca corpori. Causatur ergo primitiua est res ex qua prouenit dispositio aduentu primo aut non primo. ¶ Causa secunda est antecedens: ⁊ illa est multipliciter repletiualis humoralis complexionalis ⁊ compositionalis: ex quo patet q̃ mala complexio ⁊ dolor sunt causa antecedens. ⁊ similiter debilitas membri. ⁊ aliter non declaro: quia aliter me prolongare nolo: quia in quolibetis per me ordinatis me prolongaui. Causa ergo antecedens est ex qua prouenit dispositio aduentu non primo. ¶ Causa autem coniuncta est ipse sanguis antecedens in loco ꝗ apostemato vel. ꝗ.

Cã ergo q̃uicta ẽ ista ex q̃ prouenit dispositio aduentu p̃.

¶ Habet autem flõn quattuor tempora. principium. augmentum. statum: ⁊ declinationem. Principium declaratur per presentiam ipsarum causarum coniunctarum scilicet cum incipiunt apparere. ¶ Augmentum cognoscit̃ p adiectionẽ magnitudis ⁊ remissionis. ¶ Status aũt cognoscit̃ p aggregationẽ materiei: ⁊ illic aggregatur materia si debet aggregari. ¶ Declinatio est quando incipit tẽdere ad lenitatem ⁊ debilitatem. ⁊ si vis maiorem declarationem vide questiones per me factas de hoc. ¶ Et nota q̃ ista tempora non minus debes notare q̃z egritudinem. vnde ignoratis istis ⁊ cura egritudinis ignoratur. Et notauit auice. 4° primi cum dixit tempus egritudinis est. vt sciamus in quo tempore est egritudo. verbi gratia si egritudo est in principio super ipsum apponimus q̃ solum repercutit. ¶ Terminatur autem apostema quattuor modis. primo modo p resolutionem. secundo p sanationem. 3.° p putrefactionem. 4.° p purificationẽ. primus declarat̃ ab auic. cuz dixit: ⁊ tu qdem scis illud qõ ratifi-

Discussed gynecologic surgery and Cesarean Section

PETRUS DE ARGELLATA (1350 - 1423)

Chirurgia

Venice: Printer of Argellata, 1499.

An accomplished pupil of Guy de Chauliac, Petrus de Argellata 'was skilled in dentistry, used sutures and drainage-tubes in wounds, trephined the skull, incised the *linea alba* in post-mortem Caesarean section, and sometimes operated for hernia, stone, and fistula in ano' (Fielding Garrison).

His *Chirurgia* contains a good deal of therapeutics and, as usual, a part is devoted to gynaecology and obstetrics.

When Pope Alexander V died at Bologna in 1410, Argellata made a post-mortem examination which is described in his work' (Sarton).

Argellata is particularly noted for his detailed description of the post-mortem Cesarean section (extracting the fetus after the mother has died). While the procedure had been known since antiquity (*lex regia*), Argellata provided specific surgical instructions that were advanced for his time.

He explicitly described making the incision along the linea alba—the fibrous structure running down the midline of the abdomen. This was a crucial anatomical insight because cutting here minimizes bleeding and avoids major muscles, a technique that remains standard in abdominal surgery today.

Book Notes: Early annotations show close study of this copy and are most abundant in the chapters on wounds. Chancery folio (306 × 210mm). 131 leaves (of 132, without blank). Woodcut initials, occasional spaces with guide-letters. 18th-century sheep-backed boards.

Provenance: Previously the property of Eugene S. Flamm. Extensive annotations in at least one early hand.

References: BMC V 588; BSB-Ink A-669; Bod-inc A-378; GW 2324; Goff A-954; Hain 1638; Klebs 777.4; Osler 7414. Also F.H. Garrison, *An Introduction to the History of Medicine* (Saunders, 1924); G. Sarton, *Introduction to the History of Science* (Carnegie Institution, 1947).

Langenbeck Retells the Harrowing Story of the First Documented Vaginal Hysterectomy in History (No Anesthesia, No Antisepsis, Kirchmeyer – assistant couldn't help, used both hands and teeth to do operation) – Translated from His 1817 German Publication (below)

XI.

Geschichte einer von mir glücklich verrichteten Exstirpation der ganzen Gebärmutter.

Es fehlt uns nicht an Beyspielen von Ausrottungen der Gebärmutter aus Unwissenheit und ähnlichlich durch Unterbindung. Weisberg 1) beschreibt einen solchen Fall, wo eine Hebamme nach einer natürlichen Geburt beym Lösen der Nachgeburt den Uterus mit herausrug und abschnitt, die Frau aber geheilt ward und bis jetzt noch lebt.

Im dritten Stücke des siebten Bandes der Bibliothek für die Chirurgie von Richter wird folgender Fall mitgetheilt: Eine unvernünftige Hebamme zog nach einer leichten und glücklichen Geburt die Gebär-

No a mut-

1) Commentatio de Uteri mox post partum obtusiones rejectione persecta non lethali.

"The woman O., about 50 years old, had long suffered from pains, burning, and stabbing in the uterus. Little by little it prolapsed. There was a discharge of foul-smelling pus, which excoriated the surrounding skin. The characteristic burning and stabbing pains of carcinoma became so severe that the woman earnestly begged to be freed from her suffering by an operation. On examination I found all the signs as described: the vaginal portion of the cervix protruded somewhat beyond the *labia majora*; the *labia* around the *os uteri* were indurated, the *os* itself red and ulcerated, discharging foul pus. The inner wall of the vagina was likewise red and ulcerated, and through the vagina I could feel the uterus hardened, nodular, and greatly enlarged. The general health was still reasonably good, so that I could undertake the operation. In agreement with General-Surgeon Kirchmeyer, I performed it the next day as follows.

The woman was placed on the edge of the bed, both feet on chairs. I positioned myself between the thighs, and with scalpel and forceps separated the protruded vagina from its attachment to the uterus, without cutting through the vagina itself. Then I reached the part of the uterus which, viewed from in front, appeared tucked into the peritoneum like a cloth. I carefully separated the substance of the uterus from the peritoneum without opening it (so that the intestines could not protrude) and pulled the uterus ever further outward. I continued this separation up to the rounded upper edge of the uterine fundus, and then cut away the uterus from the peritoneum, so that only an insignificant portion of its substance remained in connection with the peritoneum. This part appeared sound. Thus, the uterus was, as it were, shelled out from the abdominal cavity, forming with the vagina an empty sac.

The hemorrhage was very severe and had to be controlled by ligatures. This was the hardest part of the operation. General-Surgeon Kirchmeyer was present, but because of gout could not assist me. I therefore controlled the bleeding myself: with my left hand I grasped the bleeding surface, passed needle and thread around it, with the fingers of my right hand formed the loop, then with my right hand pulled one end of the thread, the other end with my teeth. In this manner I placed four ligatures, and the bleeding stopped. After the operation the patient was very weak, but she soon recovered. The cavity was filled with charpie (lint). Healing progressed rapidly, and the woman remains completely healthy up to this day."

CONRAD LANGENBECK (1776 – 1851)

Geschichte einer von mir glücklich verrichteten Extirpation der ganzen Gebärmutter

***Neue Bibliothek für die Chirurgie und Ophthalmologie*, First Volume, Third Fasicle, pp. 551 to 557, 1817.**

Conrad Johann Martin Langenbeck was a leading German surgeon and anatomist of the early nineteenth century and one of the key figures in the move from premodern to modern operative surgery.

He was professor of surgery and anatomy at Göttingen and an influential teacher whose pupils shaped later German surgery. Langenbeck worked before the advent of anesthesia and antisepsis, which makes his surgical achievements—particularly in abdominal and pelvic surgery—both technically audacious and historically significant. He is best remembered in gynecologic history for performing the earliest documented vaginal hysterectomy. There were a few documented peritoneal hysterectomies up to this time including one performed by Giovanni Andrea della Croce in the sixteenth century.

In 1813, Langenbeck performed a total vaginal hysterectomy for uterine prolapse complicated by malignancy. At the time, abdominal hysterectomy was almost uniformly fatal, and even vaginal approaches were considered nearly suicidal operations.

Langenbeck chose the vaginal route to avoid opening the peritoneal cavity, thereby reducing the risks of hemorrhage and peritonitis—risks that were otherwise uncontrollable in the pre-anesthetic, pre-antiseptic era. The operation involved circumferential dissection of the cervix, ligation and division of the uterine attachments, and removal of the uterus through the vagina.

Remarkably, the patient survived, making this operation one of the first clearly successful hysterectomies in surgical history. Langenbeck's success demonstrated that removal of the uterus could be compatible with survival if approached anatomically and conservatively.

References: Leonardo p. 315. Also, Baskett TF. Hysterectomy: evolution and trends. *Best Pract Res Clin Obstet Gynaecol.* 2005 Jun;19(3):295-305; N. Senn, "The Early History of Hysterectomy," *JAMA*, Sep 21, 1895.

Portrait of Conrad Langenbeck, Professor, University of Gottingen by Ludwig Emil Grimm, Philadelphia Museum of Art, 1826

I.

Ueber Minderung der Gefahr beim Kaiserschnitte, nebst der Geschichte eines Falles, in welchem Mutter und Kind erhalten wurden.

Von

C. F. Gräfe.

In frühern Jahren war ich Zeuge zweier Kaiserschnitte, welche, wenn gleich von ausgezeichneten Männern verrichtet, dennoch mit rasch erfolgtem Tode endeten. Die sorgsamste und genaueste Beobachtung beider Fälle leitete mich auf einige Umstände, denen nach meinem Dafürhalten das Misslingen hauptsächlich beizumessen war. Von jener Zeit an dachte ich darauf, wie die supponirten gefahrbringenden Momente sicher gemieden werden könnten. Lange schon ist meinen Zuhörern das aus den fraglichen Anlässen hervorgegangene Resultat jedoch nur als Vorschlag bekannt, da ich nie Gelegenheit hatte den Kaiserschnitt selbst zu vollziehen. Diese ist mir jetzt geworden. Mutter und Kind wurden durch das eingeschlagene Verfahren erhalten, und ich achte es daher für Pflicht dasselbe der weiteren Prüfung meiner Amtsgenossen anheim zu geben.

First time a successful Cesarean Section documented in a scientific journal

KARL FERDINAND VON GRAEFE (1787 - 1840)

Ueber Minderung der Gefahr beim Kaiserschnitte, nebst der Geschichte eines Falles welchem Mutter und Kind erhalten wurde

***Journal der Chirurgie und Augenheilkunde*, Berlin: Verlage von G. Weimer, 1826.**

Karl Ferdinand von Graefe was a German surgeon and ophthalmologist . He is considered a pioneer of plastic surgery, refined numerous surgical techniques, and held the founding chair of surgery at the University of Berlin.

Cesarean Section is an ancient idea discussed in the literature well before the birth of Christ. However, examples of C-sections where the mother survived were non-existent in the literature until 1500.

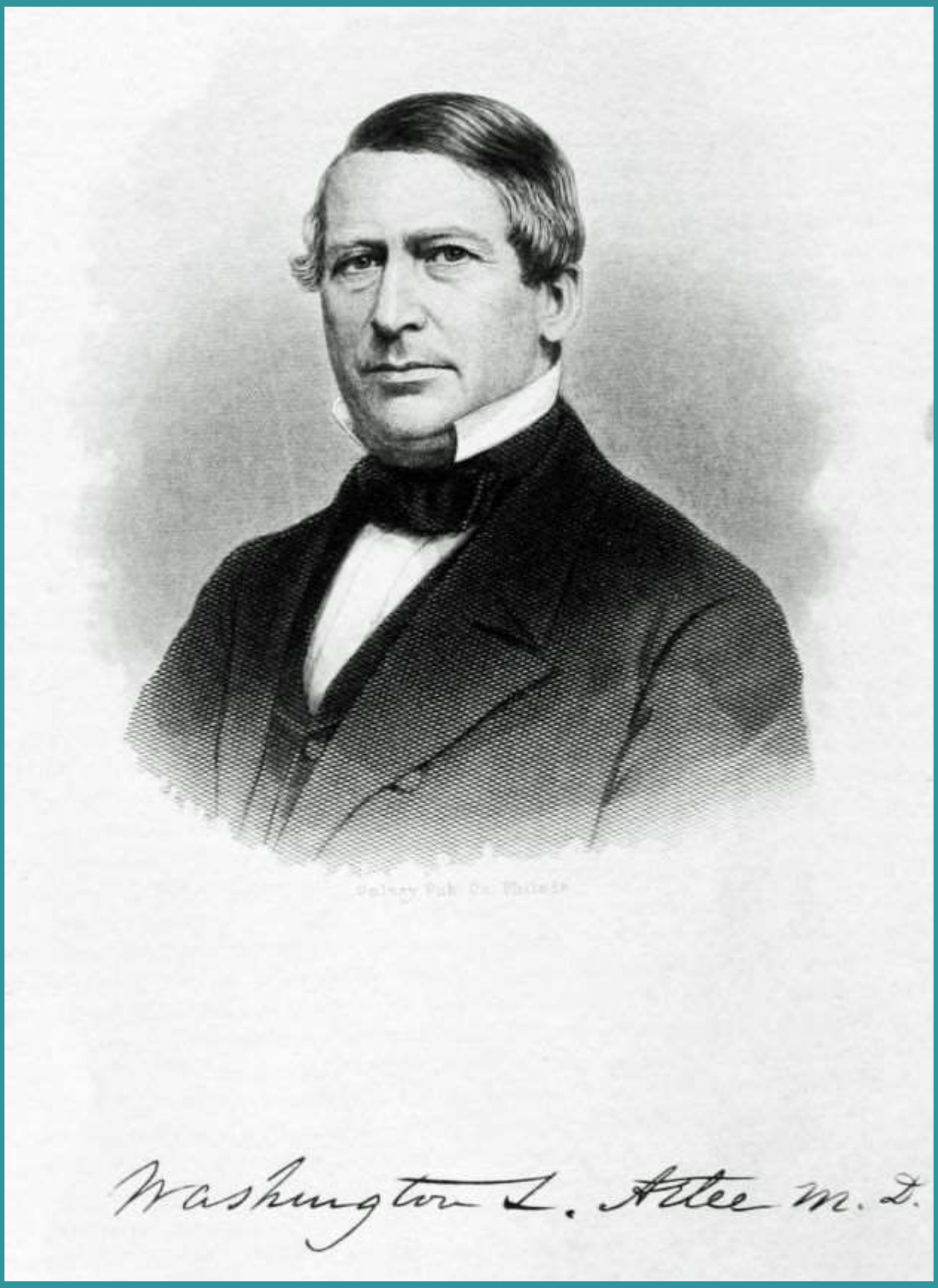
According to the National Library of Medicine (2024): “Perhaps the first written record we have of a mother and baby surviving a cesarean section comes from Switzerland in 1500 when a sow gelder, Jacob Nufer, performed the operation on his wife. The mother lived and subsequently gave birth normally to five children, including twins.”

However, this case was not documented at the time, and it was only eighty years later that it was discussed third hand in the literature. Other contemporary cases were discussed in the literature such as the operation performed by James Miranda Stuart Barry in South Africa in 1826. But this case was only later reported third hand in the literature.

Later, Hendrick van Roonhuyze reported several successful cases but also third hand.

We have searched the literature for examples of firsthand reporting of a successful operation (with clinical notes) and find that this distinction belongs to Karl Ferdinand von Graefe who carried out a successful operation in 1826 in Germany and wrote about it in an 80-page report in a surgical journal.

His operation was carried out without anesthesia but with careful cleaning of the wound site and a lower incision in the patient’s belly and uterus as later became the practice.


Washington L. Atlee M. D.

WASHINGTON L. ATLEE (1808-1878)

Case of a successful extirpation of a fibroid tumour

Reprint from *American Journal of Medical Science*, Volume 9, pp. 309-335, 1845.

ART. III.—*Case of successful Extirpation of a Fibrous Tumour of the peritoneal surface of the Uterus by the large peritoneal section.* By WASHINGTON L. ATLEE, M. D., of Lancaster, Penn., Professor of Medical Chemistry in the Medical Department of Pennsylvania College, Philadelphia.

June 8th, 1844, I was consulted, at the recommendation of Dr. G. T. Dare, of Galeaster, by Miss L. P., and received from her the following history of her case.

In the spring of 1843, she began to have frequent desires to micturate, but her attention was not particularly drawn to the circumstance until the 15th of October, 1843, when she felt, for the first time, a tumour in the right groin, about the size of a pullet's egg. About two weeks previous to this, she had been thrown from a horse, from which accident she suffered very much in her right groin, side and hip, and was confined to the house for several days. At this time she is not able to ride more than a mile without stopping to pass water, and she does so once or twice, sometimes oftener, during the night for the same purpose. She is in the habit of drinking very little in the evening, in order to prevent much disturbance from this cause at night. There has been no difficulty in the process of defecation, but she has been somewhat troubled with constipation, which she relieves with a single pill powder or a pinch of salts. Her menstruation has always been regular, but painful. It, however, has lately diminished in quantity, is sometimes clotted, and is followed for a short time by fluor albus. Twice last winter she was seized with pain in the tumour, and down the thighs, lasting about half an hour, and so excruciating as to almost produce fainting. She felt confident that the tumour was wasing away at that time, as she believed it to be in the womb.

She is 24 years of age, rather over the medium height, but always enjoyed excellent health, excepting while undergoing medical treatment for the tumour. About one week, however, after she had first met the Dr. Dare, she had an attack of inflammatory rheumatism, which continued for two weeks. Her constitution is good, the digestive functions go on well, there is no other local disease, and her muscular and nervous systems are well developed.

I examined the patient in company with my brother, and found a tumour occupying the hypogastric and right iliac regions, resting closely upon the pubic bones, being prominent above the symphysis, and gradually retreating toward the spine as the head ascended towards the umbilicus—the fundus of the tumour occupying a point one inch below the navel. The tumour was hard, resisting, somewhat uneven, and presented an edge in the right iliac region. The only tender spot on handling was on its upper surface.

No. XVIII.—APRIL, 1845. 20

Uterine fibroids are benign smooth-muscle tumors arising from the myometrium of the uterus. They are among the most common tumors in women. Fibroids vary widely in size, number, and location - producing symptoms that range from none at all to severe menorrhagia, anemia, pelvic pain, pressure on bladder or bowel, infertility, and pregnancy complications. Although benign, their anatomical position and vascularity historically makes them one of the most dangerous uterine pathologies to treat surgically, especially before anesthesia and antisepsis.

Before the nineteenth century, attempts to remove fibroids were rare and usually fatal. Ancient and medieval physicians recognized “hard swellings” or “scirrhous” enlargements of the uterus, but treatment was limited to pessaries, cautery, ligation of protruding masses, or palliative measures.

Fibroids were long regarded as inoperable, and women often endured years of disabling symptoms or died from anemia or complications. The early nineteenth century marked a turning point, driven by surgeons willing to try for removal. Washington L. Atlee was a Philadelphia-based surgeon and one of the pioneers of abdominal gynecologic surgery. In his landmark 1845 report he documented the deliberate removal of an 18-inch pedunculated fibroid from the external (subserosal) surface of the uterus via a full abdominal incision. Crucially, he avoided removing the uterus itself, preserving the organ. He secured the pedicle with three waxed silk sutures and closed the abdomen with 15 through-and-through sutures, resulting in the patient’s survival.

The case proved that fibroid surgery could be effective. Atlee’s case helped establish the conceptual and technical foundations for myomectomy, distinguishing tumor removal from hysterectomy and demonstrating that uterine fibroids were not intrinsically untouchable.

References: Leonardo p. 234; Speert America p. 180. Also see Longo (Nov 1976), “Classic pages in obstetrics and gynecology. Case of a successful extirpation of a fibrous tumor of the peritoneal surface of the uterus by the large peritoneal section. Washington Lemuel Atlee,” AJOG; Tapisiz and Altinbas, “Fibroids through the ages: a historical journey and future prospects in myomectomy,” GPM, Sep 30, 2024.

Charles Clay: An Early Attempt at Abdominal Hysterectomy

In November 1843, Charles Clay of Manchester, already experienced in ovariotomy, inadvertently confronted a massive fibroid uterus and proceeded with the first abdominal hysterectomy amid catastrophic hemorrhage; the patient died soon afterward. A similar operation performed days later by A. M. Heath ended identically. Although Clay achieved a temporary survival in 1844 after a total abdominal hysterectomy with bilateral salpingo-oophorectomy for enormous fibroids, the patient died two weeks later, underscoring the lethal risks of pre-antiseptic abdominal surgery. A decisive turning point came a decade later, in June 1853, when Walter Burnham of Lowell, Massachusetts, performed the first truly successful abdominal hysterectomy after unexpectedly encountering uterine fibroids, removing the uterus and ovaries under chloroform anesthesia—marking a crucial milestone in the evolution of gynecologic surgery.

CHARLES CLAY (1801 - 1893)

The complete handbook of obstetric surgery: or, short rules of practice in every emergency, from the simplest to the most formidable operations connected with the science of obstetricy

London: Henry Renshaw, 1856.

Charles Clay's *surgical text* is one of the earliest comprehensive English-language manuals devoted specifically to operative obstetrics, written at a moment when surgical intervention in childbirth was rapidly expanding but still extremely dangerous.

Clay, a Manchester surgeon best known for pioneering abdominal ovariotomy, sought to codify when and how surgery should be used in obstetric emergencies rather than leaving such decisions to ad hoc judgment. The handbook addresses procedures including craniotomy, embryotomy, version, forceps delivery, cesarean section, management of placenta praevia, uterine rupture, and puerperal complications. Clay's tone is practical and prescriptive, reflecting his belief that obstetric surgery should be governed by clear anatomical principles and clinical indications rather than tradition or hesitation.

The importance of Clay's Handbook lies in its role in professionalizing obstetric surgery. By separating operative obstetrics from general midwifery manuals, Clay helped define it as a distinct surgical domain requiring anatomical expertise, manual skill, and ethical judgment. The book also reflects a broader shift toward male, hospital-based obstetrics and the increasing authority of surgeon-accoucheurs. Although many of Clay's techniques were later rendered obsolete by antisepsis, safer cesarean delivery, and neonatal care, his insistence on systematic training, clear indications, and surgical responsibility profoundly influenced Victorian obstetrics. The Complete Handbook thus stands as a key text in the evolution of obstetric surgery from heroic last resort to disciplined clinical practice.

References: Baskett p. 84; Leonardo, p. 317; Moscucci p. 139; Radcliffe p. 89. Also Baskett TF. Hysterectomy: evolution and trends. Best Pract Res Clin Obstet Gynaecol. 2005 Jun;19(3):295-305; Shaw WF. Charles Clay: the father of ovariotomy in *England. J Obstet Gynaecol Br Emp* 1952; 58: 930–40.

ON THE TREATMENT

OF

VESICO-VAGINAL FISTULA.

VESICO-VAGINAL FISTULA—an abnormal communication between the bladder and vagina, allowing an involuntary discharge of urine—is produced generally by tedious labour. The impacted fœtal head, jamming the anterior vaginal parietes against the symphysis pubis, obstructs the circulation of the parts, which results in a slough of greater or less extent, according to the degree and duration of the impaction. Almost the only hope of preventing so serious a disaster under such circumstances is the timely resort to instrumental delivery. By this means I have seen the slough confined to the vaginal mucous membrane, where, otherwise, it would unquestionably have extended entirely through the vagino-vesical septum. It occurs principally in first labours where the pelvis is small, the soft parts unyielding, and the fœtal cranium large; but I have seen it in those advanced in life, who had given birth previously to many children. Authors are disposed to attribute the accident, in many cases, to the awkward use of obstetrical instruments; but, from a careful analysis of these cases, and from my own experience, I am well satisfied that for one case thus produced, their judicious application has prevented it fifty times.

Other causes produce it occasionally, such as a prolonged retention of a pessary in the vagina, a calculus or other foreign body in the bladder, abscesses, venereal ulcerations, &c. I have seen one case where the whole base of the bladder was destroyed by a corroding ulcer, which, originating in the cervix uteri, extended forward to the urethra. Whatever may be the cause of this distressing affection, it is a matter of serious importance to both surgeon and patient that it be rendered susceptible of cure.

Its diagnosis is sufficiently easy. Incontinence of urine, following a tedious labour after a lapse of from one to fifteen days, will always prove its existence. But to determine the exact size, shape, and relative position of the artificial opening requires some nicety of examination. The consequences of the involuntary discharge of urine are indeed painful. The vagina may become inflamed, ulcerated, encrusted with urinary calculi, and even contracted; while the vulva, nates, and thighs are more or less excoriated, being often covered

Designed a curative surgery for vesico-vaginal fistula, a condition responsible for thousands of deaths

JAMES MARION SIMS (1813 - 1883)

On the Treatment of Vesico-Vaginal Fistula

***American Journal of Medical Sciences*, 23(45), January 1852, 59-82.**

Vesico-vaginal fistulas were a relatively common condition in which a woman's urine leaked into her vaginal cavity from her bladder, and many regarded the fistulas as untreatable during the early 1800s.

James Marion Sims

Larry Longo (1994, Grolier Medicine): "J. Marion Sims, a native of South Carolina who practiced medicine there and in Alabama, moved to New York City in 1853 for reasons of health. Two years later he founded the Women's Hospital in New York, which opened on 4 May 1855; this was the first American institution devoted exclusively to the treatment of gynecologic disorders. There Sims and his colleagues achieved a brilliant success record for their fistula repairs and vaginal plastic operations and established modern gynecologic surgery in the United States. Sims attained international renown as one of the world's foremost gynecologists. Sims's 1852 paper contains the original description of his operation for the surgical cure of vesico-vaginal fistula. After repeated fruitless attempts (about forty in number) to cure several women suffering from this malady, Sims ultimately succeeded with the aid of silver sutures, the improved exposure provided by the knee-chest position, and a vaginal speculum now named for him. Sims's technique initiated a new era in the history of gynecology."

Unfortunately, the surgical advances Sims detailed were the result of experimental surgeries performed on enslaved Black women between 1845 and 1849 in Alabama. These women endured dozens of painful procedures without anesthesia. Consequently, Sims' work is significant not only for its surgical advance but also as a permanent record of ethical issues forcing modern readers to reckon with the reality that key medical insights were extracted from vulnerable, unconsenting subjects.

Despite his brilliant accomplishments as a surgeon on behalf of thousands of sufferers of vaginal fistulas, Sims is now in disrepute. His statue in Central Park in New York was removed in 2018 after publication of the book *Medical Apartheid*, which reported on Sims' surgeries on enslaved women.

Book Notes: Our copy is in a copy of Vol 23 of the journal in contemporary leather binding. Pages and wood engraving in excellent condition.

References: GMN 6037; Grolier Medicine 66A; McGregor (1998); Speert America p. 179.

SILVER SUTURES IN SURGERY.

THE

ANNIVERSARY DISCOURSE,

BEFORE THE

NEW YORK ACADEMY OF MEDICINE.

DELIVERED IN THE NEW BUILDING OF THE HISTORICAL SOCIETY, ON THE 18TH NOVEMBER, 1857.

BY

J. MARION SIMS, M.D.,

SURGEON TO THE WOMAN'S HOSPITAL.

(PUBLISHED BY ORDER OF THE ACADEMY.)

NEW YORK:
SAMUEL S. & WILLIAM WOOD,
389 BROADWAY.
1858.

Meaningfully improved gynecologic surgery by using silver wire as a suture material over traditional silk thread

JAMES MARION SIMS (1813 - 1883)

Silver Sutures in Surgery

Anniversary Discourse before the New York Academy of Medicine, 1857.

Sims' address to the New York Academy of Medicine argued for silver wire as a solution to many of the failures encountered in surgeries at the time. Sims outlined a technical breakthrough in curing vesicovaginal fistula—a catastrophic condition resulting from obstructed labor that left women incontinent and socially ostracized—by arguing that the specific material used for stitching was the single most critical variable in the healing process.

While other surgeons favored silk thread, Sims demonstrated that silk acted as a porous wick for bacteria, inevitably causing infection and tissue destruction that caused repairs to fail; in contrast, he presented silver wire as an inert, non-porous material that induced no inflammation and allowed wounds to close cleanly. Sims' procedure was soon adopted worldwide.

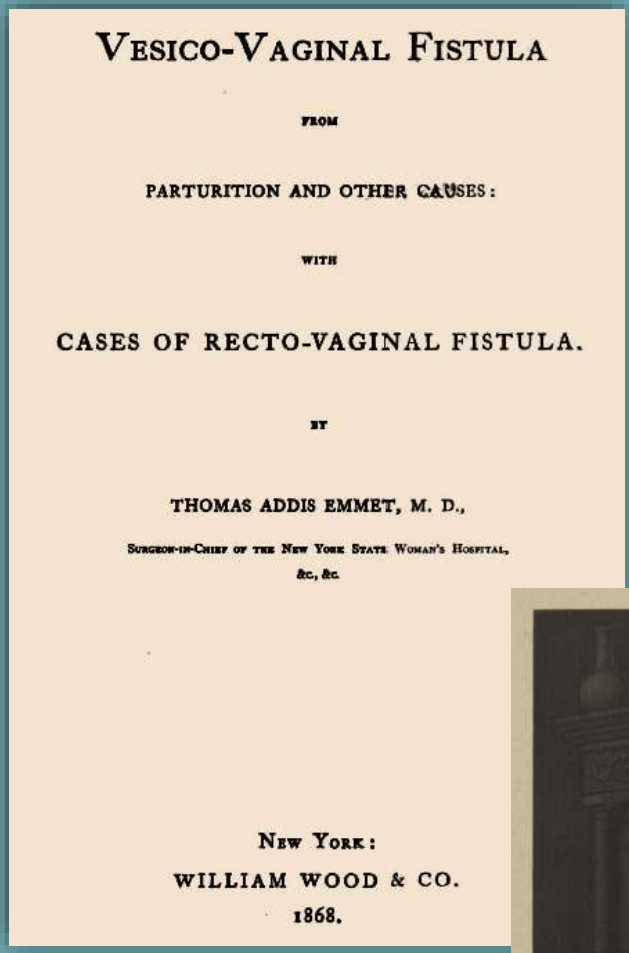
Sims founded the Women's Hospital in New York in 1855 – which was the first American institution set up to treat gynecologic disorders. This hospital became highly successful and a beacon for women with serious gynecologic issues in the U.S. Thomas Addison Emmet later took over medical leadership of this institution after Sims moved to Europe.

In 1866 Sims also wrote *Clinical Notes on Uterine Surgery. With Special References to Management of the Sterile Condition*. This was published in London and New York (we have the New York edition). Also, this book was serialized in *The Lancet*. This was written while Sims was in London during the American Civil War. This book describes Sims' duck-bill speculum and describes his research on artificial impregnation.

Sims is credited as the originator of the modern discipline of gynecology by authors such as Irving Kaiser (1978) and George Ward (1936).

Book Notes: Our copy was previously the property of John Studd, the British gynecologist.

References: GMN 5605; Grolier Medicine p. 243; Heirs of Hippocrates 1804; McGregor (1998); Speert America p. 179.



VESICO-VAGINAL FISTULA

FROM

PARTURITION AND OTHER CAUSES:

WITH

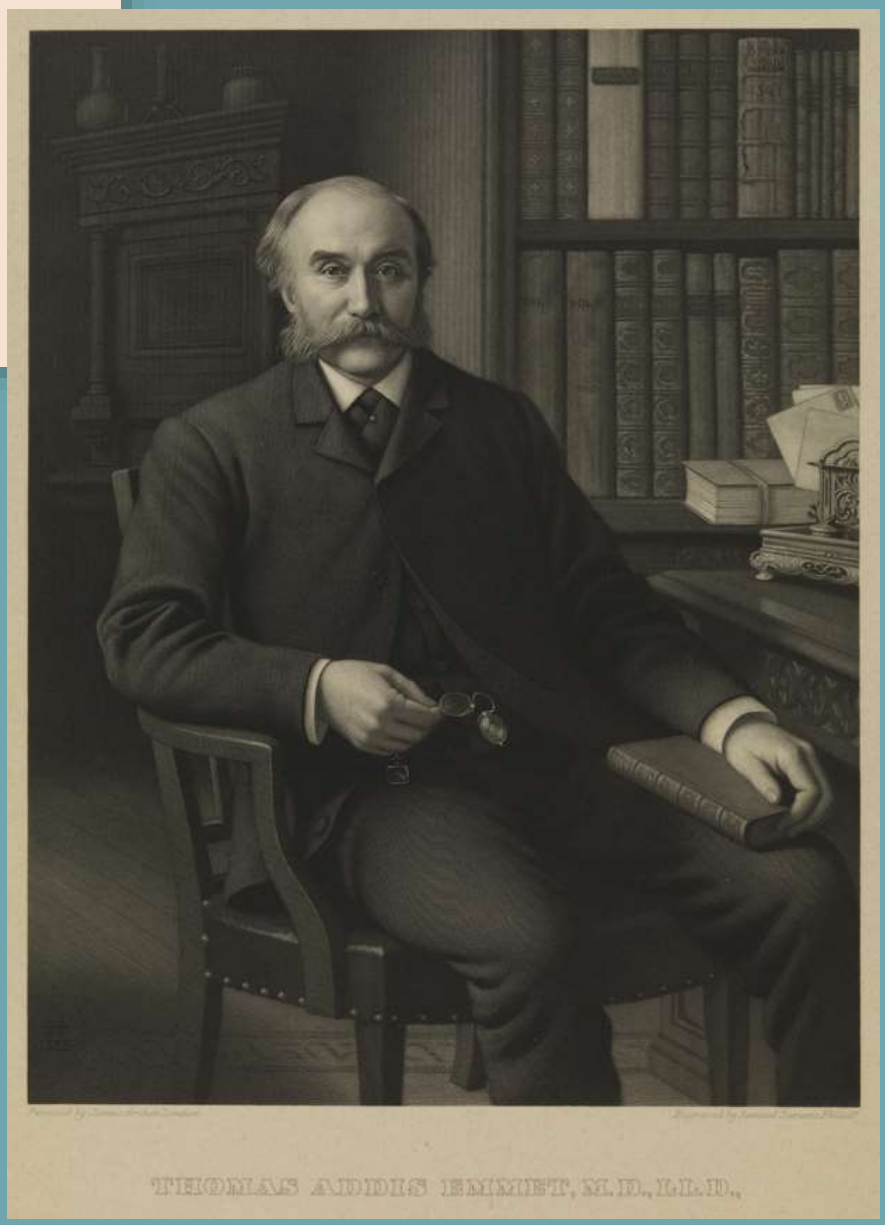
CASES OF RECTO-VAGINAL FISTULA.

BY

THOMAS ADDIS EMMET, M. D.,

SURGEON-IN-CHIEF OF THE NEW YORK STATE WOMAN'S HOSPITAL,
&c, &c.

NEW YORK:
WILLIAM WOOD & CO.
1868.



First to develop a method for reforming the urethra after its loss from vesico-vaginal fistula

THOMAS ADDIS EMMET (1829 - 1919)

Vesico-Vaginal Fistula from Parturition and Other Causes: With Cases of Recto-Vaginal Fistula (inscribed)

New York: William Wood and Co. 1868.

A vesico-vaginal fistula (VVF) is an abnormal communication between the bladder (vesica) and the vagina, resulting in continuous, involuntary leakage of urine through the vagina. In Emmet's era, the overwhelming cause was prolonged, obstructed labor. The condition was medically debilitating and socially catastrophic: affected women were incontinent, often ostracized, unable to work, and frequently abandoned by families. Recto-vaginal fistula, involving the rectum and vagina, produced similar misery with fecal incontinence.

Emmet's achievement was not simply technical repair, but conceptual reframing. He demonstrated that fistulae were surgically curable. Building on earlier efforts, including those of his mentor J. Marion Sims, Emmet refined surgical technique with meticulous attention to tissue preparation, tension-free closure, multilayer suturing, and postoperative bladder drainage.

After Marion Sims who then moved to Europe, Emmet was left in charge of their surgical hospital for women in New York. Emmet's treatment approach for fistula was derived from pure necessity. He wrote this in his 1900 article, *Reminiscences:*

"My fitness was soon to be tested, for shortly after his departure for Europe several unusually difficult cases of vesico-vaginal fistula were sent to me. As Dr. Sims had never operated on any but what I can now term simple cases, I was at first indisposed to make any effort for their relief, on the supposition they were incurable, but I was forced to realize that I must at least make the attempt. They were all cured ultimately, and I then sent for some thirty more, who had been at different times discharged as incurable and I succeeded in curing all of these. From this experience was developed a special branch of plastic surgery, which in 1868 I gave to the profession in a work on 'Vesico-vaginal Fistula from Parturition and Other Causes.' In this volume I described my method for forming the female urethra after its loss from sloughing. No successful attempt had been previously made to form this passage and the method of procedure I developed has not yet been superseded."

References: GMN 6058; McGregor (1998).

A CASE OF REMOVAL OF THE UTERINE APPENDAGES.

By LAWSON TAIT, F.R.C.S.

So much interest is being expressed in the operation which has been termed "oöphorectomy", and there is so much of a disposition to prejudge it, that I desire briefly to describe one of my recent cases in which, like many others, my only regret is that, instead of temporising so long with the patient as I did, I did not press the only real remedy which the case admitted. I have reason to believe that many unfounded rumours are abroad, that those who have adopted a wide extension of abdominal section are operating in a reckless fashion. I can only say that in my own practice I think no evidence of this will be found, and the following case will prove much to the contrary.

Mrs. L., aged 34, was sent to me by Dr. McLintock of Church Stretton in September 1878. She had been married four and a half years, and had one child in 1875. Since her confinement, she had never been well, and had suffered from symptoms which clearly were those of subinvolution and retroflexion. She had profuse menstrual hæmorrhage; and, on consulting a physician in July 1878, she was told she had a tumour behind the womb, and that the womb must be dilated and the tumour removed. For this purpose, a sponge-tent was introduced, and left in, according to her reiterated statement, for nine days. She suffered from an attack of acute "inflammation of the bowels", and was in bed for seven weeks. This incident occurred, I am pleased to say, neither in Church Stretton nor in Birmingham. When she came to me on September 24th, 1878, she was in a wretched state of exhaustion and emaciation. I found a mass on the right side of the uterus, which fluctuated indistinctly. The uterus was retroflexed, and fixed completely by perimetric effusion. I tapped the mass, and removed about four ounces of pus from what I now know was an abscess of the right ovary. She was much relieved, and returned to Church Stretton under Dr. McLintock's care, and slowly gained some strength. She never made anything like a recovery, however; and her medical attendant sent her back several times to me, and together we carried on a great variety of treatment without much benefit. The uterus remained fixed, and all efforts to replace it were so painful that she could not endure them. She could not bear intercourse; she never was a day without pain; and her life was fitly described as a burden to her and her relatives.

Dr. McLintock sent her down to me again at the end of last February, and in his letter he told me he was sure something more must be done if our patient's life was to be saved. I found that the mass on the right of the uterus was just as I had left it; that the uterus was still fixed and retroflexed; that there was now a more clearly defined mass to the left of the uterus; and that the whole roof of the pelvis was exquisitely tender to touch. Her temperature went up at night, and she had night-sweats; and, though I could feel no fluctuation, I had no doubt there was pus somewhere. I therefore advised and performed an exploratory incision on the 6th of March. I found the pelvis roofed over by adherent coils of intestine, which I lifted with much trouble. Below these, the whole of the organs were matted together, and their identification was a matter of the greatest difficulty. Finally, I succeeded in recognising the right Fallopian tube, distended into a cyst, with greatly thickened walls, and full of pus. Below it, and intimately adherent to it, lay the ovary, as large as an orange, and containing some old cheesy matter—the remains, probably, of the abscess I had tapped two years and a half before. The uterus was bound down in the *cul-de-sac* by old adhesions, and from these I relieved it. I found the left ovary adherent below the fundus; and from it the left Fallopian tube ran a circuitous course, like a sausage in appearance, and adherent to the brim of the pelvis, the uterus, and a piece of small intestine. It contained about two ounces of pus. I removed both ovaries and both tubes, cutting the latter off close to their uterine attachments. The hæmorrhage during the operation was very troublesome, but was controlled by sponge-pressure. Mr. J. Raffles Harmar assisted me, and Mr. Wright Wilson gave ether.

The patient has recovered without a bad symptom, and is perfectly free from pain for the first time since the incident of the sponge-tent. The uterus is (to-day) perfectly free, and any movement of it gives her no pain. My only regret about this case is, that I did not operate two years ago.

Robert Lawson Tait

The first successful example of an oophorectomy (removal of ovaries) that we are aware of

ROBERT LAWSON TAIT (1845 - 1899)

A Case of Removal of the Uterine Appendages

British Medical Journal, vol. 1, May 14th 1881.

Born in Edinburgh and mentored by Sir James Young Simpson, Tait was a brilliant and audacious figure who achieved numerous surgical "firsts". His career was defined by pushing the boundaries of abdominal surgery, including the first successful appendicectomy for acute appendicitis in 1880 and the use of oophorectomy for sepsis in 1872.

He practiced what some termed "Tait's Law," advocating for exploratory laparotomy in any life-threatening pelvic or abdominal condition not clearly caused by malignancy. Beyond his technical skill, Tait was a pioneer of aseptic technique; he abandoned Lister's chemical antisepsis in favor of obsessive cleansing of his hands and instruments and was among the first to ligate the ovarian pedicle and return it to the peritoneal cavity rather than exteriorizing it. His outcomes were extraordinary for the time, achieving a mortality rate of only 6 percent in his second series of 50 ovariotomies.

Robert Lawson Tait's 1881 article documents a pivotal surgical intervention in the treatment of chronic pelvic disease.

In this brief but impactful two-page report, Tait describes an oophorectomy - the surgical removal of the Fallopian Tubes and ovaries—a procedure then referred to as the removal of the "uterine appendages"—to address severe inflammatory conditions. By reporting a specific case of success, Tait provided clinical evidence for a procedure that would eventually become known as the "Tait operation," which targeted life-threatening pelvic infections and ectopic pregnancies that were previously considered medically hopeless.

By 1884, Tait reported a series of five cases with four complete cures, eventually establishing a life-saving procedure where only one out of forty subsequent patients died.

To our knowledge, Tait was the first to successfully remove the ovaries of a patient. In 1809 Ephraim McDowell had successfully removed a large ovarian tumor in the United States. And, at about the same time as Tait, both Robert Battey and Alfred Heger also began to perform oophorectomies.

Tait was a fierce advocate for active surgical interference in cases of pelvic disease, often clashing with more conservative practitioners who favored non-invasive *materia medica*. This paper was part of his broader effort to professionalize gynecologic surgery, shifting it from a desperate "heroic" measure of last resort to a standardized, life-saving discipline.

References: GMN 6075; Leonardo p. 339; Moscucci p. 155-156; Radcliffe p. 90.f

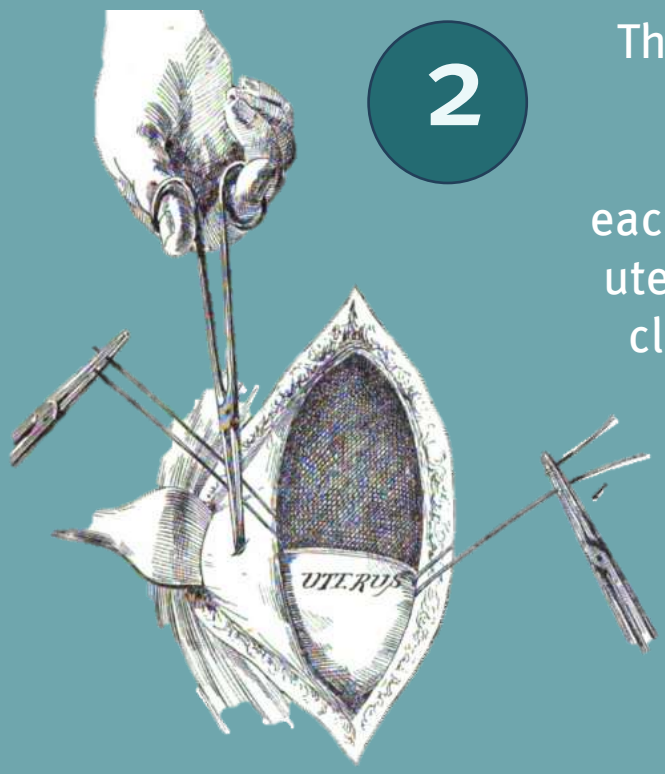
Key Elements of Gilliam's Operation for Prolapse

1

Use Button Forceps

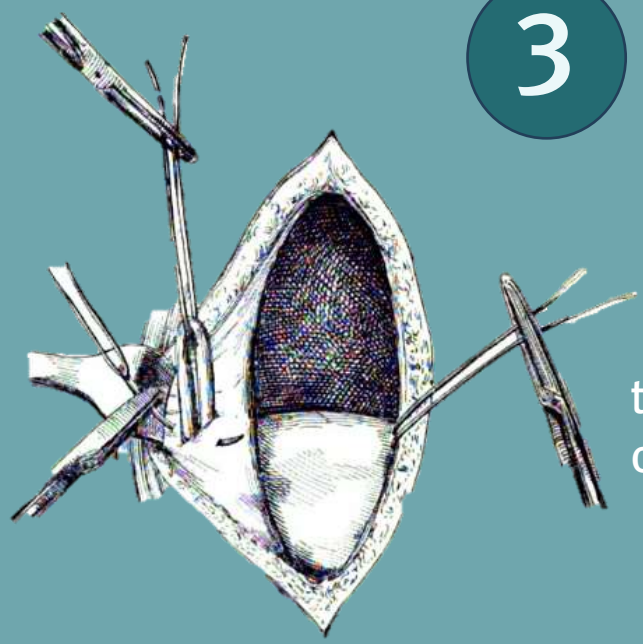
2

Thread around the round ligament on each side of the uterus. Hold by clamp forceps



3

The perforating forceps is withdrawn, bringing after it the round ligament, through the base of which a suture is being passed.



Described a new, highly effective operation to treat uterine prolapse

DAVID TOD GILLIAM (1844 - 1923)

Round-ligament Ventrosuspension of the Uterus: A New Method

The American Journal of Obstetrics and Diseases of Women and Children, 1900, vol. 41, no. 267.

David Tod Gilliam

In 1900 David Tod Gilliam introduced a novel operative solution to one of the most persistent problems in nineteenth-century gynecology: uterine retrodisplacement and prolapse. At the turn of the century, these conditions were widely believed to cause chronic pelvic pain, menstrual disorders, infertility, and "nervous" symptoms, yet available treatments—pessaries, cautery, or hysterectomy—were either ineffective or excessively radical. Gilliam proposed a conservative, anatomically reasoned alternative that aimed to restore normal uterine position while preserving the organ and reproductive potential.

Gilliam sought to improve upon previous suspension methods, such as the Olshausen or Kelly procedures, which often resulted in restricted uterine mobility or significant complications during subsequent pregnancies. His "new method" involved making a small abdominal incision, drawing a loop of each round ligament through the rectus muscle and fascia, and securing them externally. This approach ensured a secure, durable suspension that allowed the uterus to remain in a natural, forward-leaning (anteverted) position while still permitting the mobility required for potential gestation.

Gilliam emphasized the simplicity and reproducibility of the operation, presenting it as a rational improvement over earlier suspension methods that relied on suturing the uterus directly to the abdominal wall. He reported favorable early outcomes, including durable uterine support and symptomatic improvement, and argued that the procedure respected physiological principles rather than imposing artificial fixation.

"Gilliam's operation" was rapidly adopted and modified, becoming one of the most widely taught procedures for uterine displacement in the twentieth century. It marked a shift away from destructive or ablative operations toward organ-preserving gynecologic surgery.

References: Baskett p. 154; GMN 6111.

Key Elements of The Robotic Prolapse Procedure

ROBOTIC-ASSISTED LAPAROSCOPIC SACROCOLPOPEXY FOR TREATMENT OF VAGINAL VAULT PROLAPSE

DAVID S. DiMARCO, GEORGE K. CHOW, MATTHEW T. GETTMAN, AND DANIEL S. ELLIOTT

ABSTRACT

Introduction. To describe and demonstrate the use and benefit of robotic-assisted laparoscopic sacrocolpopexy in the treatment of posthysterectomy vaginal vault prolapse.

Technical Considerations. The procedure combines the use of standard laparoscopy with the daVinci robotic system. The patient is placed in the dorsal lithotomy position. One camera port, two robotic ports, and two standard laparoscopic ports are placed transperitoneally. Standard laparoscopic dissection, in combination with an intravaginal retractor, is used for initial anterior and posterior vaginal mobilization and exposure of the sacral promontory. The daVinci robot is then docked and used to suture a silicone Y-shaped graft from the vagina to the sacral promontory. Culdoplasty, with plication of the uterosacral ligaments, is then performed, with the final step, retroperitonealization of the graft.

Conclusions. A total of 5 women have undergone this procedure, 3 with concomitant pubovaginal sling placement. All 5 women were discharged after 24 hours. No complications from the sacrocolpopexy were reported; however, 1 patient experienced transient vaginal bleeding related to the pubovaginal portion of the case. No recurrent anterior, posterior, or apical prolapse has occurred at mean of 4 months of follow-up. Using a robotic system for laparoscopic sacrocolpopexy facilitated precise intracorporeal suture placement so that the procedure could be done in a fashion similar to that of the open method. Robotic-assisted laparoscopic sacrocolpopexy may provide the same long-term durability of open sacrocolpopexy with the benefit of a minimally invasive approach. UROLOGY **63**: 373–376, 2004. © 2004 Elsevier Inc.

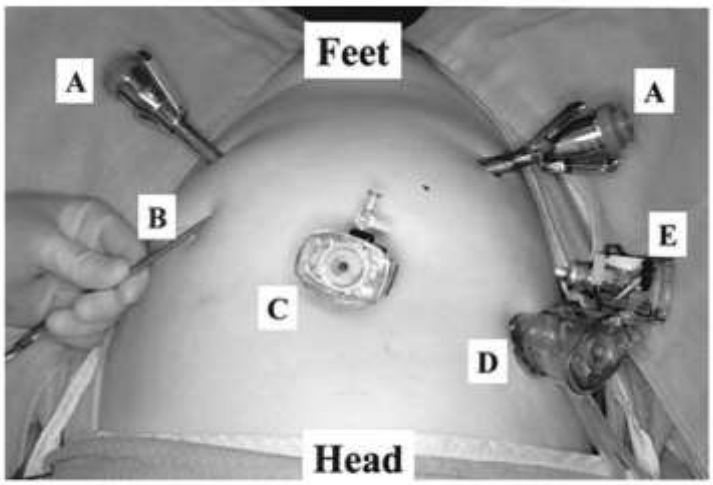


FIGURE 1. *Transperitoneal port placement: A, 8-mm robotic ports placed at inferior lateral rectus; B, Prolene suture to retract sigmoid colon; C, 12-mm camera port; D, 10-mm port at superior lateral rectus; and E, 5-mm port placed inferiorly subcostal.*

The da Vinci robot is an integrated computer-based system consisting of two interactive robotic arms, a camera arm, and a remote control with three-dimensional vision capability. The da Vinci robot uses instruments with 6 degrees of freedom, which provides the same flexibility as the human wrist. The working robotic arms are attached to reusable 8-mm trocars, and the camera is placed through a standard 12-mm laparoscopic port. For optimal robot function and to minimize the risk of collisions, the angle created by the camera port and each working robotic port should be obtuse and the distance between the ports at least one hand-breadth.

DAVID S. DI MARCO (1972 - PRESENT)

Robotic-assisted laparoscopic sacrocolpopexy for treatment of vaginal vault prolapse

Urology 63: (with Chow GK, Gettman MT, Elliott DS.), 2004.

Di Marco's 2004 paper, "Robotic-assisted laparoscopic sacrocolpopexy for treatment of vaginal vault prolapse," documented the first institutional experience with using the da Vinci Surgical System to treat high-grade pelvic organ prolapse. The procedure involves a minimally invasive approach where a synthetic Y-shaped mesh is sutured to the vaginal apex and then anchored to the anterior longitudinal ligament of the sacral promontory. This provides a durable "internal suspension" for the vagina, which is eventually covered by the peritoneum to prevent bowel complications.

David S. Di Marco
Mayo Clinic

The primary innovation described by Di Marco and his colleagues was the integration of robotic technology with standard laparoscopy to overcome the technical limitations of conventional "stick" laparoscopic surgery. The robotic system provided surgeons with three-dimensional vision, increased magnification, and seven degrees of freedom in instrument movement, which significantly simplified the complex task of deep pelvic suturing. For patients, this innovation offered the "gold standard" durability of traditional open abdominal surgery but with the benefits of a minimally invasive technique, including significantly decreased hospital stays (typically overnight) and minimal blood loss.

The implications for patients since this landmark publication have been largely positive, establishing robotic sacrocolpopexy as a highly effective care approach. Success rates reported since 2004 have been consistently high, with anatomic (objective) success rates ranging between 79% and 100%. Subjective success rates—how cured patients feel—range from 88% to 97%, with patient satisfaction often exceeding 90%. While the procedure is durable, approximately 10% of patients may experience some form of prolapse recurrence over the long term, and reoperation rates for apical recurrence are very low, estimated at roughly 0.8%.

6

Menopause

For most of recorded history, menopause was not understood as a discrete biological transition but rather as a dangerous and morally charged moment in a woman's life.

Early modern physicians interpreted the cessation of menstruation through humoral theory: menstrual blood was believed to purge excess or corrupt humors, and its disappearance was therefore thought to cause internal congestion, "plethora," or toxic accumulation.

During the Medieval and Renaissance periods, this view persisted. Midwifery texts and early medical treatises often described the "change of life" as a time of physical and emotional peril. Women reaching this age were sometimes marginalized, and their symptoms were often attributed to spiritual or character failings rather than biological shifts. There was little concept of "hormones"; instead, the focus remained on the physical absence of blood and the subsequent "cooling" of the female temperament.

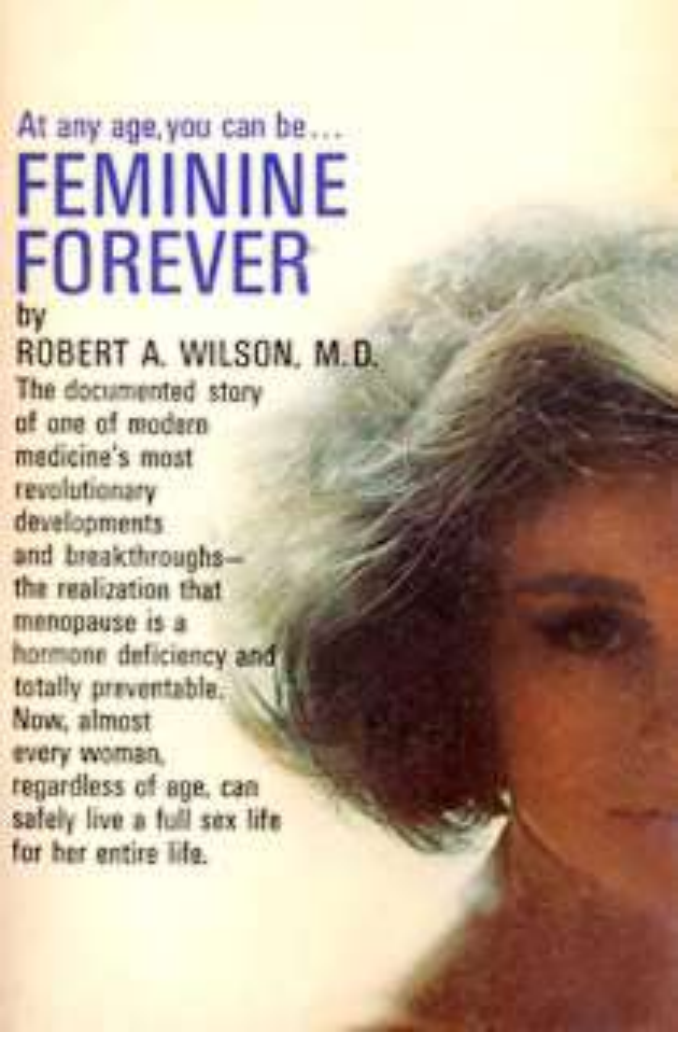
Eighteenth- and early nineteenth-century medical texts described menopause—often termed the critical age or la ménopause—as a period marked by nervous instability, flushes of heat, palpitations, melancholy, hysteria, and even insanity.

These symptoms were rarely distinguished from broader cultural anxieties about aging women, fertility loss, and social role disruption. Menopause thus entered medical discourse less as a normal life stage than as a pathological crisis requiring vigilance and intervention.

A decisive transformation occurred in the late nineteenth and early twentieth centuries with the rise of experimental physiology and endocrinology. The ovary, once viewed primarily as a reproductive organ, emerged as an endocrine gland whose secretions exerted systemic effects.

The 1960s Saw Medicalization of Hormone Deficiency

The identification of internal secretions and the isolation of ovarian hormones reframed menopause as a state of hormone deficiency rather than dangerous retention. This reconceptualization paralleled broader shifts in medicine: disease became molecular and biochemical, and women's midlife symptoms were increasingly interpreted through laboratory science rather than moral theory. Still, therapeutic options remained limited, and menopause was often medicalized without effective treatment.



The modern era of menopause management began in the mid-twentieth century with the clinical use of estrogens. Figures such as Fuller Albright demonstrated that estrogen deficiency was responsible for postmenopausal osteoporosis, providing the first clear link between menopause and a major chronic disease.

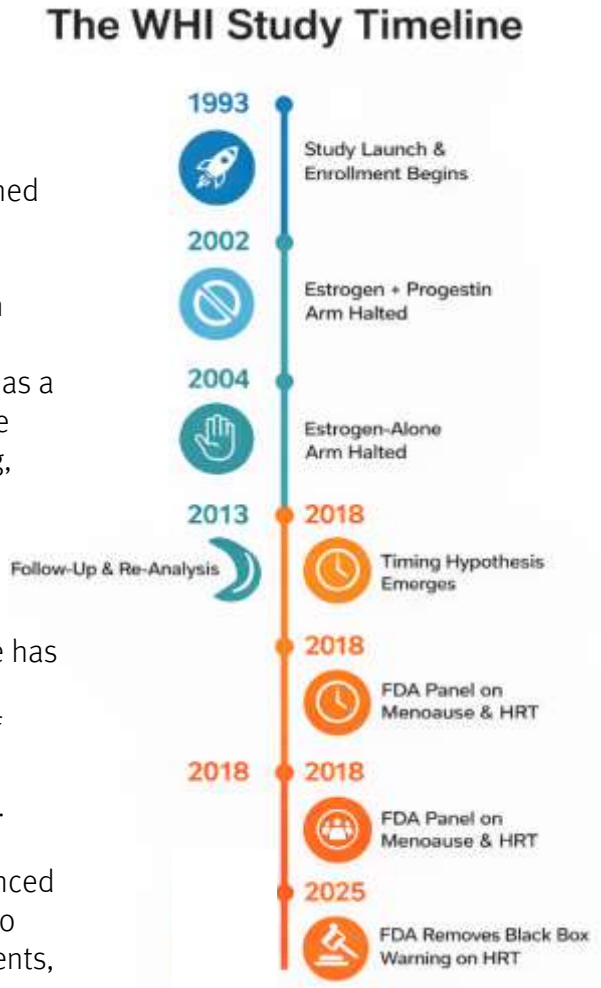
This discovery led to the first major publication to change menopausal treatment: Robert A. Wilson's 1966 book, *Feminine Forever*. Wilson argued that menopause was not a natural transition but a "deficiency disease" that required medical correction. He championed the use of Estrogen Replacement Therapy (ERT) as a "cure" for aging. This publication was immensely influential, leading to a major increase in hormone use. However, it was later heavily criticized for its patriarchal tone and for being funded by the pharmaceutical industry.

Hormone therapy moved menopause decisively into the realm of treatable physiology. By the 1960s, estrogens were widely prescribed for vasomotor symptoms, urogenital atrophy, and later for long-term disease prevention. Menopause was reframed not as a crisis but as a deficiency like diabetes or hypothyroidism—an analogy that powerfully shaped clinical practice.

Late in the 20th century menopause was increasingly portrayed as an estrogen-deficiency syndrome associated with aging, and chronic illness.

By the 1980s and 1990s, millions of women in high-income countries were taking long-term HRT, often with little distinction between symptomatic treatment and preventive medicine.

The WHI Bombshell



The publication of the Women's Health Initiative (WHI) hormone trials in the early 2000s marked a profound rupture in this narrative. The demonstration that combined estrogen–progestin therapy increased risks of breast cancer, thromboembolism, and stroke in older postmenopausal women triggered a dramatic decline in HRT use and forced a reappraisal of decades of assumptions. Menopause was no longer framed simply as a deficiency to be corrected indefinitely, but as a life stage whose management required careful attention to timing, individual risk, and therapeutic goals. This moment represents one of the most consequential course corrections in modern women's health.

In the decades since WHI, understanding of menopause has matured and diversified. The concept of a universal menopausal experience has given way to recognition of heterogeneity shaped by genetics, body composition, reproductive history, socioeconomic status, and culture.

Hormone therapy has been rehabilitated in a more nuanced form—short-term, symptom-driven, and initiated close to the menopausal transition—while nonhormonal treatments, lifestyle interventions, and patient-centered decision-making have gained prominence.

A number of effective non-hormonal drug options for menopausal symptoms have entered the market. Importantly, menopause is now studied not only as an endocrine event but as a neurovascular, metabolic, and immunologic transition with implications for long-term health.

In the 21st century, the conversation has moved toward a more balanced, individualized approach with increasing interest on healthspan and the management of diseases of aging.

We now recognize that menopause involves a spectrum of experiences, and the perspective is shifting from the management of menopausal symptoms per se to the female life experience after 50. By 2040 more than half of women in industrialized countries will be alive after 50 and, thus, there is an ever growing imperative to identify opportunities for improved health in this period.

DE

LA MÉNOPAUSE,

OU

DE L'AGE CRITIQUE DES FEMMES;

TRAITÉ dans lequel sont exposés la description anatomique et physiologique de l'utérus à la ménopause, les changemens que cette époque opère tant sur le physique que sur le moral de la Femme, les moyens hygiéniques qui doivent être alors employés, enfin les maladies qui surviennent ordinairement à l'âge critique.

PAR CH. P. L. DE GARDANNE,

Docteur en médecine de la Faculté de Paris, Médecin de charité du 3.e Arrondissement, Membre du Cercle Médical, de la Société Physico-médicale de Moscow, etc.

Propter solum uterum mulier est id quod est.

VANHELMONT.

SECONDE ÉDITION.

A PARIS,

CHEZ MÉQUIGNON-MARVIS, LIBRAIRE,

RUE DE L'ÉCOLE DE MÉDECINE, N.o 3, PRÈS CELLE DE LA HARPE.

1821.

CHARLES-PIERRE-LOUIS DE GARDANNE (1788 - 1858)

De La Ménopause Ou De L'âge Critique Des Femmes

Paris: Mequignon, 1821.

Charles-Pierre-Louis de Gardanne’s 1821 treatise is historically important because it introduced the term "ménopause" into the medical lexicon.

Before Gardanne, the end of female fertility was referred to by vague or ominous terms like the "climacteric," "the dodging time," or simply "cessation". By combining the Greek words men (month) and pausis (cessation), Gardanne created a specific, clinical label for the phenomenon. This act of naming was crucial; it transformed the cessation of menstruation from a mere symptom of aging into a distinct physiological event and a legitimate subject of scientific inquiry. Substantively, the text reflects the prevailing 19th-century medical anxiety regarding female physiology.

Gardanne framed menopause not merely as a natural transition, but as a "critical age" (l'âge critique) fraught with danger. Influenced by the humoral theory that still lingered in French medicine, he believed that the cessation of menstrual bleeding left women vulnerable to a host of illnesses—such as gout, dropsy, and uterine cancer—because the "impurities" once expelled by the body were now retained. In his view, the uterus was the central regulator of a woman's health, and its retirement was a moment of physiological instability that required close medical supervision.

The legacy of Gardanne’s work lies in its role in the "medicalization" of aging women. By defining menopause as a specific medical category with associated risks, he established the physician as the necessary manager of this life stage. His recommended treatments—which included bloodletting (using leeches to mimic the lost menstrual flow), dietary restrictions, and spa treatments—set a precedent for viewing menopause as a condition to be treated rather than a life stage to be experienced. This perspective laid the early groundwork for the pathologization of menopause that would dominate gynecology for the next two centuries, eventually evolving into the 20th-century focus on hormone deficiency and replacement.

References: Downham Moore (2022); Mattern p. 272.

THE PARATHYROID GLANDS
AND
METABOLIC BONE DISEASE

SELECTED STUDIES

BY

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BALTIMORE
THE WILLIAMS & WILKINS COMPANY
1948

Albright details his discovery of postmenopausal osteoporosis, linking the disease to estrogen deficiency

FULLER ALBRIGHT (1900 - 1969) AND EDWARD REIFENSTEIN JR. (1908 - 1975)

The Parathyroid Glands and Metabolic Bone Disease: Selected Studies

Baltimore, Williams and Wilkins, 1948.

Published in 1948 by Fuller Albright and Edward C. Reifenstein Jr., *The Parathyroid Glands and Metabolic Bone Disease: Selected Studies* is one of the first and most important texts in the field of endocrinology and mineral metabolism. The book summarized decades of Albright's clinical research at Massachusetts General Hospital, providing a physiological framework for how the body regulates calcium and phosphorus.

By using meticulous "metabolic balance studies," the authors moved beyond simple observation to quantify exactly how various hormones and diseases altered bone density and mineral excretion.

The core of the work focuses on the classification and pathology of bone disorders, most notably the distinction between osteoporosis, osteomalacia, and osteitis fibrosa cystica. Albright famously identified osteoporosis as a disorder of bone matrix—a failure of the osteoblasts to lay down protein scaffolding—rather than a failure of mineralization. It is in this volume that Albright detailed his discovery of postmenopausal osteoporosis, linking the disease to estrogen deficiency and forever changing the medical approach to aging and women's health.

Beyond osteoporosis, the treatise provided the first clear descriptions of hyperparathyroidism and hypoparathyroidism, as well as the groundbreaking discovery of pseudohypoparathyroidism. This latter discovery represented the first time in medical history that a disease was attributed to "target-organ resistance," where the body produces a hormone but the tissues fail to respond to it.

Fuller Albright 1949
(courtesy, NLM)

Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women

Principal Results From the Women's Health Initiative Randomized Controlled Trial

Writing Group for the Women's Health Initiative Investigators

Context Despite decades of accumulated observational evidence, the balance of risks and benefits for hormone use in healthy postmenopausal women remains uncertain.

Objective To assess the major health benefits and risks of the most commonly used combined hormone preparation in the United States.

Design Estrogen plus progestin component of the Women's Health Initiative, a randomized controlled primary prevention trial (planned duration, 8.5 years) in which 16608 postmenopausal women aged 50-79 years with an intact uterus at baseline were recruited by 40 US clinical centers in 1993-1998.

Interventions Participants received conjugated equine estrogens, 0.625 mg/d, plus medroxyprogesterone acetate, 2.5 mg/d, in 1 tablet (n=8506) or placebo (n=8102).

Main Outcomes Measures The primary outcome was coronary heart disease (CHD) (nonfatal myocardial infarction and CHD death), with invasive breast cancer as the primary adverse outcome. A global index summarizing the balance of risks and benefits included the 2 primary outcomes plus stroke, pulmonary embolism (PE), endometrial cancer, colorectal cancer, hip fracture, and death due to other causes.

Results On May 31, 2002, after a mean of 5.2 years of follow-up, the data and safety monitoring board recommended stopping the trial of estrogen plus progestin vs placebo because the test statistic for invasive breast cancer exceeded the stopping boundary for this adverse effect and the global index statistic supported risks exceeding benefits. This report includes data on the major clinical outcomes through April 30, 2002. Estimated hazard ratios (HRs) (nominal 95% confidence intervals [CIs]) were as follows: CHD, 1.29 (1.02-1.63) with 286 cases; breast cancer, 1.26 (1.00-1.59) with 290 cases; stroke, 1.41 (1.07-1.85) with 212 cases; PE, 2.13 (1.39-3.25) with 101 cases; colorectal cancer, 0.63 (0.43-0.92) with 112 cases; endometrial cancer, 0.83 (0.47-1.47) with 47 cases; hip fracture, 0.66 (0.45-0.98) with 106 cases; and death due to other causes, 0.92 (0.74-1.14) with 331 cases. Corresponding HRs (nominal 95% CIs) for composite outcomes were 1.22 (1.09-1.36) for total cardiovascular disease (arterial and venous disease), 1.03 (0.90-1.17) for total cancer, 0.76 (0.69-0.85) for combined fractures, 0.98 (0.82-1.18) for total mortality, and 1.15 (1.03-1.28) for the global index. Absolute excess risks per 10000 person-years attributable to estrogen plus progestin were 7 more CHD events, 8 more strokes, 8 more PEs, and 8 more invasive breast cancers, while absolute risk reductions per 10000 person-years were 6 fewer colorectal cancers and 5 fewer hip fractures. The absolute excess risk of events included in the global index was 19 per 10000 person-years.

Conclusions Overall health risks exceeded benefits from use of combined estrogen plus progestin for an average 5.2-year follow-up among healthy postmenopausal US women. All-cause mortality was not affected during the trial. The risk-benefit profile found in this trial is not consistent with the requirements for a viable intervention for primary prevention of chronic diseases, and the results indicate that this regimen should not be initiated or continued for primary prevention of CHD.

JAMA. 2002;288:321-333 www.jama.com

For editorial comment see p 366.

Author Information and Financial Disclosures appear at the end of this article.

THE WOMEN'S HEALTH INITIATIVE (WHI) focuses on defining the risks and benefits of strategies that could potentially reduce the incidence of heart disease, breast and colorectal cancer, and fractures in postmenopausal women. Between 1993 and 1998, the WHI enrolled 161809 postmenopausal women in the age range of 50 to 79 years into a set of clinical trials (trials of low-fat dietary pattern, calcium and vitamin D supplementation, and 2 trials of postmenopausal hormone use) and an observational study at 40 clinical centers in the United States.[1] This article reports principal results for the trial of combined estrogen and progestin in women with a uterus. The trial was stopped early based on health risks that exceeded health benefits over an average follow-up of 5.2 years. A parallel trial of estrogen alone in women who have had a hysterectomy is being continued, and the planned end of this trial is March 2005, by which time the average follow-up will be about 8.5 years.

The WHI clinical trials were designed in 1991-1992 using the accumulated evidence at that time. The primary outcome for the trial of estrogen plus progestin was designated as coronary heart disease (CHD). Potential cardioprotection was based on generally

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Found that, on balance, HRT for menopause was harmful when used as a progestin/estrogen combo

JACQUES ROSSOUW AND WHI INVESTIGATORS

Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial

Journal of the American Medical Association, 288(3):321-333, July 17, 2002.

This article reports the principal results from the Women's Health Initiative (WHI) randomized controlled trial, which investigated the risks and benefits of combined estrogen plus progestin therapy in healthy postmenopausal women. The study enrolled 16,608 women aged 50–79 with an intact uterus, assigning them to receive either a daily combined hormone tablet or a placebo. Originally planned for 8.5 years, the trial was stopped early after an average follow-up of 5.2 years because the data showed that the health risks of the regimen exceeded its benefits, specifically crossing a safety boundary for increased risk of invasive breast cancer.

The trial's results revealed a significant increase in several serious health conditions among women taking the combined hormones compared to the placebo group. Specifically, the researchers found increased hazard ratios for coronary heart disease (1.29), invasive breast cancer (1.26), stroke (1.41), and pulmonary embolism (2.13). While the therapy did provide some benefits, such as a reduced risk of colorectal cancer (0.63) and hip fractures (0.66), the "global index" used to summarize the overall balance of risks and benefits supported the conclusion that the harm outweighed the advantages. All-cause mortality, however, remained unaffected during the trial period.

The implications of these findings were profound, as they directly challenged long-standing observational evidence that suggested hormone therapy provided cardioprotective benefits for postmenopausal women. The WHI investigators concluded that combined estrogen and progestin should not be initiated or continued for the primary prevention of coronary heart disease. This landmark study led to a major shift in clinical practice, emphasizing that the risk-benefit profile for this specific regimen was inconsistent with the requirements for a viable intervention for chronic disease prevention in healthy women.

References: Mattern p. 298.

Original Investigation

Menopausal Hormone Therapy and Health Outcomes During the Intervention and Extended Poststopping Phases of the Women's Health Initiative Randomized Trials

JoAnn E. Manson, MD, DrPH; Rowan T. Chlebowski, MD, PhD; Marcia L. Stefanick, PhD; Aaron K. Aragaki, MS; Jacques E. Rossouw, MD; Ross L. Prentice, PhD; Garnet Anderson, PhD; Barbara V. Howard, PhD; Cynthia A. Thomson, PhD, RD; Andrea Z. LaCroix, PhD; Jean Wactawski-Wende, PhD; Rebecca D. Jackson, MD; Marian Limacher, MD; Karen L. Margolis, MD, MPH; Sylvia Wassertheil-Smoller, PhD; Shirley A. Beresford, PhD; Jane A. Cauley, DrPH; Charles B. Eaton, MD, MS; Margery Gass, MD, NCMP; Judith Hsia, MD; Karen C. Johnson, MD, MPH; Charles Kooperberg, PhD; Lewis H. Kuller, MD, DrPH; Cora E. Lewis, MD, MSPH; Simin Liu, MD, ScD; Lisa W. Martin, MD; Judith K. Ockene, PhD; Mary Jo O'Sullivan, MD; Lynda H. Powell, PhD; Michael S. Simon, MD, MPH; Linda Van Horn, PhD, RD; Mara Z. Vitolins, DrPH, RD; Robert B. Wallace, MD, MSc

IMPORTANCE Menopausal hormone therapy continues in clinical use but questions remain regarding its risks and benefits for chronic disease prevention.

OBJECTIVE To report a comprehensive, integrated overview of findings from the 2 Women's Health Initiative (WHI) hormone therapy trials with extended postintervention follow-up.

DESIGN, SETTING, AND PARTICIPANTS A total of 27 347 postmenopausal women aged 50 to 79 years were enrolled at 40 US centers.

INTERVENTIONS Women with an intact uterus received conjugated equine estrogens (CEE; 0.625 mg/d) plus medroxyprogesterone acetate (MPA; 2.5 mg/d) (n = 8506) or placebo (n = 8102). Women with prior hysterectomy received CEE alone (0.625 mg/d) (n = 5310) or placebo (n = 5429). The intervention lasted a median of 5.6 years in CEE plus MPA trial and 7.2 years in CEE alone trial with 13 years of cumulative follow-up until September 30, 2010.

MAIN OUTCOMES AND MEASURES Primary efficacy and safety outcomes were coronary heart disease (CHD) and invasive breast cancer, respectively. A global index also included stroke, pulmonary embolism, colorectal cancer, endometrial cancer, hip fracture, and death.

RESULTS During the CEE plus MPA intervention phase, the numbers of CHD cases were 196 for CEE plus MPA vs 159 for placebo (hazard ratio [HR], 1.18; 95% CI, 0.95-1.45) and 206 vs 155, respectively, for invasive breast cancer (HR, 1.24; 95% CI, 1.01-1.53). Other risks included increased stroke, pulmonary embolism, dementia (in women aged ≥65 years), gallbladder disease, and urinary incontinence; benefits included decreased hip fractures, diabetes, and vasomotor symptoms. Most risks and benefits dissipated postintervention, although some elevation in breast cancer risk persisted during cumulative follow-up (434 cases for CEE plus MPA vs 323 for placebo; HR, 1.28 [95% CI, 1.11-1.48]). The risks and benefits were more balanced during the CEE alone intervention with 204 CHD cases for CEE alone vs 222 cases for placebo (HR, 0.94; 95% CI, 0.78-1.14) and 104 vs 135, respectively, for invasive breast cancer (HR, 0.79; 95% CI, 0.61-1.02); cumulatively, there were 168 vs 216, respectively, cases of breast cancer diagnosed (HR, 0.79; 95% CI, 0.65-0.97). Results for other outcomes were similar to CEE plus MPA. Neither regimen affected all-cause mortality. For CEE alone, younger women (aged 50-59 years) had more favorable results for all-cause mortality, myocardial infarction, and the global index (nominal $P < .05$ for trend by age). Absolute risks of adverse events (measured by the global index) per 10 000 women annually taking CEE plus MPA ranged from 12 excess cases for ages of 50-59 years to 38 for ages of 70-79 years; for women taking CEE alone, from 19 fewer cases for ages of 50-59 years to 51 excess cases for ages of 70-79 years. Quality-of-life outcomes had mixed results in both trials.

CONCLUSIONS AND RELEVANCE Menopausal hormone therapy has a complex pattern of risks and benefits. Findings from the intervention and extended postintervention follow-up of the 2 WHI hormone therapy trials do not support use of this therapy for chronic disease prevention, although it is appropriate for symptom management in some women.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT00000611

JAMA. 2013;310(13):1353-1368. doi:10.1001/jama.2013.278040

Editorial page 1349

Author Video Interview at jama.com

Supplemental content at jama.com

Author Affiliations: Author affiliations are listed at the end of this article.

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HRT beneficial for women in 50s and 60s while estrogen only HRT not associated with higher breast cancer risk

JOANNE MANSON AND COLLEAGUES

Menopausal Hormone Therapy and Health Outcomes During the Intervention and Extended Poststopping Phases of the Women's Health Initiative Randomized Trials

Journal of the American Medical Association, October 2, 2013.

This paper reanalyzed health outcomes from the Women's Health Initiative (WHI) randomized trials of HRT. The study reassessed two hormone therapy regimens—combined estrogen plus progestin in women with a uterus, and estrogen alone in women with prior hysterectomy—tracking outcomes including coronary heart disease, stroke, venous thromboembolism, breast cancer, colorectal cancer, fractures, diabetes, and all-cause mortality.

The key finding was that overall risks and benefits were age- and timing-dependent: women who initiated hormone therapy closer to menopause (ages 50–59) had more favorable benefit–risk profiles than older women, particularly for all-cause mortality and some cardiovascular outcomes, while older initiators experienced higher risks.

Importantly, the paper clarified long-term effects after discontinuation. Many risks observed during the intervention phase attenuated or disappeared after stopping therapy, while some benefits—such as reduced fractures—persisted. For breast cancer, outcomes diverged by regimen: combined estrogen–progestin therapy was associated with an increased incidence of breast cancer that persisted after cessation, whereas estrogen-alone therapy showed a reduced incidence and mortality from breast cancer over extended follow-up. Neither regimen significantly affected long-term all-cause mortality.

This paper marked a pivotal reframing of the WHI legacy. Early WHI results (2002–2004) had led to a dramatic decline in HRT use by highlighting cardiovascular and cancer risks in older postmenopausal women, often extrapolated to all women. Manson et al. helped establish the "timing hypothesis", aligning WHI data with observational studies suggesting that initiating HRT near menopause may confer symptom relief and skeletal benefits with acceptable risk in appropriately selected women.

7

Female Cancers

The history of cancer spans millions of years, with the earliest written human evidence of female cancers in ancient Egypt (c. 3000 BCE) and the first description in the Edwin Smith Papyrus.

In ancient Greek medicine, authors such as Hippocrates and later Galen recognized hard uterine or breast masses, ulceration, foul discharge, and wasting as ominous signs, but they lacked a coherent concept of malignancy. Hippocrates named it karkinos (crab) around 400 BCE, attributing it to an imbalance of black bile, a theory that persisted for centuries, though Romans and Greeks also tried surgery and cauterization.

Cancers of the breast and womb were recognized in this early literature and these diseases were often shrouded in mystery or dismissed as incurable.

Paul of Aegina (c. 625–690 CE), a Byzantine physician whose work shaped medical practice for nearly a thousand years, provided one of the first descriptions of the surgical removal of the breast. Unlike many of his predecessors who avoided invasive procedures in women, Paul offered explicit instructions for treating uterine and vaginal conditions, including hemorrhages and tumors, helping to normalize operative gynecology within mainstream medicine.

Breast cancer was more accessible to intervention than uterine cancer, and several medieval surgeons advocated early excision, often followed by cauterization.

The uterus, by contrast, remained mysterious, hidden, and symbolically charged; cancer of the womb was typically diagnosed only after advanced ulceration and bleeding.

An early breast cancer patient

The seventeenth and eighteenth centuries brought incremental but important shifts. Surgeons such as Johannes Scultetus emphasized careful observation, early diagnosis, and complete excision for breast cancer, anticipating later oncologic principles.

At the same time, obstetrics and gynecology began to professionalize, especially in Europe. However, female cancers remained largely untreatable. Vaginal examinations were limited, internal anatomy poorly visualized, and operations constrained by catastrophic bleeding. The distinction between benign fibroids and malignant uterine tumors was often blurred, a diagnostic problem that would persist well into the nineteenth century.

The 19th Century Sees Major Progress in Pathology and Surgery

The nineteenth century transformed gynecologic oncology through pathology, anesthesia, and antisepsis. Microscopic pathology—pioneered by Johannes Müller—established that cancers were diseases of disordered cells rather than corrupted humors, fundamentally redefining malignancy.

The 1800s brought a major acceleration in the treatment of cancers of the reproductive system. In 1801, Friedrich Benjamin Osiander performed the first deliberate surgical excision of the vaginal portion of the cervix for malignant disease. Operating without anesthesia or modern infection control, Osiander's bravery proved that local control of cervical malignancy was surgically possible.

Lacking further insights, humanity's main instinct with respect to cancers was to seek their removal. By the late 19th century, surgeons began attempting ever more radical approaches. In 1878, for example, Wilhelm Alexander Freund systematized total hysterectomy to treat uterine and cervical cancer through complete removal of these organs.

Twentieth Century Has Seen the Most Progress by Far

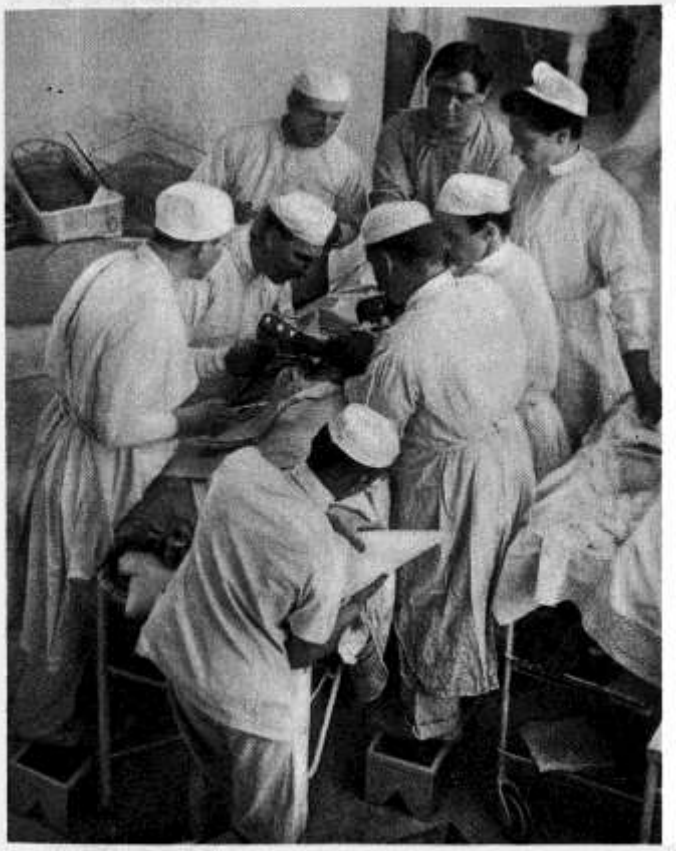
The early 1900s saw the standardization of these radical techniques. Ernst Wertheim revived and extended Freund's work in his landmark 1900 paper, advocating for the abdominal removal of not just the uterus, but the parametria and regional lymph nodes. Walter Sigwart further standardized the procedure.

William Halsted took a similar approach to breast cancer, attacking tumors by seeking radical mastectomy of the breast.

While surgeons perfected their craft, others looked for ways to attack cancer at the molecular level. Paul Ehrlich and Sahachiro Hata's 1910 discovery of Salvarsan introduced the visionary concept of the "magic bullet"—a drug that could seek out and destroy diseased cells without harming normal tissue.

This laid the intellectual foundation for modern chemotherapy – which was first tried after WWII.

Therapeutically, the mid-twentieth century saw the rise of radiation therapy and cytotoxic chemotherapy, expanding treatment options beyond surgery. In gynecologic cancers, radiation became especially important for cervical cancer, while chemotherapy gained traction in ovarian cancer—a disease notorious for late diagnosis and diffuse intraperitoneal spread.



Dr. Halsted's First Operation in the New Surgical Amphitheatre in 1904

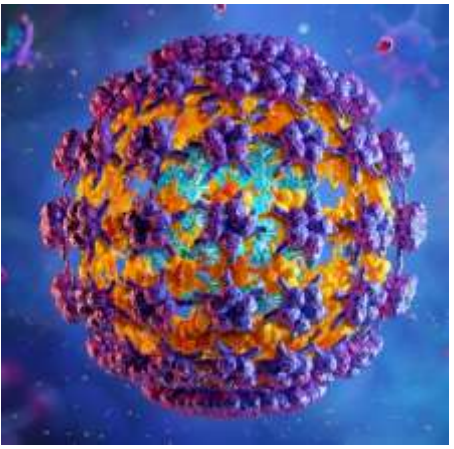
The introduction of platinum-based regimens in the 1970s and 1980s significantly improved survival for ovarian cancer patients, marking one of the first effective systemic treatments for a gynecologic malignancy. Breast cancer treatment evolved in parallel, with randomized trials—most notably those led by Bernard Fisher—demonstrating that less radical surgery combined with radiation and systemic therapy could achieve survival equivalent to mastectomy, dismantling Halsted's dominance.

Detection and Prevention Strategies Have Shined in the Twentieth Century

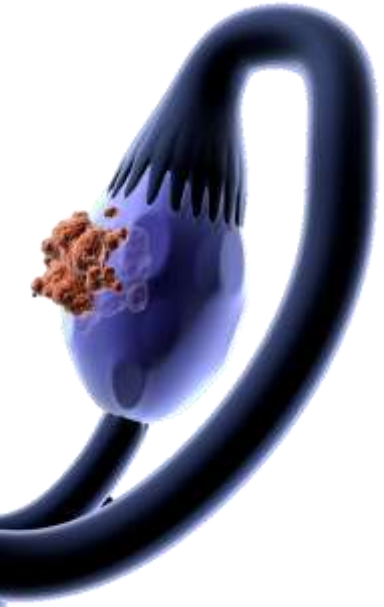
Two of the most impactful public health triumphs of the century arrived mid-way. In 1943, George Papanicolaou and Herbert Traut published *Diagnosis of Uterine Cancer by the Vaginal Smear*, introducing the "Pap Smear". This innovation allowed for the detection of cervical cancer before a tumor was even visible, eventually reducing mortality rates in developed nations by over 70%.

Likewise, in 1951, Raúl Leborgne vitalized mammography by inventing a compression apparatus that improved image quality, allowing for the detection of the microcalcifications of the breast.

The late twentieth and early twenty-first centuries marked the molecular and targeted era.



zur Hausen's work associating HPV with cervical cancer was one of the most important breakthroughs in medicine of the 20th century.



Ovarian cancer deaths remain far too high.

In breast cancer, Dennis Slamon's identification of HER2 amplification and the development of trastuzumab validated the concept that cancers could be stratified and treated based on molecular drivers rather than anatomy alone.

In cervical cancer, Harald zur Hausen's demonstration that human papillomavirus causes malignancy led directly to prophylactic vaccines, making cancer prevention possible at a biological level rather than solely through screening. These advances represent a profound shift: from treating cancer after it arises to preventing it altogether.

Huge Progress Against Cervical and Breast Cancer

Looking back over the centuries we have seen a female cancer go from a death sentence to a situation where long-term survival is very possible. Cervical cancer has arguably seen the most revolutionary change. Five hundred years ago, it was a silent, agonizing killer. Today, it is one of the only cancers we can theoretically eliminate from the planet. The Pap Smear combined with the HPV vaccine have combined to reduce the incidence of cervical cancer by more than 75%. Cervical cancer was once a top-two cancer killer of women and today ranks as #14.

The American Society of Clinical Oncology (ASCO) highlighted the "Top 5 advances in 50 years of Modern Oncology" in 2014, and second on the list was the approval of the HPV vaccine to prevent cervical cancer.

Breast cancer is another area where deaths are down substantially. In the 16th century, surgery for breast cancer (when attempted) was performed without anesthesia and was largely considered futile. The two big changes have been mammography and targeted therapy.

With targeted therapy we moved from "slash and burn" (radical mastectomies) to precision medicine. We now identify specific "drivers" like HER2 or Hormone Receptors and use drugs like Tamoxifen or Herceptin to shut the cancer down with far less collateral damage. The net result is that today the 5-year survival rate for localized breast cancer is 99%. Today, the biggest challenge is reducing death rates from triple negative breast cancer.

Ovarian Cancer Remains a Major Area of Unmet Need

Ovarian cancer remains the most lethal of the gynecologic cancers. In 2025 there were approximately 20,000 new cases in the U.S. with nearly 65% mortality. Ovarian cancer remains the leading cause of death from gynecologic cancers in the U.S.

The concept of cytoreductive (debulking) surgery was first articulated by Joe Vincent Meigs in 1934, though it did not gain broad acceptance until the mid-1970s, when C. Thomas Griffiths demonstrated an association between smaller residual tumor volume and improved survival.

Despite debulking surgery, the fundamental problem remains: detection.

There is still no effective "Pap smear" for the ovaries. Because the ovaries sit deep in the pelvis, tumors can grow quite large without causing symptoms. Most women (about 75%) are still diagnosed at Stage III or IV, where the cancer has already spread. While new drugs like PARP inhibitors are helping women live longer, we are still waiting for a breakthrough in early screening.

PARP inhibitors have shown high potential but only for women with BRCA mutations or homologous recombination deficiency.

Joe Vincent Meigs (1892 – 1963) was an early innovator in treating ovarian and cervical cancers.

Uterine Cancer Also Calls for Additional Progress

Uterine cancer is another troubling disease. The American Cancer Society projects ~69,120 new uterine cancer cases in the U.S. in 2025. Close to 14,000 women will have died from this disease in the U.S. in 2025. Uterine cancer is currently the most common gynecologic malignancy in the U.S. and the fourth most common cancer among women overall. Endometrial cancer accounts for ~90% of uterine cancers.

Unlike almost every other major cancer, where rates are stable or falling, uterine cancer is increasing. Uterine cancer is one of the few cancers where the death rate is actually rising (up about 1.5% per year recently). While we are getting better at treating the common, slow-growing "Type 1" tumors, there is a sharp rise in aggressive, non-hormonal "Type 2" tumors (like serous carcinoma).

Type 2 don't respond to standard hormone treatments and are much more likely to be fatal. There is some hope here. New drugs like Pembrolizumab (Keytruda) and Dostarlimab have shown "unprecedented" results for advanced cases that previously had no hope. For the first time in decades, the "standard of care" for advanced uterine cancer is being rewritten.

The incidence of uterine cancer is unfortunately rising.

PAVLI AEGINETAE TOTIVS REI MEDICAE LIBRI VII. AD PROFECTIONEM PARATI, ET BREVI SVMMA OMnem artem complectentes. Per IANVM Cornarium medicū Physicum Latina lingua cōscripti.

IANI CORNARII MEDICI PHYSICI, DOlabellarum, in Paulum Aeginetam medicum, libri VII.

Cum Indice rerum & uerborum locupletissimo.

Cum Cæsareæ Maiest. Gratia & Priuilegio ad decennium.

BASILEAE PER IOANNES HERVAGIOS ANNO D. M. LVI.

Johann Henrich Helmas me possidet. 1637.

92334

First description of surgical removal of breast and deep knowledge of gynecology

PAUL OF AEGINA (c. 625 - 690 CE)

De medica materia libri septe

Venice: Mense Octobri, 1532

Ricci (p. 196 to 200) gives a detailed description of Paul of Aegina's many contributions to gynecology. "The extreme practicality of the text and its consequent use doubtless accounts for its rarity today. Its section on surgery, Book VI, has been called the principal medical work of the Byzantine era" (Stillwell, *The Awakening Interest in Science*, 473).

Paul described practical management of difficult childbirth, retained placenta, uterine hemorrhage, prolapse, abscesses, fistulae, and gynecological tumors, often recommending manual techniques, instruments, and operative interventions when conservative measures failed. Unlike earlier authors who avoided invasive procedures in women,

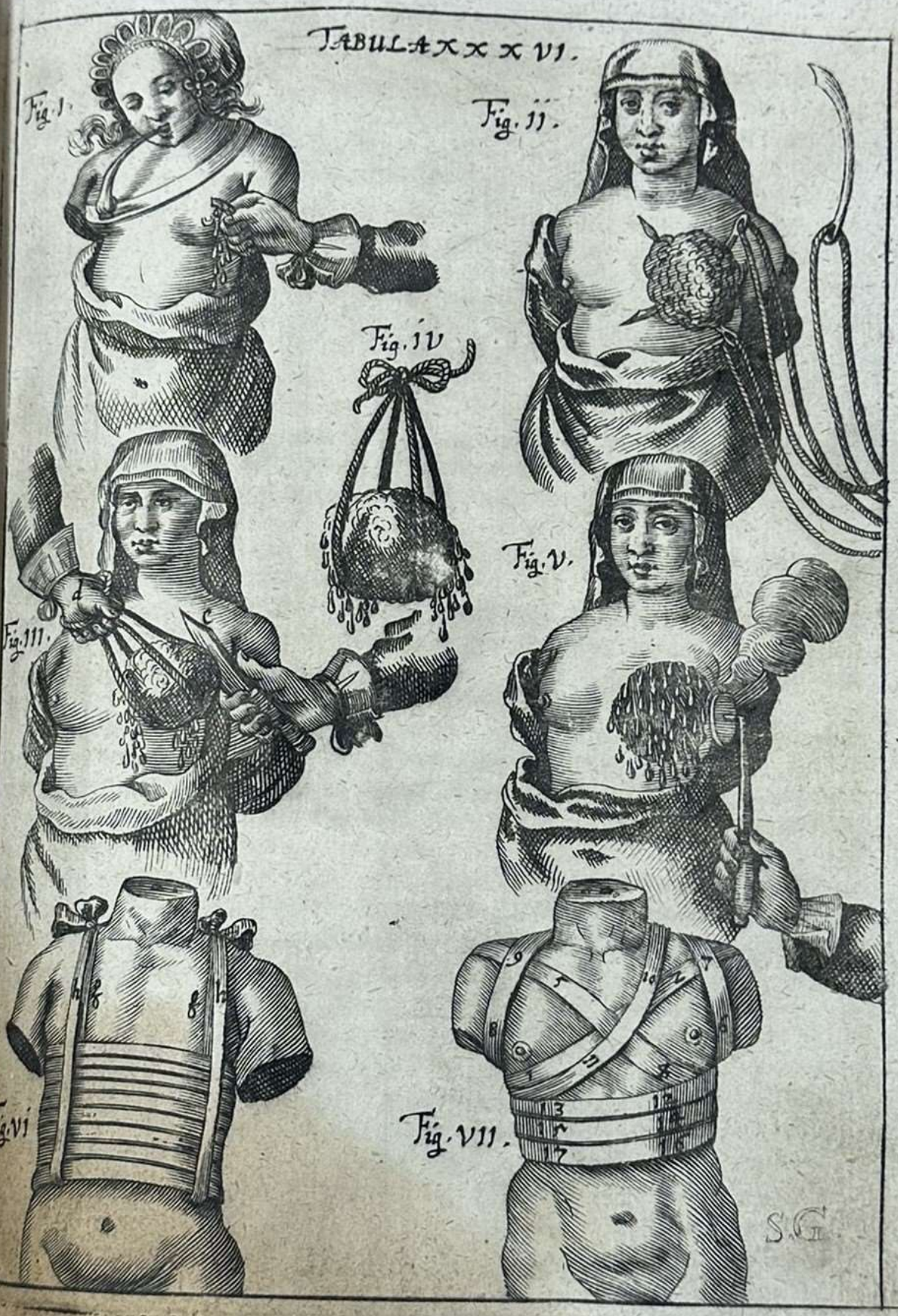
Paul gave explicit instructions for surgical treatment of uterine and vaginal conditions, helping normalize operative gynecology within mainstream medicine.

His pharmacological sections also preserved extensive knowledge of emmenagogues, fertility treatments, contraceptives, and abortifacients, reflecting the realities of reproductive care in late antiquity. Through its translation into Arabic and Latin, Paul of Aegina's Epitome became one of the most enduring foundations of medieval and early modern obstetrics and gynecology, shaping women's healthcare practice for nearly a millennium.

Book Notes: Folio (260 x 190 mm). 460 (of 466 leaves, without 3 blanks and leaves S7 woodcut, e6 text and ee7 printer's device). 11 full-page hand-colored woodcuts (of 12) of anatomical man, ages of man and animals. Vellum binding.

Provenance: Augustus Frederick, Duke of Sussex (1773-1843, bookplate); John Duncanson (bookplate); Edmund McClure (bookplate); Eric Saxton.

References: Du Moulin (1993, p. 12), GMN 5549, Haagensen 14; Leonardo p. 141; Ricci p. 196, Stillwell 473.


TABULA XXXVI.
Fig. I.
Fig. II.
Fig. IV
Fig. V.
Fig. III.
Fig. VI
Fig. VII.
S.G.

Developed safe surgical methods for breast removal in the case of cancer

JOHANNES SCULTETUS (1644 - 1726)

Wund-Artzneyisches, Zeng-Haus in zween Theil abgetheilt; Welches aus dem Lateinischen von dess

Frankfurt: Gudrucht bey Johann Gerlin, 1666.

Johannes Scultetus (1595–1645), a German surgeon best known for his landmark work *Armamentarium Chirurgicum* (first published posthumously), here in its first German edition (*Wund-Artzneyisches*), made important early contributions to the understanding and surgical treatment of breast cancer.

A meticulous observer and gifted illustrator, Scultetus compiled one of the most comprehensive surgical manuals of the seventeenth century, richly illustrated with detailed woodcuts of instruments and operative techniques. In his sections on cancer mammae, he described the disease as a hard, painful tumor of the breast that often became ulcerated and emitted a foul odor—characteristics consistent with malignant progression. He stressed careful palpation and visual examination for diagnosis and noted the disease's tendency to recur after surgery, anticipating the later recognition of cancer's infiltrative nature.

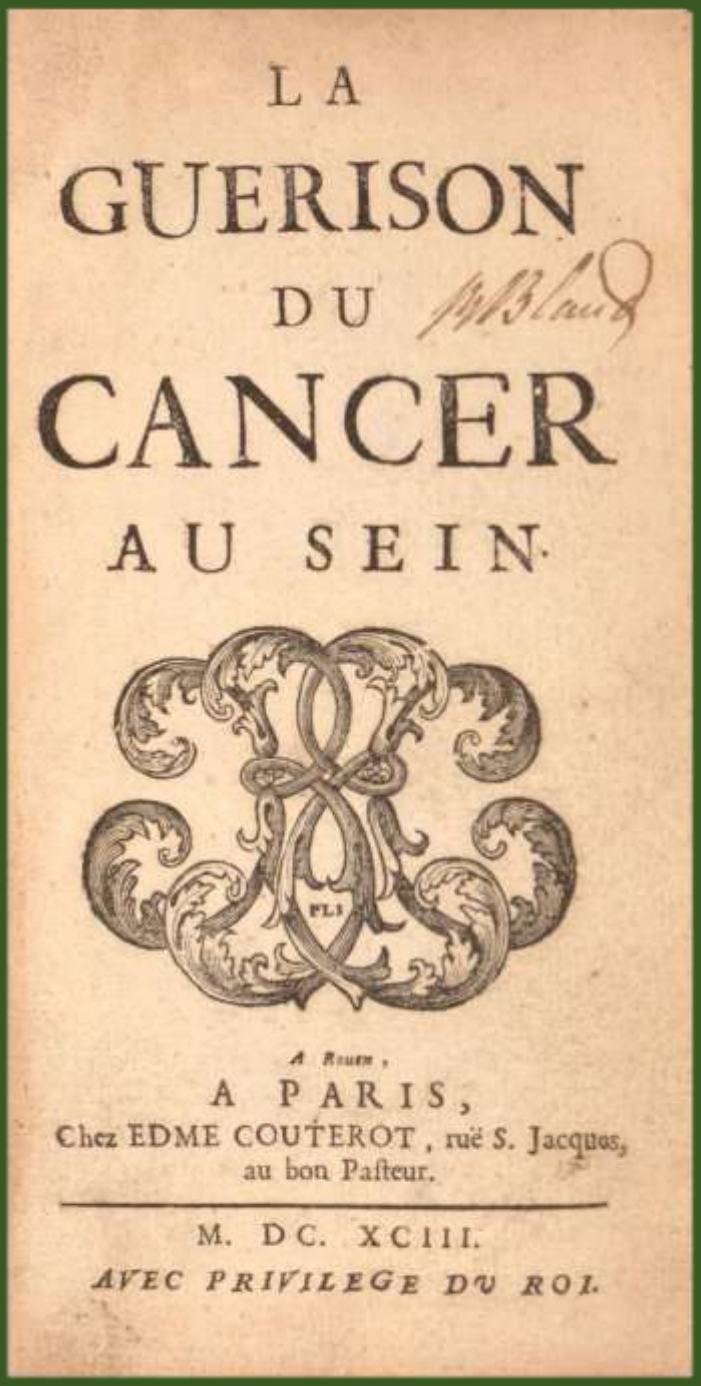
His operative recommendations included complete excision of the affected breast, cauterization of the wound margins and the use of ligatures to control hemorrhage—practices that made his surgical methods safer than those of his contemporaries.

Beyond his surgical innovations, Scultetus' *Armamentarium* provided an anatomically precise and visually accessible foundation for subsequent generations of surgeons. While still working within a humoral framework—attributing breast cancer to corrupted black bile—Scultetus advanced the practical treatment of the disease by emphasizing early excision, cleanliness and wound management rather than speculative remedies.

Book Notes: Title in red/black, [3] 263pp., [33] leaves: 56 plates. 185 x 120mm. Rebound in quarter calf.

Provenance: Previously the property of Kenneth F. Russell, Royal College of Surgeons, Australia. We have Russell's German ed (1666) and Latin ed. (1656). Book has signature on title page of Joannis Chemelvode, likely John Molyvdos, an Ottoman Greek scholar, physician and monk (1657-1719) who is regarded as the last living member of the Byzantine royal family.

References (1655 ed.): GMN 5571; Heirs of Hippocrates 466; Krivatsy 10759; Leonardo p. 203; Norman 1912; Radcliffe 47; Waller 8792; VD 17, 39:153208L.



LA
GUERISON
DU
CANCER
AU SEIN.

A Rouen,
A PARIS,
Chez EDME COUTEROT, ruë S. Jacques,
au bon Pasteur.

M. DC. XCIII.
AVEC PRIVILEGE DU ROI.

First monograph on breast cancer

HOUPPEVILLE, GUILLAUME DE (1644 - 1726)

La guérison du cancer au sein

Rouen: Chez Edmé Couterot, 1693.

Houppeville's book translated as *The Cure of Breast Cancer*, published in Paris in 1720, is the earliest monograph devoted entirely to breast cancer.

Houppeville, a surgeon of Rouen, sought to bring clinical observation and practical treatment to what had long been considered an incurable and mysterious disease.

His treatise discusses the visible and palpable signs of breast cancer, its progression and the characteristic hardness and pain that distinguished malignant tumors from benign swellings.

He also explored the emotional and physiological origins of the disease—often attributing it to "black bile" and melancholy—but combined this with firsthand surgical experience and an early appreciation of the disease's local invasiveness.

Houppeville outlined a therapeutic approach that included topical applications, cauterization and cautious surgical excision—methods reflecting both the limited tools of his era and a strikingly realistic understanding of cancer's tendency to recur.

He emphasized the importance of early intervention before ulceration and metastasis and his tone was both compassionate and pragmatic.

He supported his recommendations with citations from Hippocrates, Galen, Falloppio, Fabricius ab Aquapendente, Paré, Scultetus, Zacutus, Ettmuller, Tulp, and Roderigo de Castro. He praises German surgeon Fabry von Hilden for his description of breast extirpation.

Book Notes: 8vo. Printed folding table, lithographed plate, 5 half-tone plates. Publisher's printed wrappers.

Provenance: Previously owned by Jan Muhlbauer.

References: Krivatsy 6078, Robinson (1986), Sakofras and Safioleas (2010); Waller 4941.

Friedrich Benjamin Osiander

FRIEDRICH BENJAMIN OSIANDER (1759 - 1822)

Heilung des Mutterkrebses und krankhafter Auswüchse aus der Gebärmutter durch den Schnitt

In *Hufelands Journal der Practifchen Arzneykunde und Wundarzneykunft*, Berlin, Bd. 16, St. 3, S. 133–135, 1803.

Osiander (1759–1822) was a prominent German obstetrician and early gynecologic surgeon, best known for introducing operative approaches to diseases of the uterus at a time when such interventions were considered exceptionally dangerous. He served as professor of obstetrics at the University of Göttingen and was a leading figure in the institutionalization of academic obstetrics in late Enlightenment Germany.

His 1803 article "Heilung des Mutterkrebses und krankhafter Auswüchse aus der Gebärmutter durch den Schnitt" ("Cure of uterine cancer and pathological growths of the uterus by incision") is a landmark in the early history of operative gynecology.

In this paper, Osiander reported what is generally regarded as the first deliberate surgical excision of the vaginal portion of the cervix for malignant disease.

Karamanou, Salakos, Grammatikakis and Androutsos (2017) write "The operation which was performed by the braver surgeons at the beginning of the 19th century was the excision of the carcinomatous cervix. In 1801, Friedrich Benjamin Osiander performed the first excision of the vaginal portion of the cervix. Between 1801 and 1808 he carried out eight operations of this kind with success and he managed also to easily restrain the subsequent hemorrhage. In the following years, several surgeons cited his method mentioning that it was the only worthy treatment in cases of cervical malignancy"

Osiander's article details operative technique, which involved transvaginal excision of the diseased cervical portion using cutting instruments, performed without anesthesia and under extremely limited conditions of hemostasis and infection control. Osiander emphasized careful patient selection—restricting the operation to cases in which disease appeared confined to the cervix—and reported symptomatic improvement and local control in selected patients.

References: Leonardo, p. 360; N. Senn, "The Early History of Hysterectomy," *JAMA*, Sep 21, 1895.

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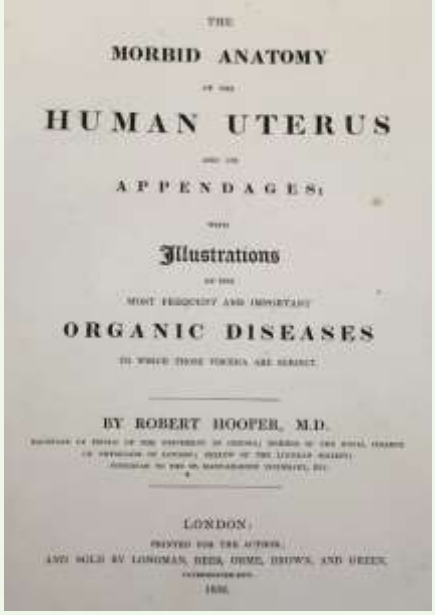
ROBERT HOOPER (1773 - 1825)

The Morbid Anatomy of the Human Uterus

London: Longman, Rees, Orme, Brown and Green, 1832


THE
MORBID ANATOMY
OF THE
HUMAN UTERUS
AND ITS
APPENDAGES;
WITH
Illustrations
OF THE
MOST FREQUENT AND IMPORTANT
ORGANIC DISEASES
TO WHICH THOSE VISCERA ARE SUBJECT.
BY ROBERT HOOPER, M.D.
LONDON:
PRINTED FOR THE AUTHOR,
AND SOLD BY LONGMAN, REES, ORME, BROWN, AND GREEN.
1832.

Robert Hooper's 1832 work, *The Morbid Anatomy of the Human Uterus and its Appendages*, is a landmark of pathological illustration, distinguished by its high-quality hand-colored aquatint plates. Hooper, an experienced London physician and pathologist, aimed to provide a systematic visual record of "organic diseases" such as tumors, ulcers, and inflammatory conditions of the female reproductive system. This was to accompany his first work *The Morbid Anatomy of the Human Brain* published four year before.

Unlike earlier texts that often relied on stylized or semi-abstract sketches, Hooper's illustrations were celebrated for their extraordinary realism and "morbid" accuracy, capturing the specific textures, colors, and vascular patterns of diseased tissue as they appeared during dissection.

The treatise is organized to lead the reader through the various pathologies of the uterus, ovaries, and fallopian tubes, providing clear clinical descriptions alongside the visual evidence. Hooper was particularly focused on the classification of uterine tumors (which he referred to as "substances") and the varying stages of cervical carcinoma, which he documented with unflinching detail. By providing such a rigorous atlas of disease, Hooper contributed to the shifting medical paradigm that sought to ground women's health in observable anatomical changes rather than the "humoral" theories of the past. His work remains a primary source for understanding the evolution of gynecological pathology

Book Notes: 4to (335 x 274 mm). [8], 67 [1] pp. 22 fine hand-coloured lithographed, stipple-engraved or aquatint plates after Howship and Kirkland. Original boards.

Provenance: Presentation copy from the author to University of Glasgow library, inscribed on front free endpaper.

References: Osler 7574 (original drawings); Wellcome II, 298.

Opposite Page: Plate XV: Carcinoma of the Uterus

Ueber

den feinern Bau

und

die Formen

der krankhaften Geschwülste

...

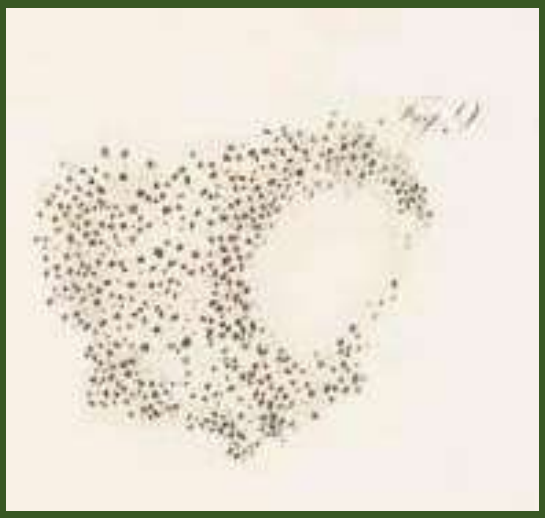
Dr. Johannes Müller,

In zwei Lieferungen.

Erste Lieferung.

Berlin.

1838.



Described cancer physiology at the cell level – allowing real insight into cancer for the first time.

JOHANNES PETER MÜLLER (1801 - 1858)

Ueber den feinern Bau und die Formen der krankhaften Geschwülste

Berlin: G. Reimer, 1838.

Daniel de Moulin (1993, p. 68): "Johannes Müller (1801–58), professor of anatomy and physiology in Berlin, may well be looked upon as the founder of cancer histology.

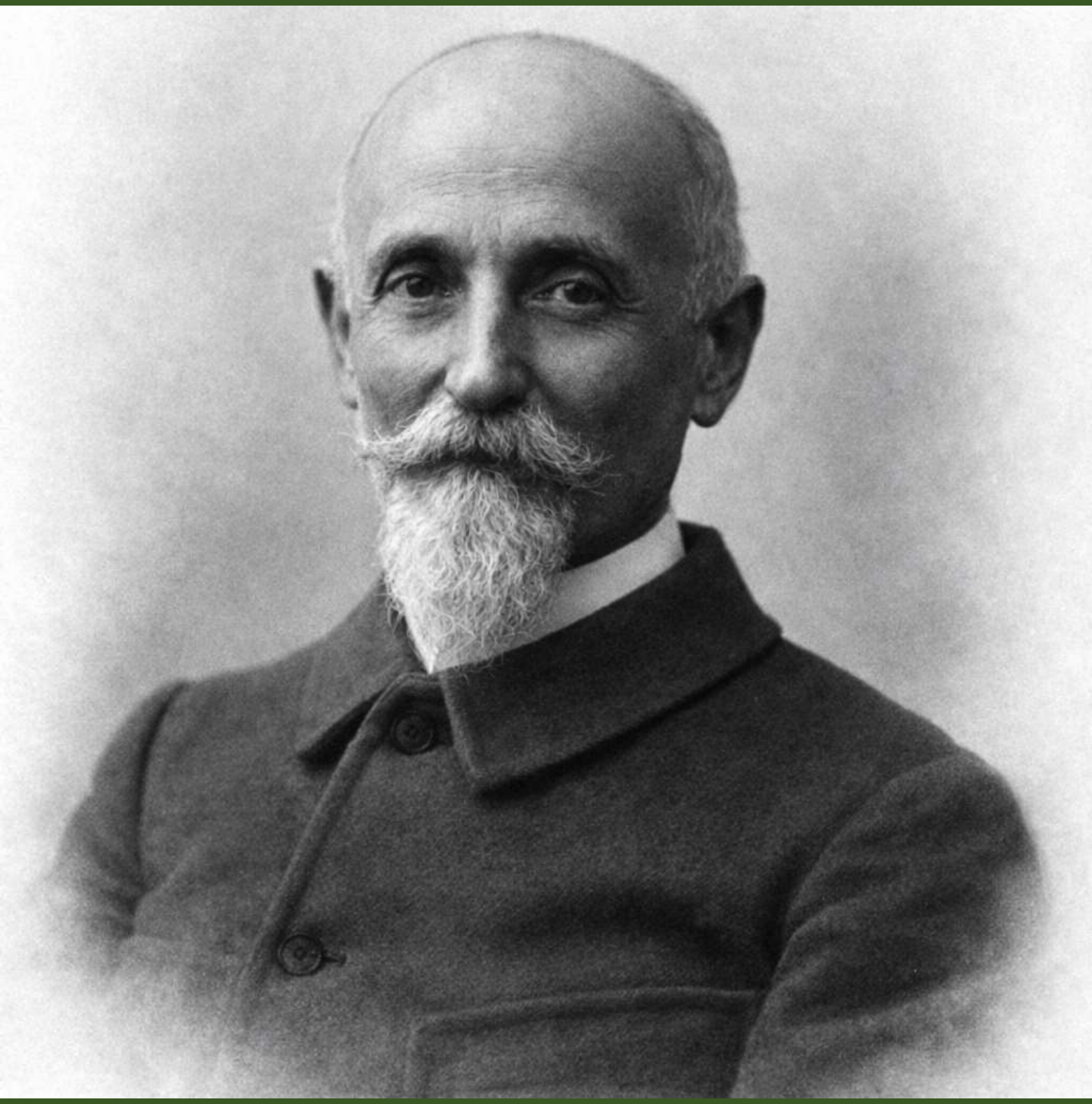
Müller was an exceptionally versatile scientist who introduced modern experimental physiology in Germany. Microscopic anatomy was receiving much attention in his department, and it was probably no coincidence that, in the same year (1838), Theodor Schwann, who was working in Müller's department, described the animal cell and Müller himself published his treatise *Über den feinern Bau and die Formen der krankhaften Geschwülste*, which was to become a classic in the history of cancerology. He established that pathologic growth consists of cells, just like any other tissue. In contrast to normal structures, however, the natural proportions had disappeared. The elements of form of cancerous growths are analogous to those of the normal elements of form of the body itself, or correspond with 'embryonic formations', as he called them, i.e. parts of tissue which are in a state of development. Most prominent amongst the cellular constituents of malignant growths were 'kugelartige Zellen', vesicular cells, containing granules or a single somewhat bigger nucleus, or even entire young cells. These he looked upon as the actual 'seminium morbi'.

A second type of cellular elements consisted of 'tailed bodies', which Müller regarded as connective tissue cells in an early stage of maturation."

Publication Notes: Folio, 1 leaf, 60 pp., 1 leaf, 4 illustrations by Schumann, Troschel, and Müller, engraved plates by Grüzmacher, half-leather binding.

References: GMN 2612; Haagensen 41; Speert p. 102. Also Long, *A History of Pathology*, 187-89.

Wilhelm Alexander Freund



WILHELM ALEXANDER FREUND (1833 - 1917)

Eine neue Methode der Exstirpation des Ganzen Uterus

***Samlung Klinischer Vorträge no. 133, Gynäkologie*, vol. 41, pp. 911-924, Breitkopf & Härtel, 1878.**

Freund's 1878 paper was a major step forward in surgical gynecology. He was the first to systematize an abdominal approach for total hysterectomy. Before, most attempts to remove the uterus were performed vaginally, which offered limited visibility and was often impossible to carry out. Freund's "new method" used a midline laparotomy to provide direct visual access to the pelvic organs, allowing for the ligation of the broad ligaments and the controlled separation of the uterus from the bladder and rectum.

Larry Longo wrote of this work in 1977: "Freund, of Breslau, successfully performed the first hysterectomy for carcinoma. Others had suggested, as much as a century earlier, that the cancerous uterus could be surgically extirpated, and several workers had performed abdominal hysterectomy for other conditions. However, it is to Freund that the credit belongs for inventing the operation along principles upon which modern radical hysterectomy for carcinoma of the cervix is based. The operation, performed on a 62-year-old woman, employed several innovations. The patient was tilted to elevate the pelvis (12 years before Trendelenburg's description of this position); the patient was thoroughly scrubbed with a 10 per cent solution of carbolic acid; a midline incision was made, and the intestines were carefully wrapped in warm carbolized towels and placed on the abdomen. A stout ligature on the fundus allowed the uterus to be lifted upward. Ligatures were successively placed around the Fallopian tubes, the broad ligaments, and the blood vessels. The bladder was dissected off the uterus, and an opening was made through the cul-de-sac into the vagina. The uterus was gradually removed as all remaining connections were severed. Then the pelvis was thoroughly reperitonealized."

Freund He almost simultaneously published an abstract (Klin. Wochenschr. 15: 417, 1878) and a more extended account (*Zentralbl. Gynaekol.* 2: 265, 1878) of this epochal operation. Despite his success, the appalling mortality rate associated with the procedure caused it to fall into disrepute for several decades. Other gynecologists such as E. Ries, A. K. Mackenrodt, P. Zweifel, and A. S. G. Döderlein added useful modifications, but it remained for the genius of Ernest Wertheim to successfully revive and extend this approach.

References: Haagensen 76; O'Dowd and Phillipp 555; Ricci (1945) p. 235; Speert 633. Also see Larry Longo, "Eine neue Methode der Exstirpation des ganzen Uterus: Wilhelm Alexander Freund," *AJOG*, 128(1), 117, 1977.

THE RESULTS OF OPERATIONS FOR THE CURE OF CANCER OF THE BREAST PERFORMED AT THE JOHNS HOPKINS HOSPITAL FROM JUNE 1889, TO JANUARY, 1894.

By WILLIAM S. HALSTED, M.D.,

Professor of Surgery, Johns Hopkins University, Surgeon-in-chief to the Johns Hopkins Hospital.

Reprinted from The Johns Hopkins Hospital Reports, Vol. IV, No. 6.

Promoted the radical mastectomy for breast cancer treatment

WILLIAM HALSTED (1852 - 1922)

The Results of Operations for the Cure of Cancer of the Breast Performed at the Johns Hopkins Hospital from June, 1889, to January, 1894.

Reprint from: The Johns Hopkins Hospital Reports, Vol. IV, No. 6 (1894-1895). Baltimore, 1894-1895.

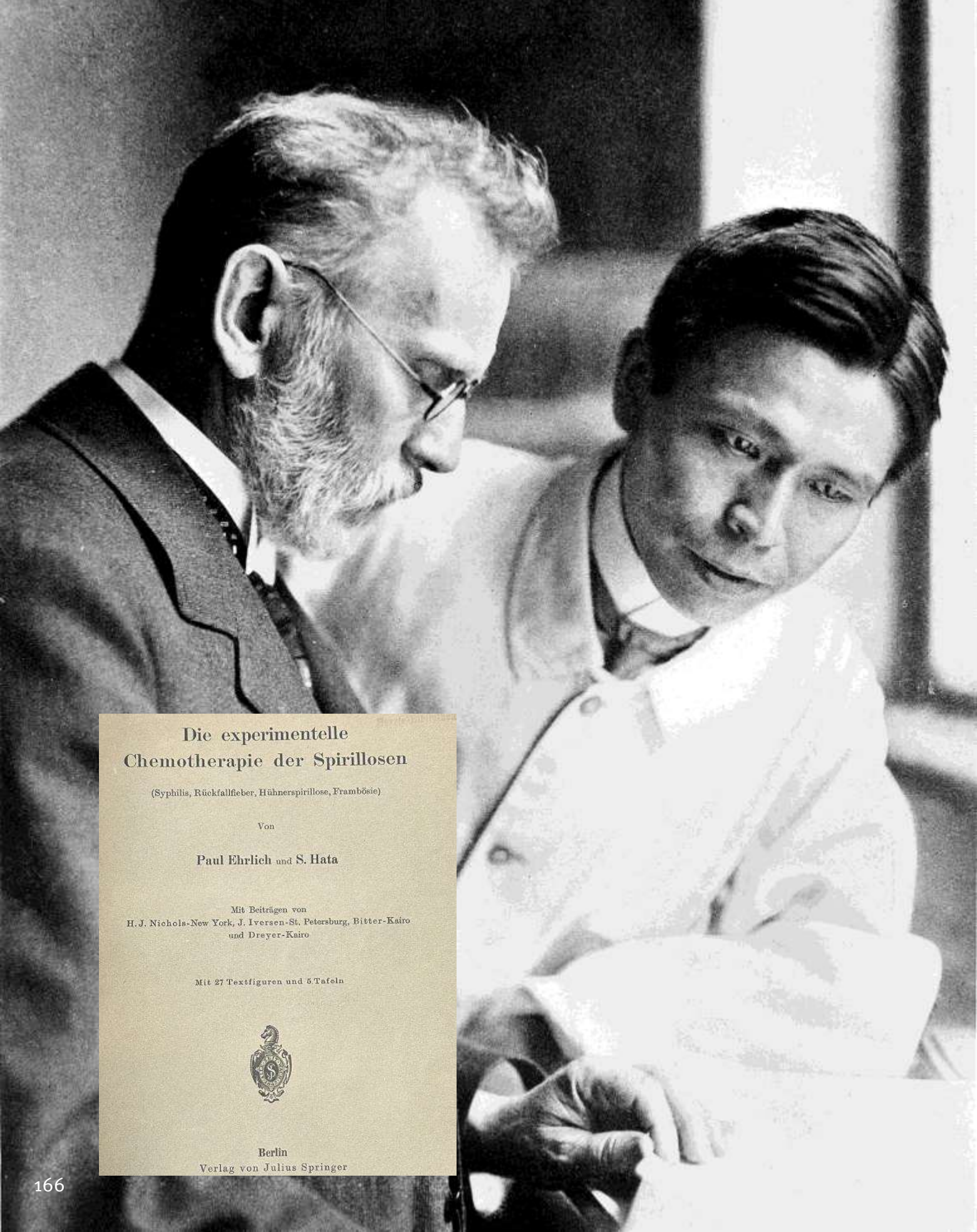
Halsted's presented one of the earliest systematic analyses of breast cancer outcomes in the United States. Compiled by surgeons under his leadership, the report documented the results of 50 consecutive breast cancer operations performed during the hospital's first five years. Halsted described in detail his radical mastectomy technique, which involved *en bloc* removal of the breast, underlying pectoral muscles and axillary lymph nodes—a method designed to achieve complete local eradication of the disease. The study meticulously recorded recurrence rates, survival outcomes and postoperative complications, reflecting a new era of scientific rigor in surgical oncology through careful case documentation and long-term follow-up.

The report's findings demonstrated that local recurrence rates were significantly reduced with the radical approach compared to earlier, more limited operations and that patients treated with complete resection experienced longer periods of disease-free survival. Halsted's conclusions—that breast cancer can spread in an orderly, regional fashion through contiguous tissue and lymphatic channels—formed the theoretical foundation of modern surgical oncology for decades. Though later challenged by systemic theories of cancer dissemination, the 1894–1895 Johns Hopkins report represented a pivotal milestone in the history of breast cancer surgery.

Publication Notes: 8vo. Printed folding table, lithographed plate, 5 half-tone plates. Publisher's printed wrappers.

Provenance: Previously the property of Haskell Norman and Jan Muhlbauer.

References: Ades (2017), De Moulin (1993), Ekmektzoglou (2009), GMN 5777, Hajdu (2012), Lukong (2017), Mukherjee (2002), Norman 983, Thoms 132.



Die experimentelle
Chemotherapie der Spirillosen

(Syphilis, Rückfallfieber, Hühnerspirillose, Frambösie)

Von

Paul Ehrlich und S. Hata

Mit Beiträgen von
H. J. Nichols-New York, J. Iversen-St. Petersburg, Bitter-Kairo
und Dreyer-Kairo

Mit 27 Textfiguren und 5 Tafeln

Berlin
Verlag von Julius Springer

Identified the possibility of targeted drugs at the cellular level for cancer and other diseases.

PAUL EHRLICH (1852 - 1922) and SAHACHIRO HATA (1873 - 1938)

Die experimentelle Chemotherapie der Spirillosen

Berlin: Verlag von Julius Springer, 1910.

In 1910, Paul Ehrlich and his Japanese collaborator Sahachiro Hata achieved a breakthrough in targeted drug therapy with their discovery of Salvarsan (arsphenamine), the first effective treatment for syphilis.

Although this work did not directly impact cancer treatment, it revolutionized medical thinking about how diseases—including cancer—could be attacked selectively at the cellular level.

Ehrlich and Hata introduced the visionary concept of the “magic bullet” (Zauberkugel)—a compound that could seek out and destroy disease-causing cells without harming normal tissues. This idea laid the intellectual foundation for chemotherapy and, by extension, modern targeted cancer therapy.

Ehrlich’s early experiments on dye-binding and cell receptors also anticipated the later development of monoclonal antibodies and receptor-specific anticancer drugs. By introducing the principles of selectivity, receptor targeting and chemical precision, Ehrlich and Hata’s 1910 discovery became a distant but essential ancestor of treatments that now define breast cancer care.

"This was the first chapter in the history of chemotherapy, later stages being marked by the discovery of prontosil and the brilliantly successful sulpha drugs, including the well-known 'M. & B. 693' which was to save the life of Winston Churchill at a critical point in the Second World War" (PMM).

Book Notes: 8vo. Printed folding table, lithographed plate, 5 half-tone plates. Publisher's printed wrappers.

Provenance: Formerly owned by Max Bircher-Benner, Zurich. Best known for developing Bircher Muesli and coining the term “whole food diet”.

References: GMN 2403, Heirs of Hippocrates 2159; Lilly, p. 259; Osler 1697; Waller 2707.

Die Technik der Radikaloperation

bei

Uterus-Karzinoms

von

Privatdozent Dr. med. Walter Sigwart
Assistent an der Königl. Universitäts-Frauenklinik zu Berlin

Mit 19 Tafeln und 27 Abbildungen im Text.

Wiesbaden.
Verlag von J. F. Bergmann.
1899

Improved on the radical hysterectomy for the treatment of uterine cancer

WALTER SIGWART

Die Technik der Radikaloperationen des Uterus-Karzinoms

Aachen and Weisbaden: Bergmann, 1911.

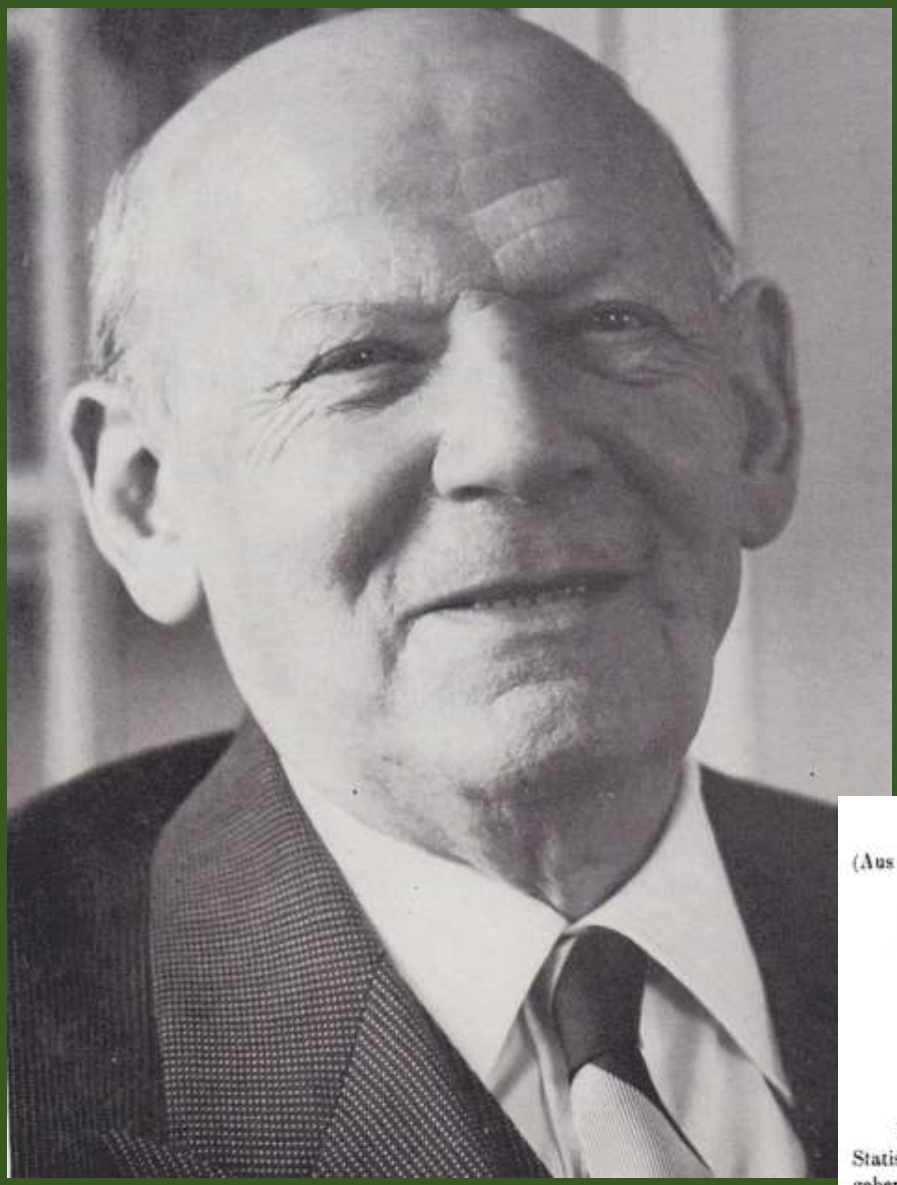
At the time of the publication of this book, Walter Sigwart was a prominent surgeon at the University Women's Clinic in Berlin, working under the mentorship of Ernst Bumm, one of the leading obstetricians of the era. The book is most famous for its extraordinary collection of large-format, hand-colored lithographs that provide a step-by-step anatomical guide to the radical abdominal hysterectomy. It meticulously chronicles the "Bumm-Sigwart" variation of the radical operation, emphasizing the vital importance of anatomical precision and the systematic dissection of pelvic lymph nodes to combat the spread of cervical and uterine cancers.

The importance of this work lies in its role as a transition point between the pioneer phase of radical surgery and its standardization. While the basic principles of the radical hysterectomy were established by Ernst Wertheim just over a decade earlier, Sigwart's text elevated the procedure by focusing on the "surgical field" as a three-dimensional space. His detailed illustrations of the ureter's course and the vascular supply of the pelvis were revolutionary, offering surgeons a visual clarity that previous texts lacked. By documenting successful outcomes and refined techniques for protecting the urinary tract during extensive tissue removal, Sigwart helped move radical surgery from a high-mortality experimental procedure toward a reproducible surgical standard that saved countless women from what was then a certain death sentence.

Sigwart's 1911 treatise laid the groundwork for modern surgical staging and the preservation of pelvic autonomic nerves. His insistence on the total removal of the parametria (the connective tissue adjacent to the uterus) remains a core tenet of radical surgery for cervical cancer today.

Book Notes: 45 pages. Quarto. 36,5 x 28,5 cm. With 3 illustrations in the text and 13 full-page black-and-white plates; Our copy is a former library copy with several institutional stamps and markings.

Provenance: Title page signature indicates prior ownership of a Dr. Max Richter.



XXVII.

(Aus der Königl. chirurg. Universitätsklinik in Berlin. — Director: Geh. Med.-Rath Prof. Dr. A. Bier.)

Beiträge zur Pathologie und Klinik der Mammacarcinome.

Von

Dr. Albert Salomon.

(Hierzu Tafel IX und 25 Textfiguren.)

Die vorliegende Arbeit ist entstanden aus dem Wunsche, eine Statistik der Mammakrebse nach anatomischen Gesichtspunkten zu geben und die Beziehungen zwischen Anatomie und Klinik der Brustkrebse nach einheitlichen Principien zur Darstellung zu bringen. Schon Billroth schreibt in seinem Buche „Ueber die Krankheiten der Brustdrüse" gelegentlich der Besprechung der Mammakrebse, dass auf die anatomische Differenz der Formen bisher gar keine Rücksicht genommen werden konnte, weil sich darüber keine genügend genauen Notizen vorfinden. Auch in den zahlreichen in der Folge erschienenen Publicationen über das Mammacarcinom und seine operative Behandlung finden sich über diesen Punkt im Vergleich zu anderen sehr ausführlich berücksichtigten Momenten, wie über vorangegangene Traumen, Entzündungen, Beziehungen zur Geburt und Erblichkeit, zum Alter usw. meist nur sehr spärliche Angaben. Häufig erfährt man nur, dass die mikroskopische Untersuchung in allen Fällen Krebs ergeben hat und dieselben meist scirrhöser Natur waren. So unterscheidet Henry z. B. nur zwischen weichen und harten Krebsen, von denen die ersteren 95 pCt. der Tumoren ausmachen sollen. Detaillirte Angaben über Heilungsprocente bei verschiedenen Formen des Brustkrebses finden sich in zwei amerikanischen Statistiken von Halstead, sowie von Greenow und Simmons, auch G. B. Schmidt und Finsterer konnten einige Angaben über die Histologie der geheilten Fälle

Archiv für klin. Chirurgie. Bd. 101. Heft 3. 38

Photograph of Microcalcifications in breast tissue

First to show how an X-ray can tell breast cancer vs. non-cancer via microcalcifications, setting up the potential for a mammogram.

ALBERT SALOMON (1883 - 1976)

Beiträge zur Pathologie und Klinik der Mammacarcinome

Archiv für Klinische Chirurgie 101, 573-663, Berlin, Verlag von August Hirschwald, 1913.

Albert Salomon was a German surgeon and pathologist who made the first systematic study of x-ray imaging of the breast, laying the foundation for modern mammography.

In 1913, while working at the University of Berlin, Salomon examined over 3,000 mastectomy specimens using x-rays to correlate radiographic findings with histologic features of breast tumors. He demonstrated that malignant tumors produced distinctive calcifications and irregular densities on x-ray films, distinguishing them from benign lesions. This pioneering correlation between radiology and pathology showed that breast cancer could be identified through non-invasive imaging, decades before clinical mammography became a diagnostic standard.

However, Salomon never linked this new method to the idea of trying to find breast cancer in healthy women.

Although Salomon's work was largely forgotten for years—due partly to the upheavals of World War I and II—his 1913 monograph, *Beiträge zur Pathologie und Klinik der Mammakarzinome*, became a cornerstone of mammographic science once rediscovered in the mid-20th century. Later researchers such as Stafford L. Warren, Raúl Leborgne and Robert Egan built on Salomon's insights, developing clinical mammography for cancer screening in the 1930s–1950s. Salomon is now recognized as the founding figure of mammography, having been the first to prove that breast x-rays could reveal the internal morphology of cancer and thus transform both diagnosis and early detection.

Book Notes: 8°, (2), pp. 573-668, 25 text figures and 1 color plate, fine half-linen binding.

References: GMN 13264, Lukong (2017), Picard, JD (1998). "History of Mammography". Bulletin de l'Académie Nationale de Médecine. 182 (8): 1613-1620.

DIAGNOSIS OF UTERINE CANCER BY THE VAGINAL SMEAR

GEORGE N. PAPANICOLAOU, M.D., Ph.D.
Department of Anatomy, Cornell University Medical College

AND

HERBERT F. TRAUT, M.D.
Department of Obstetrics and Gynecology, Cornell University Medical College and the New York Hospital

NEW YORK: THE COMMONWEALTH FUND
1943

Now Published by
HARVARD UNIVERSITY PRESS
Cambridge, Massachusetts

PLATE B

The birth of the Pap Smear. Before this monograph, cervical cancer was the leading cause of cancer death in women.

GEORGE PAPANICOLAOU (1883 - 1962)

Diagnosis of Uterine Cancer by the Vaginal Smear

Cambridge: Harvard University Press, 1943.

George Papanicolaou

This monograph is one of the most important and impactful publications in the history of women's health.

Before this monograph, cervical cancer was the leading cause of cancer death in women, primarily because it was often detected only after reaching an advanced, incurable stage. Cervical cancer was also a top five killer of women overall.

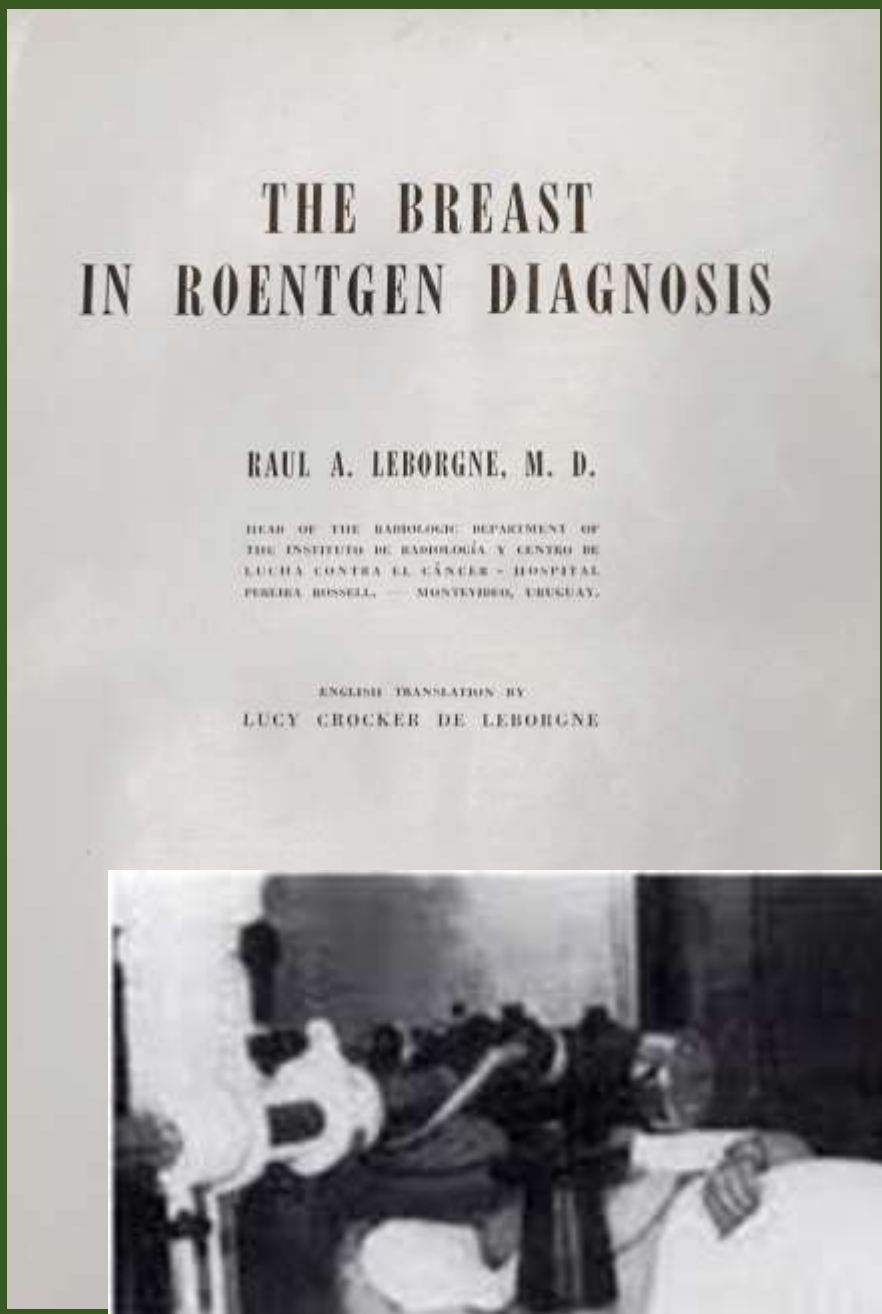
The mechanics of the "Pap Smear" were rooted in Papanicolaou's earlier research on the estrous cycle of guinea pigs, where he discovered that vaginal secretions contained "exfoliated" cells that mirrored the physiological state of the reproductive organs. He realized that the same principle applied to humans: the cervix and uterus naturally shed cells into the vaginal vault. By collecting these cells with a simple pipette or swab, spreading them on a slide, and applying a specialized polychromatic stain (the "Pap stain"), clinicians could observe microscopic nuclear changes—such as enlargement, irregularity, and hyperchromatism—that signaled the presence of cancer even before a physical tumor was visible to the naked eye.

This work led to the first successful mass-screening program for any cancer. In the decades following its adoption, the incidence and mortality rates of cervical cancer in developed nations dropped by over 70%.

This success paved the way for the modern field of diagnostic cytology and the development of subsequent screening technologies for other organ systems. Papanicolaou's work remains the "gold standard" example of how basic biological research into animal cycles can yield a life-saving clinical application that defines a century of public health.

Many millions of lives have been saved by this innovation. Despite the success of the test, cervical cancer still claimed approximately 350,000 lives globally in 2022. Over 90% of these deaths currently occur in low- and middle-income countries where access to regular Pap smears or modern high-performance tests is limited.

References: O'Dowd and Philipp p. 547; Speert p. 256.



THE BREAST
IN ROENTGEN DIAGNOSIS

RAUL A. LEBORGNE, M. D.

HEAD OF THE RADIOLOGIC DEPARTMENT OF THE INSTITUTO DE RADIOLOGÍA Y CENTRO DE LUCHA CONTRA EL CÁNCER - HOSPITAL PEREIRA ROSSELL, — MONTEVIDEO, URUGUAY.

ENGLISH TRANSLATION BY
LUCY CROCKER DE LEBORGNE

An early patient getting one of the first mammograms in history.

Created first practical approach to mammography – a technology that would save millions of lives

RAÚL ALFREDO LEBORGNE (1907 - 1986)

The Breast in Roentgen Diagnosis

Impresora Uruguaya S.A.; Constable, 1953.

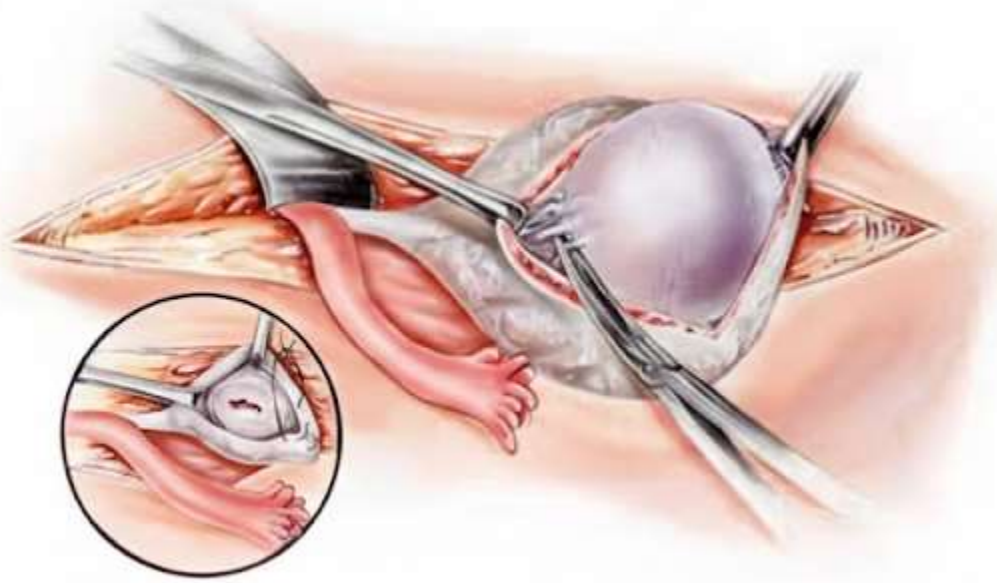
Raúl Alfredo Leborgne

Discovered in 1895, x-rays were all the rage in the early 1900s, dramatically illuminating the insides of the human body, showing bones in detail. There were even attempts to use x-ray machines to find cancer in breasts. Breast cancer certainly deserved attention, since it was and is one of the most common cancers, but differentiating soft tissue in the first x-ray machines was problematic. In 1930 Stafford Warren, a radiologist from New York, performed a study indicating x-rays might perform better than doctors at finding breast cancer, but his published article didn't excite too many and progress remained slow, with small advances occurring in fits and halts. The potential to use x-rays to find breast cancer was apparent. If cancer could be found before it spreads, it could more easily be treated and irradicated.

Raul Leborgne vitalized mammography with a key publication in 1951. He was a radiologist from Uruguay and one of his insights still makes patients cringe yet was crucial to the development of mammograms. Leborgne devised an apparatus that would squeeze a patient's breast between a cone and a compression pad to hold it flat while an x-ray was taken. He introduced this technique in 1949 and reported his findings in a landmark publication in 1951. This compression enhanced the quality of the images. Using it, he was better able to see small structures and use spot/magnification.

He was the first to report the significance of radiographically detectable microcalcifications, “which may be seen in extensive as well as incipient lesions.” Finding them in 30% of cancers, Leborgne gave radiologists something more to look for. His methods set the stage for our current techniques and for improved detection and diagnosis. Mammography became routine in the 1970s and has continued to improve. Since 1990 it has helped reduce breast cancer mortality 40%. (Science Heroes).

References: Lukong (2017).



Griffiths Reinvigorated the Idea of Ovarian Cancer Debulking Surgery

Validated debulking surgery for ovarian cancer by showing that smaller residual tumor volume predicts improved survival

C. THOMAS GRIFFITHS (1931 – 2002)

Surgical resection of tumor bulk in the primary treatment of ovarian carcinoma

NCI Monograph 42, 1976, 101-104.

C. Thomas Griffiths trained under Joe Meigs at the Massachusetts General Hospital in Boston. He spent much of his career as a professor and clinician at the Harvard Medical School and the Dana-Farber Cancer Institute, where he championed the integration of aggressive surgery with emerging chemotherapy regimens.

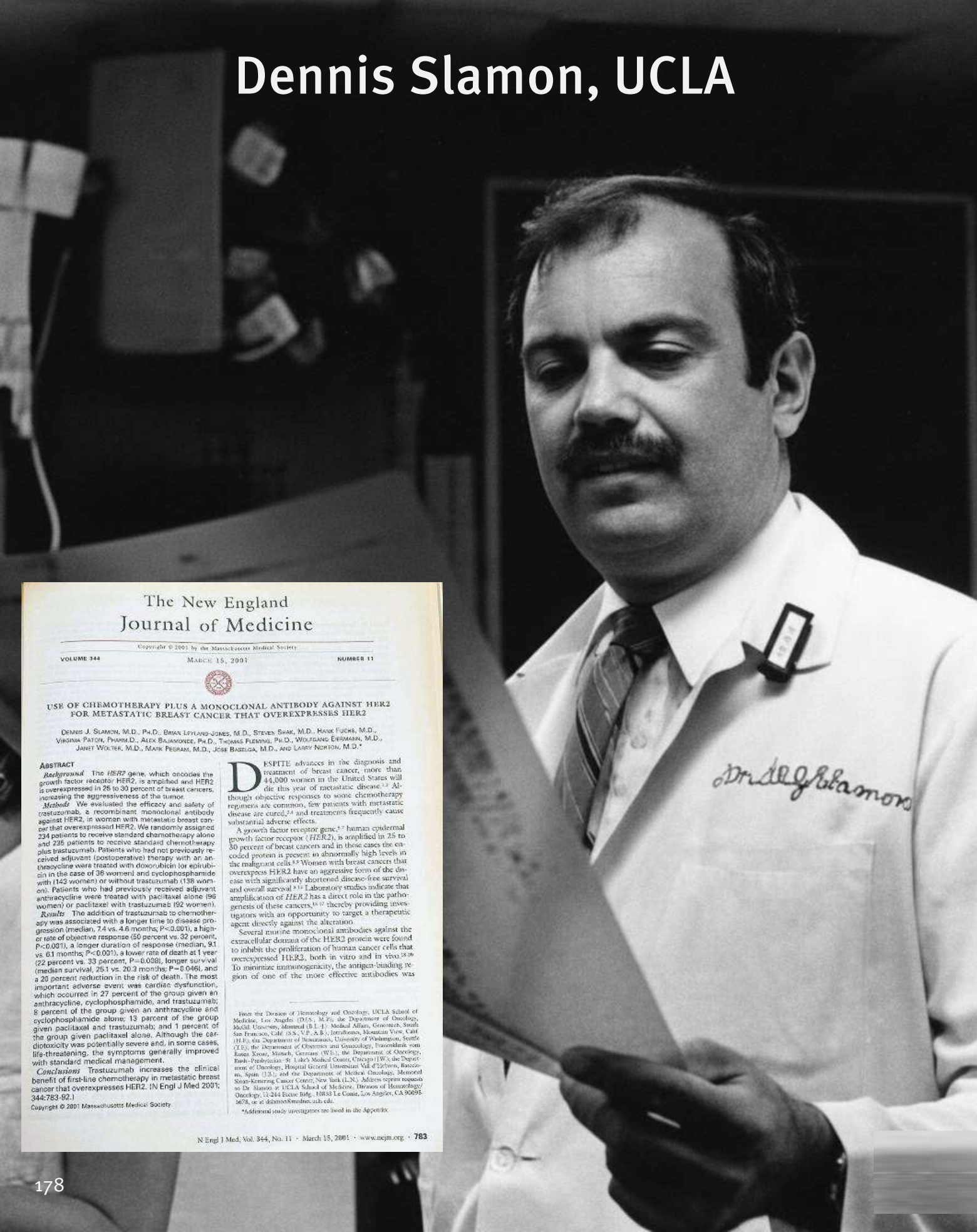
This paper provided the first quantitative evidence that the size of residual tumor left after surgery is the main determinant of survival. Prior to Griffiths, the standard of care for advanced ovarian cancer was often limited to a simple biopsy or conservative surgery, as many surgeons believed that removing only a portion of a disseminated tumor was futile. While Dr. Joe V. Meigs had conceptualized the idea of "debulking" as early as 1934, the practice lacked proof and was largely ignored for forty years. Griffiths used a then-novel regression analysis to study 102 patients with advanced disease, showing that survival was directly related to the maximum diameter of residual tumor masses. He demonstrated that survival was uniformly poor if the largest remaining tumor exceeded 1.5 cm in diameter, regardless of the total amount removed.

This paper moved ovarian cancer treatment from a passive diagnostic approach to an aggressive surgical specialty. It provided a biological rationale for surgery: reducing tumor bulk increases the number of rapidly dividing cells, which are more susceptible to chemotherapy, and improves drug delivery to smaller, well-perfused implants.

This "debulking" strategy remains the cornerstone of ovarian cancer treatment today, though the definition of "optimal" has since been refined from Griffiths' 1.5 cm down to 1 cm or, ideally, no visible residual disease. Modern innovations, such as neoadjuvant chemotherapy with robotic-assisted cytoreduction, continue to build on Griffith's ideas.

References: Schorge JO et al., "Meigs to modern times: The evolution of debulking surgery in advanced ovarian cancer." *Gynecologic Oncology*, June 2018; 149(3):447-454.

Dennis Slamon, UCLA



The New England
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VOLUME 344 MARCH 15, 2001 NUMBER 11

USE OF CHEMOTHERAPY PLUS A MONOCLONAL ANTIBODY AGAINST HER2 FOR METASTATIC BREAST CANCER THAT OVEREXPRESSES HER2

DENNIS J. SLAMON, M.D., PH.D., BRIAN LEYLAND-JONES, M.D., STEVEN SHAK, M.D., HANK FUCHS, M.D., VIRGINIA PATON, PHARM.D., ALEX BAJAMONDE, PH.D., THOMAS FLEMING, PH.D., WOLFGANG EIERMANN, M.D., JANET WOLTER, M.D., MARK PEGRAM, M.D., JOSE BASELGA, M.D., AND LARRY NORTON, M.D.*

ABSTRACT

Background The *HER2* gene, which encodes the growth factor receptor HER2, is amplified and HER2 is overexpressed in 25 to 30 percent of breast cancers, increasing the aggressiveness of the tumor.

Methods We evaluated the efficacy and safety of trastuzumab, a recombinant monoclonal antibody against HER2, in women with metastatic breast cancer that overexpressed HER2. We randomly assigned 234 patients to receive standard chemotherapy alone and 235 patients to receive standard chemotherapy plus trastuzumab. Patients who had not previously received adjuvant (postoperative) therapy with an anthracycline were treated with doxorubicin (or epirubicin in the case of 36 women) and cyclophosphamide with (143 women) or without trastuzumab (138 women). Patients who had previously received adjuvant anthracycline were treated with paclitaxel alone (96 women) or paclitaxel with trastuzumab (92 women).

Results The addition of trastuzumab to chemotherapy was associated with a longer time to disease progression (median, 7.4 vs. 4.6 months; P<0.001), a higher rate of objective response (50 percent vs. 32 percent, P<0.001), a longer duration of response (median, 9.1 vs. 6.1 months; P<0.001), a lower rate of death at 1 year (22 percent vs. 33 percent, P=0.008), longer survival (median survival, 25.1 vs. 20.3 months; P=0.046), and a 20 percent reduction in the risk of death. The most important adverse event was cardiac dysfunction, which occurred in 27 percent of the group given an anthracycline, cyclophosphamide, and trastuzumab; 8 percent of the group given an anthracycline and cyclophosphamide alone; 13 percent of the group given paclitaxel and trastuzumab; and 1 percent of the group given paclitaxel alone. Although the cardiotoxicity was potentially severe and, in some cases, life-threatening, the symptoms generally improved with standard medical management.

Conclusions Trastuzumab increases the clinical benefit of first-line chemotherapy in metastatic breast cancer that overexpresses HER2. (N Engl J Med 2001; 344:783-92.)

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DESPITE advances in the diagnosis and treatment of breast cancer, more than 44,000 women in the United States will die this year of metastatic disease.[1,2] Although objective responses to some chemotherapy regimens are common, few patients with metastatic disease are cured,[3,4] and treatments frequently cause substantial adverse effects.

A growth factor receptor gene,[5-7] human epidermal growth factor receptor 2 (*HER2*), is amplified in 25 to 30 percent of breast cancers and in these cases the encoded protein is present in abnormally high levels in the malignant cells.[8,9] Women with breast cancers that overexpress HER2 have an aggressive form of the disease with significantly shortened disease-free survival and overall survival.[8-10] Laboratory studies indicate that amplification of *HER2* has a direct role in the pathogenesis of these cancers,[11-17] thereby providing investigators with an opportunity to target a therapeutic agent directly against the alteration.

Several murine monoclonal antibodies against the extracellular domain of the HER2 protein were found to inhibit the proliferation of human cancer cells that overexpressed HER2, both in vitro and in vivo.[18-20] To minimize immunogenicity, the antigen-binding region of one of the more effective antibodies was

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*Additional study investigators are listed in the Appendix.

Discovered role of HER2 in breast cancer and fought to get Herceptin to the market

DENNIS SLAMON (1942 - PRESENT)

Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2

New England Journal of Medicine, Volume 384 March 15, 2001 (with co-authors).

Dennis J. Slamon transformed the treatment of breast cancer through the discovery and clinical validation of HER2 (human epidermal growth factor receptor 2) as a therapeutic target. Slamon and his team at UCLA in the 1980s identified that amplification of the HER2/neu gene occurred in approximately 20–30% of breast cancers and was associated with aggressive tumor behavior and poor prognosis. This insight led to the development of trastuzumab (Herceptin), a monoclonal antibody designed to block HER2 signaling. Despite skepticism and funding challenges, Slamon's persistence culminated in a new biologically targeted therapy that marked a paradigm shift—from nonspecific cytotoxic chemotherapy to precision oncology based on molecular profiling. Other key contributors included Virginia Paton, Jose Baselga and Larry Norton.

In his 2001 New England Journal of Medicine paper, Slamon and colleagues reported the results of a randomized clinical trial showing that adding trastuzumab to standard chemotherapy significantly improved overall survival and time to disease progression in women with metastatic HER2-positive breast cancer. The study demonstrated that Herceptin reduced the risk of death by about one-third and produced durable responses even in advanced disease. These findings validated HER2 as a critical oncogenic driver and established trastuzumab as the first successful targeted therapy for solid tumors. Slamon's work not only revolutionized the management of HER2-positive breast cancer but also opened the door for subsequent generations of targeted and antibody-based treatments, profoundly influencing the trajectory of modern cancer therapy.

References: ASCO Foundation (2025), Ekmektzoglou (2009), Lukong (2017), Sanli (2022).

Harald zur Hausen, Received the Nobel Prize for Medicine in 2008, for Linking HPV to Cervical Cancer

Source: *Miguel Villagran / Getty Images*

First paper to suggest that cervical cancer was caused by Human Papilloma Virus Rather than Herpes Viruses

HARALD ZUR HAUSEN (1937 - 2023)

Condylomata Acuminata and Human Genital Cancer

Cancer Research 36 p. 794, Feb 1976.

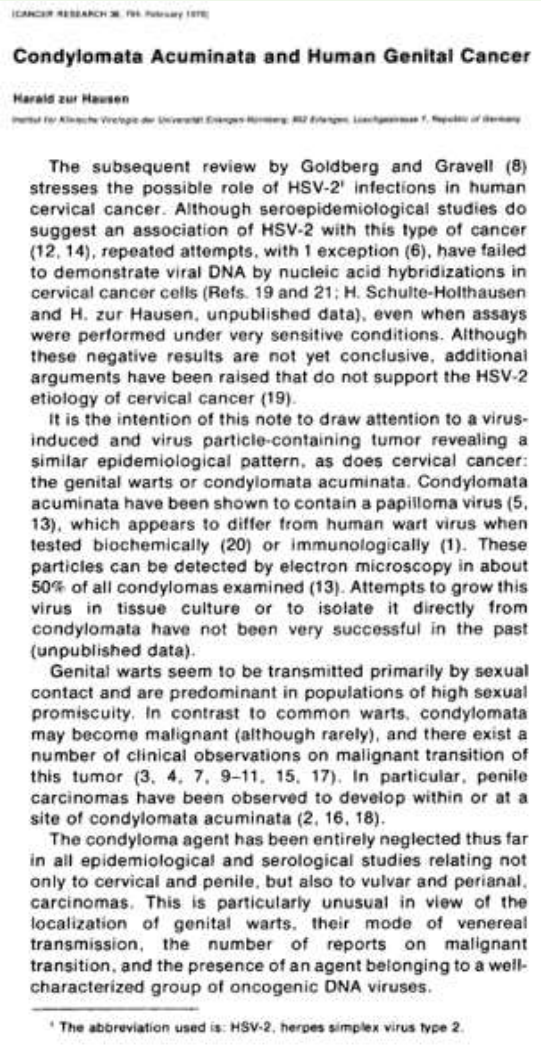
Harald zur Hausen's 1976 paper published in *Cancer Research* hypothesized that HPV was the cause of cervical cancer for the first time. In the article, zur Hausen directly challenged the then-dominant scientific consensus that Herpes Simplex Virus Type 2 (HSV-2) caused cervical cancer.

He described his repeated failure to detect HSV-2 DNA in cervical tumor samples and instead drew attention to medical reports of genital warts (*condylomata acuminata*)—known to be caused by HPV—progressing to malignancy. He proposed that if analyzed with the right techniques, these tumors would be found to harbor integrated viral genetic information. The paper wasn't long. Shown at right in its entirety, the publication had only four paragraphs.

Harald zur Hausen was a German physician-virologist with a background in identifying infectious causes of human cancers. He received his medical degree in 1960. By 1972, he had become the chairman of clinical virology at the University of Erlangen-Nuremberg, where he shifted his focus toward cervical cancer etiology.

The implications of this 1976 hypothesis were transformative for global health. While initially met with skepticism by a scientific community favoring the herpes theory, the paper set zur Hausen and his team on a decade-long search that eventually led to the isolation of HPV 16 (in 1983) and HPV 18 (in 1984) from cervical cancer biopsies. These findings provided the necessary evidence for virus-cancer causality, eventually leading to the development of prophylactic HPV vaccines approved in 2006.

For this groundbreaking work, zur Hausen was awarded the Nobel Prize in Physiology or Medicine in 2008.



Condylomata Acuminata and Human Genital Cancer

Harald zur Hausen

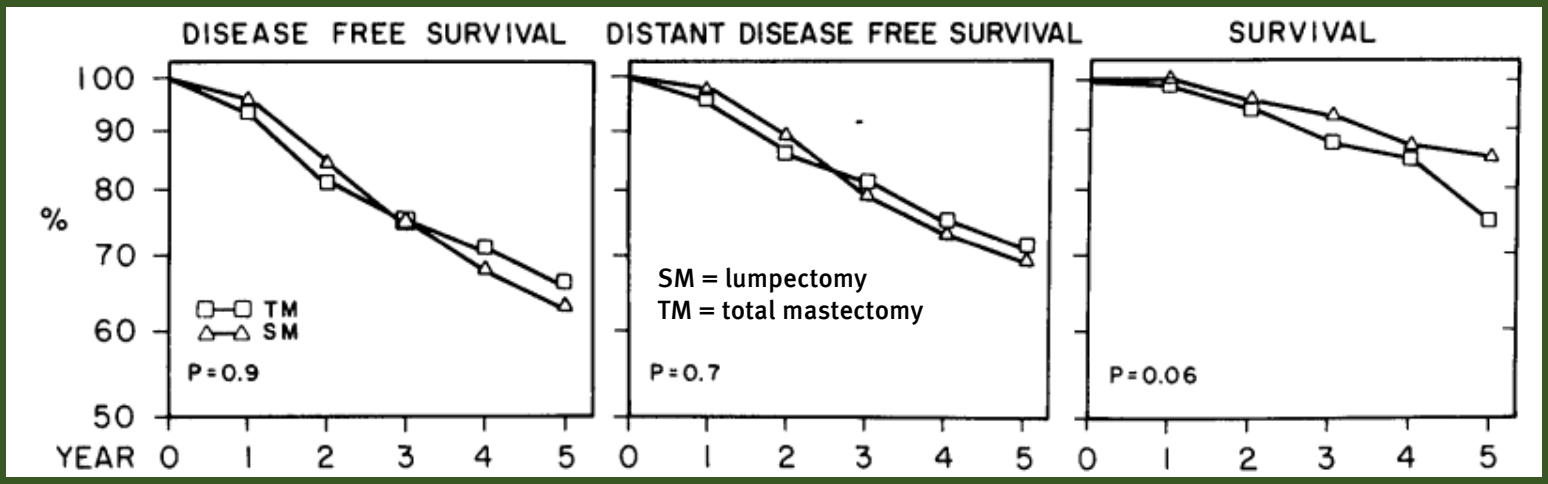
The subsequent review by Goldberg and Gravell (8) stresses the possible role of HSV-2[1] infections in human cervical cancer. Although seroepidemiological studies do suggest an association of HSV-2 with this type of cancer (12, 14), repeated attempts, with 1 exception (6), have failed to demonstrate viral DNA by nucleic acid hybridizations in cervical cancer cells (Refs. 19 and 21; H. Schulte-Holthausen and H. zur Hausen, unpublished data), even when assays were performed under very sensitive conditions. Although these negative results are not yet conclusive, additional arguments have been raised that do not support the HSV-2 etiology of cervical cancer (19).

It is the intention of this note to draw attention to a virus-induced and virus particle-containing tumor revealing a similar epidemiological pattern, as does cervical cancer: the genital warts or condylomata acuminata. Condylomata acuminata have been shown to contain a papilloma virus (5, 13), which appears to differ from human wart virus when tested biochemically (20) or immunologically (1). These particles can be detected by electron microscopy in about 50% of all condylomas examined (13). Attempts to grow this virus in tissue culture or to isolate it directly from condylomata have not been very successful in the past (unpublished data).

Genital warts seem to be transmitted primarily by sexual contact and are predominant in populations of high sexual promiscuity. In contrast to common warts, condylomata may become malignant (although rarely), and there exist a number of clinical observations on malignant transition of this tumor (3, 4, 7, 9–11, 15, 17). In particular, penile carcinomas have been observed to develop within or at a site of condylomata acuminata (2, 16, 18).

The condyloma agent has been entirely neglected thus far in all epidemiological and serological studies relating not only to cervical and penile, but also to vulvar and perianal, carcinomas. This is particularly unusual in view of the localization of genital warts, their mode of venereal transmission, the number of reports on malignant transition, and the presence of an agent belonging to a well-characterized group of oncogenic DNA viruses.

[1] The abbreviation used is: HSV-2, herpes simplex virus type 2.



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Volume 312 MARCH 14, 1985 Number 11

FIVE-YEAR RESULTS OF A RANDOMIZED CLINICAL TRIAL COMPARING TOTAL MASTECTOMY AND SEGMENTAL MASTECTOMY WITH OR WITHOUT RADIATION IN THE TREATMENT OF BREAST CANCER

Bernard Fisher, M.D., Madeline Bauer, Ph.D., Richard Margolese, M.D., Roger Poisson, M.D., Yosef Pilch, M.D., Carol Redmond, Sc.D., Edwin Fisher, M.D., Norman Wolmark, M.D., Melvin Deutsch, M.D., Eleanor Montague, M.D., Elizabeth Saffer, B.A., Lawrence Wickerham, M.D., Harvey Lerner, M.D., Andrew Glass, M.D., Henry Shibata, M.D., Peter Deckers, M.D., Alfred Ketcham, M.D., Robert Oishi, M.D., and Ian Russell, M.D.

Abstract In 1976 we began a randomized trial to evaluate breast conservation by a segmental mastectomy in the treatment of Stage I and II breast tumors ≤4 cm in size. The operation removes only sufficient tissue to ensure that margins of resected specimens are free of tumor. Women were randomly assigned to total mastectomy, segmental mastectomy alone, or segmental mastectomy followed by breast irradiation. All patients had axillary dissections, and patients with positive nodes received chemotherapy.

Life-table estimates based on data from 1843 women indicated that treatment by segmental mastectomy, with or without breast irradiation, resulted in disease-free, distant-disease–free, and overall survival at five years that was no worse than that after total breast removal. In fact, disease-free survival after segmental mastectomy plus radiation was better than disease-free survival after total mastectomy ($P = 0.04$), and overall survival after segmental mastectomy, with or without radiation, was better than overall survival after total mastectomy ($P = 0.07$, and 0.06, respectively). A total of 92.3 per cent of women treated with radiation remained free of breast tumor at five years, as compared with 72.1 per cent of those receiving no radiation ($P<0.001$). Among patients with positive nodes 97.9 per cent of women treated with radiation and 63.8 per cent of those receiving no radiation remained tumor-free ($P<0.001$), although both groups received chemotherapy.

We conclude that segmental mastectomy, followed by breast irradiation in all patients and adjuvant chemotherapy in women with positive nodes, is appropriate therapy for Stage I and II breast tumors ≤4 cm, provided that margins of resected specimens are free of tumor. (N Engl J Med 1985; 312:665-73.)

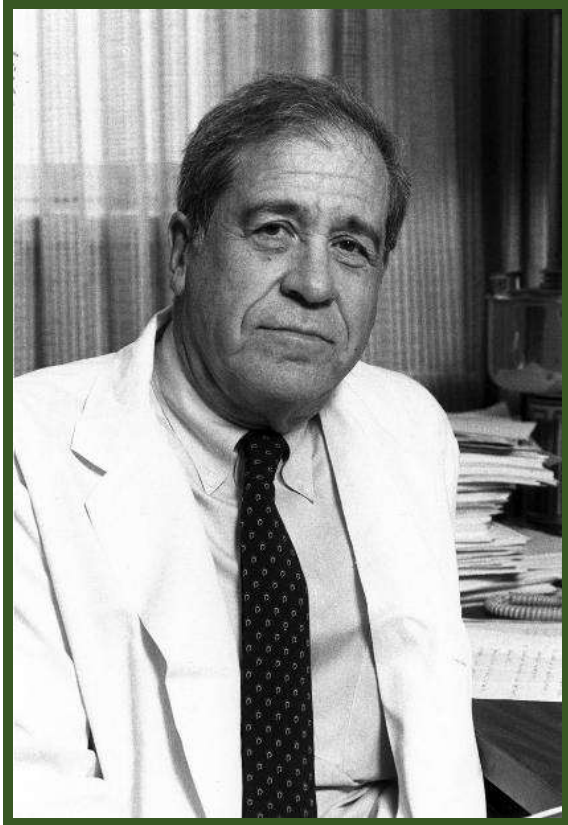
ANECDOTAL information has been presented by the pioneers[1-6] and more recent proponents[7-11] of breast preservation for the management of primary breast cancer. Although they have not clearly determined the relative merits of such a therapeutic approach by comparing it directly with more conventional methods of management, those observers have demonstrated that patients could survive free of disease after limited surgery and radiation therapy. The rationale that was employed to justify the use of the regimen is obscure. There was no biologic principle that directed the endeavor. In many instances the procedure was performed because patients refused a recommended radical mastectomy.[2] Thus, despite early and more recent efforts, important issues remain that preclude the universal acceptance and use of a more conservative approach to breast-cancer management.

From the National Surgical Adjuvant Breast Project Headquarters, Room 914 Scaife Hall, 3550 Terrace St., Pittsburgh, PA 15261, where reprint requests should be addressed to Dr. Bernard Fisher. (See Appendix I for a list of participating institutions and principal investigators.)

Supported by Public Health Service Grants from the National Cancer Institute (NCI-U10-CA-12027 and NCI-U10-CA-34211) and by a grant from the American Cancer Society (ACS-RC-13).

Even the few clinical trials that have evaluated breast conservation[12-15] have failed to establish definitively the worth of such therapy.

Our findings in a previous clinical trial (Protocol B-04) indicated that patients treated by total mastectomy without axillary-node dissection and pectoral-muscle removal were at no higher risk of distant disease or death than were those undergoing a Halsted radical mastectomy.[16] In view of these findings and because of the increasing practice of breast conservation despite the paucity of information available from clinical trials to determine its efficacy, we began a new study (Protocol B-06) in 1976 to evaluate the worth of local tumor excision with or without radiation therapy. The operation employed, a segmental mastectomy, completely abandoned conventional concepts of cancer surgery, removing only enough breast tissue to ensure that the margins of the resected surgical specimen were free of tumor. The study was designed to determine (1) the effectiveness of segmental mastectomy for breast preservation, (2) whether radiation therapy reduces the incidence of tumor in the ipsilateral breast after segmental mastectomy, (3) whether breast



Showed unambiguously that lumpectomy for breast cancer followed by radiation did not have worse outcomes than radical mastectomy

BERNARD FISHER (1918 - 2019)

Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer

***New England Journal of Medicine*, 347:1233–1241, 2002.**

In this 2002 *New England Journal of Medicine* paper, Bernie Fisher and colleagues from the National Surgical Adjuvant Breast and Bowel Project (NSABP B-06 trial) reported the twenty-year outcomes of a randomized clinical study comparing three surgical approaches for breast cancer.

The study enrolled over 1,800 women with stage I or II invasive breast cancer and randomly assigned them to one of three treatment groups: total mastectomy, lumpectomy alone, or lumpectomy followed by radiation therapy. After two decades of follow-up, Fisher and colleagues found no significant difference in overall survival or disease-free survival among the three groups. Women who underwent lumpectomy plus irradiation had slightly lower local recurrence rates than those treated with lumpectomy alone, but survival outcomes were equivalent to those of total mastectomy.

This long-term analysis confirmed that breast-conserving surgery combined with radiation is as effective as mastectomy in treating early-stage breast cancer, fundamentally changing surgical oncology and patient care.

The oncology journal and website *OncLive* described Bernie Fisher's research as "launching the breast cancer community into the modern era" and honored him with a Giants of Cancer Care award for his work that ultimately ended the standard practice of performing the Halsted radical mastectomy, a treatment that had been in place for more than 75 years. Fisher also received a Lasker award in 1985. Thanks to Fisher, notes another major oncology journal, breast-cancer survival rates have improved worldwide.

References: Ben-Dror (2022), Lukong (2017), Olson (2002), Sanli (2022).

Nubia Calero Munoz is a researcher in Columbia who overcame humble beginnings to become a world leader in identifying human papillomavirus (HPV) as the cause of cervical cancer, leading to vaccines like Gardasil®.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Epidemiologic Classification of Human Papillomavirus Types Associated with Cervical Cancer

Nubia Muñoz, M.D., F. Xavier Bosch, M.D., Silvia de Sanjosé, M.D., Rolando Herrero, M.D., Xavier Castellsagué, M.D., Keerti V. Shah, Ph.D., Peter J.F. Snijders, Ph.D., and Chris J.L.M. Meijer, M.D., for the International Agency for Research on Cancer Multicenter Cervical Cancer Study Group*

ABSTRACT

BACKGROUND
Infection with human papilloma virus (HPV) is the main cause of cervical cancer, but the risk associated with the various HPV types has not been adequately assessed.

METHODS
We pooled data from 11 case–control studies from nine countries involving 1918 women with histologically confirmed squamous-cell cervical cancer and 1928 control women. A common protocol and questionnaire were used. Information on risk factors was obtained by personal interviews, and cervical cells were collected for detection of HPV DNA and typing in a central laboratory by polymerase-chain-reaction–based assays (with MY09/MY11 and GP5+/6+ primers).

RESULTS
HPV DNA was detected in 1739 of the 1918 patients with cervical cancer (90.7 percent) and in 259 of the 1928 control women (13.4 percent). With the GP5+/6+ primer, HPV DNA was detected in 96.6 percent of the patients and 15.6 percent of the controls. The most common HPV types in patients, in descending order of frequency, were types 16, 18, 45, 31, 33, 52, 58, and 35. Among control women, types 16, 18, 45, 31, 6, 58, 35, and 33 were the most common. For studies using the GP5+/6+ primer, the pooled odds ratio for cervical cancer associated with the presence of any HPV was 158.2 (95 percent confidence interval, 113.4 to 220.6). The odds ratios were over 45 for the most common and least common HPV types. Fifteen HPV types were classified as high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82); 3 were classified as probable high-risk types (26, 53, and 66); and 12 were classified as low-risk types (6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, and CP6108). There was good agreement between our epidemiologic classification and the classification based on phylogenetic grouping.

CONCLUSIONS
In addition to HPV types 16 and 18, types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 should be considered carcinogenic, or high-risk, types, and types 26, 53, and 66 should be considered probably carcinogenic.

The key contribution of this paper was not to show that HPV is associated with cervical cancer.

This had already been shown before in work by Harald zur Hausen in the 1970s and 1980s

Rather, the contribution was to show that a relatively narrow set of HPV types were responsible for cancer. This meant that a vaccine was feasible. The information from this trial was rapidly used to create the first cervical cancer prevention vaccine Gardasil.

Dr. Munoz was nominated for the Nobel Prize for her work that led up to Gardasil – a vaccine that has saved or will save the lives of millions of women.

90% of Cervical Cancer Associated with HPV DNA. But certain types of HPV are much more likely to be associated with the cancer

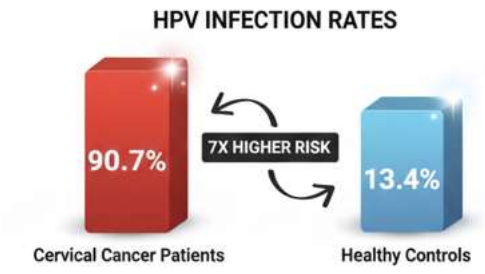
NUBIA CALERO MUNOZ (1940 – PRESENT) AND COLLEAGUES

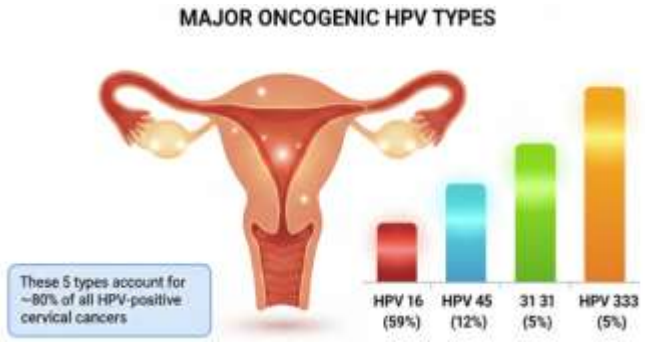
Epidemiologic classification of human papillomavirus types associated with cervical cancer

New England Journal of Medicine, Feb 6, 2003, Volume 384

The 2003 study by Muñoz et al., published in The New England Journal of Medicine, presents a comprehensive epidemiologic classification of human papillomavirus (HPV) types based on their association with cervical cancer. Researchers pooled data from 11 case-control studies across nine countries, analyzing 1,918 women with histologically confirmed squamous-cell cervical cancer and 1,928 control women. Using polymerase-chain-reaction (PCR)-based assays to detect and type HPV DNA, the study aimed to establish clear-cut criteria for identifying high-risk and low-risk HPV types, providing essential data for screening programs and vaccine development.

The results revealed that HPV DNA was present in 90.7% of cervical cancer patients compared to only 13.4% of control subjects4. In studies using the most sensitive primers ($GP5+/6+$), the pooled odds ratio for cervical cancer associated with any HPV infection was 158.25. The most common types found in cancer patients, in descending order of frequency, were HPV 16, 18, 45, 31, 33, 52, 58, and 35. Notably, HPV 16 alone was the most prevalent type globally, detected in 58.9% of cancer cases7. The study also found that the risk of cancer did not significantly increase with multiple HPV infections compared to a single infection.





Based on these findings, the authors classified 15 HPV types as high-risk (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82), three as probable high-risk (26, 53, and 66), and 12 as low-risk (6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, and CP6108). This epidemiologic classification showed remarkable concordance with existing phylogenetic groupings. The researchers concluded that since eight specific HPV types account for 95% of HPV-positive cervical cancer cases, a vaccine targeting the most common types could potentially prevent the vast majority of cervical cancers worldwide.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 10, 2007 VOL. 356 NO. 19

Quadrivalent Vaccine against Human Papillomavirus to Prevent High-Grade Cervical Lesions

The FUTURE II Study Group*

ABSTRACT

BACKGROUND

Human papillomavirus types 16 (HPV-16) and 18 (HPV-18) cause approximately 70% of cervical cancers worldwide. A phase 3 trial was conducted to evaluate a quadrivalent vaccine against HPV types 6, 11, 16, and 18 (HPV-6/11/16/18) for the prevention of high-grade cervical lesions associated with HPV-16 and HPV-18.

METHODS

In this randomized, double-blind trial, we assigned 12,167 women between the ages of 15 and 26 years to receive three doses of either HPV-6/11/16/18 vaccine or placebo, administered at day 1, month 2, and month 6. The primary analysis was performed for a per-protocol susceptible population that included 5305 women in the vaccine group and 5260 in the placebo group who had no virologic evidence of infection with HPV-16 or HPV-18 through 1 month after the third dose (month 7). The primary composite end point was cervical intraepithelial neoplasia grade 2 or 3, adenocarcinoma in situ, or cervical cancer related to HPV-16 or HPV-18.

RESULTS

Subjects were followed for an average of 3 years after receiving the first dose of vaccine or placebo. Vaccine efficacy for the prevention of the primary composite end point was 98% (95.89% confidence interval [CI], 86 to 100) in the per-protocol susceptible population and 44% (95% CI, 26 to 58) in an intention-to-treat population of all women who had undergone randomization (those with or without previous infection). The estimated vaccine efficacy against all high-grade cervical lesions, regardless of causal HPV type, in this intention-to-treat population was 17% (95% CI, 1 to 31).

CONCLUSIONS

In young women who had not been previously infected with HPV-16 or HPV-18, those in the vaccine group had a significantly lower occurrence of high-grade cervical intraepithelial neoplasia related to HPV-16 or HPV-18 than did those in the placebo group. (ClinicalTrials.gov number, NCT00092534.)

Address reprint requests to Dr. Laura A. Koutsky at the Department of Epidemiology, University of Washington, Box 359933, Lake Union Place, Suite 300, 1914 N. 34th St., Seattle, WA 98103, or at kouts@u.washington.edu.

*Members of the Females United to Unilaterally Reduce Endo/Ectocervical Disease (FUTURE) II Study Group, who vouch for the completeness and accuracy of the data, are listed in the Appendix, along with other study participants.

N Engl J Med 2007;356:1915-27.

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Definitive clinical trial evidence showed that Gardasil (a vaccine against HPV) saves lives

FUTURE II STUDY GROUP

Quadrivalent Vaccine against Human Papillomavirus to Prevent High-Grade Cervical Lesions

New England Journal of Medicine, 356:1915–1927, 2007.

This 2007 paper discussed a landmark Phase III clinical trial that definitively established the efficacy of the quadrivalent HPV vaccine (Gardasil) in preventing cervical cancer. In a randomized, double-blind study involving over 12,000 women aged 15 to 26, researchers found that the vaccine was 98% effective in preventing high-grade cervical intraepithelial neoplasia (CIN grade 2 or 3) and adenocarcinoma in situ associated with HPV types 16 and 18 among women who had not yet been exposed to the virus. Crucially, the study also noted that the efficacy dropped significantly (to roughly 44%) in the "intention-to-treat" population—which included women who were already infected—thereby providing the critical scientific evidence that vaccination works best prior to sexual debut.

The original Gardasil (quadrivalent) was approved by the U.S. FDA on June 8, 2006. Gardasil 9 was approved by the FDA in December 2014. Approximately 35 million doses are administered each year.

Gardasil (and other HPV vaccines) has fundamentally altered the landscape of women's health, making cervical cancer a preventable disease. The vaccine has changed the day-to-day medical reality for millions of women by reducing invasive procedures and anxiety.

A recent large Swedish study found an 88% reduction in cervical cancer risk for girls vaccinated before age 17. Crucially, it showed that even women vaccinated later (up to age 30) saw a significant benefit (53% reduction), debunking the myth that the vaccine is useless if you are already sexually active.

Modeling studies incorporating real-world vaccine effectiveness estimate that tens of millions of cervical cancer cases and several million deaths will be averted globally by the end of the 21st century if current HPV vaccination programs are sustained and expanded. Even under conservative assumptions, the WHO estimates that HPV vaccination alone could prevent over 300,000 deaths per year once vaccinated cohorts age, when combined with screening.

Integrated genomic characterization of endometrial carcinoma

The Cancer Genome Atlas Research Network*

We performed an integrated genomic, transcriptomic and proteomic characterization of 373 endometrial carcinomas using array- and sequencing-based technologies. Uterine serous tumours and ~25% of high-grade endometrioid tumours had extensive copy number alterations, few DNA methylation changes, low oestrogen receptor/progesterone receptor levels, and frequent *TP53* mutations. Most endometrioid tumours had few copy number alterations or *TP53* mutations, but frequent mutations in *PTEN*, *CTNNB1*, *PIK3CA*, *ARID1A* and *KRAS* and novel mutations in the SWI/SNF chromatin remodelling complex gene *ARID5B*. A subset of endometrioid tumours that we identified had a markedly increased transversion mutation frequency and newly identified hotspot mutations in *POLE*. Our results classified endometrial cancers into four categories: *POLE* ultramutated, microsatellite instability hypermutated, copy-number low, and copy-number high. Uterine serous carcinomas share genomic features with ovarian serous and basal-like breast carcinomas. We demonstrated that the genomic features of endometrial carcinomas permit a reclassification that may affect post-surgical adjuvant treatment for women with aggressive tumours.

Endometrial cancer arises from the lining of the uterus. It is the fourth most common malignancy among women in the United States, with an estimated 49,500 new cases and 8,200 deaths in 2013 (ref. 1). Most patients present with low-grade, early-stage disease. The majority of patients with more aggressive, high-grade tumours who have disease spread beyond the uterus will progress within 1 year (refs 2, 3). Endometrial cancers have been broadly classified into two groups[4]. Type I endometrioid tumours are linked to oestrogen excess, obesity, hormone-receptor positivity, and favourable prognosis compared with type II, primarily serous, tumours that are more common in older, non-obese women and have a worse outcome. Early-stage endometrioid cancers are often treated with adjuvant radiotherapy, whereas serous tumours are treated with chemotherapy, similar to advanced-stage cancers of either histological subtype. Therefore, proper subtype classification is crucial for selecting appropriate adjuvant therapy.

Several previous reports suggest that *PTEN* mutations occur early in the neoplastic process of type I tumours and co-exist frequently with other mutations in the phosphatidylinositol-3-OH kinase (PI(3)K)/AKT pathway[5,6]. Other commonly mutated genes in type I tumours include *FGFR2*, *ARID1A*, *CTNNB1*, *PIK3CA*, *PIK3R1* and *KRAS*[7–9]. Microsatellite instability (MSI) is found in approximately one-third of type I tumours, but is infrequent in type II tumours[10]. *TP53*, *PIK3CA* and *PPP2R1A* mutations are frequent in type II tumours[11,12]. Most of these studies have been limited to DNA sequencing only with samples of heterogeneous histological subtypes and tumour grades. We present a comprehensive, multiplatform analysis of 373 endometrial carcinomas including low-grade endometrioid, high-grade endometrioid, and serous carcinomas. This integrated analysis provides key molecular insights into tumour classification, which may have a direct effect on treatment recommendations for patients, and provides opportunities for genome-guided clinical trials and drug development.

Results

Tumour samples and corresponding germline DNA were collected from 373 patients, including 307 endometrioid and 66 serous (53) or mixed histology (13) cases. Local Institutional Review Boards approved all tissue acquisition. The clinical and pathological characteristics of the samples generally reflect a cross-section of individuals with recurrent endometrial cancer[2,3] (Supplementary Table 1.1). The median follow-up of the cohort was 32 months (range, 1–195 months); 21% of the patients have recurred, and 11% have died. Comprehensive molecular analyses were performed at independent centres using six genomic or proteomic platforms (Supplementary Table 1.2). MSI testing performed on all samples using seven repeat loci (Supplementary Table 1.3) found MSI in 40% of endometrioid tumours and 2% of serous tumours.

Somatic copy number alterations

Somatic copy number alterations (SCNAs) were assessed in 363 endometrial carcinomas. Unsupervised hierarchical clustering grouped the tumours into four clusters (Fig. 1a). The first three copy-number clusters were composed almost exclusively (97%) of endometrioid tumours without significant differences in tumour grades. Cluster 1 tumours were nearly devoid of broad SCNAs, averaging less than 0.5% genome alteration, with no significant recurrent events. Cluster 1 tumours also had significantly increased non-synonymous mutation rates compared to all others (median 7.2×10^{-6} versus 1.7×10^{-6} mutations per megabase (Mb), $P < 0.001$). Copy-number clusters 2 and 3 consisted mainly of endometrioid tumours, distinguished by more frequent 1q amplification in cluster 3 than cluster 2 (100% of cluster 3 tumours versus 33% of cluster 2 tumours) and worse progression-free survival ($P = 0.003$, log-rank versus clusters 1 and 2; Fig. 1b).

Most of the serous (50 out of 53; 94%) and mixed histology (8 out of 13; 62%) tumours clustered with 36 (12%) of the 289 endometrioid tumours, including 24% of grade 3 and 5% of grade 1 or 2, into copy-number cluster 4; a single group characterized by a very high degree of SCNAs (Supplementary Fig. 2.1; focal SCNAs with false discovery rate (FDR) < 0.15, and Supplementary Data 2.1). Cluster 4 tumours were characterized by significantly recurrent previously reported focal amplifications of the oncogenes *MYC* (8q24.12), *ERBB2* (17q12) and *CCNE1* (19q12)[13], and by SCNAs previously unreported in endometrial cancers including those containing *FGFR3* (4p16.3) and *SOX17* (8q11.23). Cluster 4 tumours also had frequent *TP53* mutations (90%),

*Lists of participants and their affiliations appear at the end of the paper.

Showed that endometrial cancer should be classified by the sequencer rather than the microscope to achieve optimal treatment

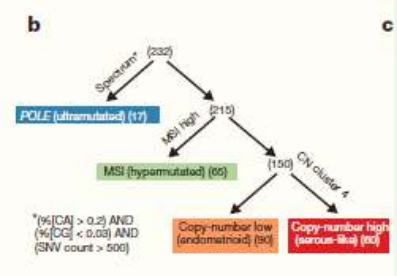
DOUGLAS LEVINE AND THE TCGA Network

Integrated genomic characterization of endometrial carcinoma

Nature, 497, 67–73, May 2, 2013.

This 2013 publication by The Cancer Genome Atlas (TCGA) Research Network represents a fundamental paradigm shift in gynecologic oncology.

By performing an exhaustive molecular analysis of 373 endometrial tumors—utilizing genomic, transcriptomic, and proteomic technologies—the study identified four distinct prognostic subgroups: POLE (ultramutated), microsatellite instability (MSI) hypermutated, copy-number low, and copy-number high. This work moved the field beyond a purely descriptive, microscope-based understanding of the disease to a definitive molecular classification, revealing that tumors with similar physical appearances under a slide could have drastically different genetic drivers and clinical outcomes.



This paper led to a four level classification system for endometrial cancers of the uterus.

The most profound impact of this article was its functional update to the long-standing "Bokhman Model." Since 1983, clinicians had relied on Jan Bokhman's two-type framework, which categorized tumors as either Type I (estrogen-dependent, low-grade) or Type II (estrogen-independent, high-grade). The TCGA data demonstrated that this two-type model was oversimplified and sometimes misleading.

Most notably, the study revealed that approximately 25% of "high-grade" endometrioid tumors (traditionally Type I) actually shared a genomic profile with the more aggressive serous carcinomas (Type II). By reclassifying these tumors into the four molecular subgroups, the TCGA provided a more accurate predictor of patient survival than traditional histopathology alone, particularly identifying the POLE group as having an exceptionally favorable prognosis regardless of how "aggressive" the cells looked.

Clinically, the TCGA classification has been integrated into international guidelines (such as those from ESGO, ESTRO, and ESP), enabling "de-escalation" of treatment for women with POLE mutations who might otherwise have been over-treated with toxic chemotherapy.

N.Y.U.

8

Women's Liberation

The women's liberation movement of the 1970s represented a pivotal moment in modern social history, redefining women's relationships to their bodies, their health, and the institutions that governed both.

Emerging from earlier feminist activism and shaped by civil rights, antiwar, and New Left movements, second-wave feminism challenged deeply entrenched inequalities in law, culture, and medicine.

This movement took place amidst broader societal change and unrest triggered by the Vietnam War and an increasing penchant for activism among the younger generation.

Prior to the 1970s, healthcare systems in many Western countries were overwhelmingly patriarchal. Medical research largely centered on male bodies, male physicians dominated the profession, and women's pain, reproductive choices, and mental health concerns were frequently dismissed or pathologized. Pregnancy and childbirth were increasingly medicalized, often removing decision-making power from women themselves. Contraception and abortion were tightly regulated. In 1970 only 7% of all OB/GYNs in the U.S. were female and issues of sexism were very real for women at the time.

The women's liberation movement reframed healthcare as a political issue rather than a purely medical one. Feminists argued that women's unequal treatment in medicine reflected broader systems of gender oppression. Reproductive health became a central focus: access to birth control, safe and legal abortion, accurate sexual education, and respectful maternity care were framed as essential to women's freedom and equality.

Bodily Autonomy

At the heart of the movement's approach to healthcare was the concept of bodily autonomy—the idea that women have the right to make informed decisions about their own bodies without coercion or paternalistic control.

Doctors frequently withheld diagnoses or treatment options from female patients, believing women were too "emotional" to handle complex medical realities. This took place against a social backdrop that had systematically displaced women from traditional medical roles, excluded them from medical leadership roles and, in many cases, had cast them as bad actors such as witches. [see Ehrenreich and English (1973)]. The standard treatment for breast cancer was the radical mastectomy—a disfiguring surgery often performed without a biopsy-confirmed diagnosis or the patient's prior consent to the extent of the surgery.

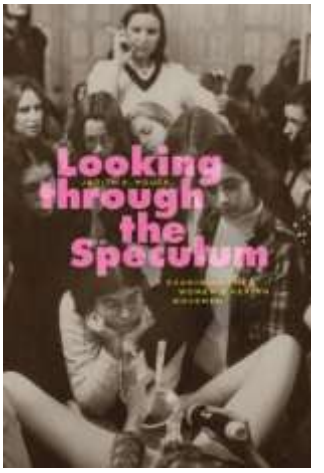
Feminists challenged laws that restricted abortion and contraception, arguing that forced pregnancy limited women's economic independence, educational opportunities, and full participation in public life. As illustrated below, organizing played a crucial role. Women established health collectives, abortion services, and self-help clinics, which emphasized shared knowledge and demystification of medical authority.

Source: University of Ottawa Archives and Special Collections

Self-Help

A major element of enhanced autonomy in a world that was perceived to offer paternalistic medical services to women is self-help. Women sought to do their own pelvic exams and to teach one other how to do it.

The desire to overcome issues with access and equity in care was a key catalyst of the second-wave feminist movement of the 1960s and 1970s. Judith Houck (2024, p. 9) writes: "Women's health activism was inspired by and part of second-wave feminism, a movement beginning in the 1960s and focused on increasing women's rights and securing women's liberation… As with earlier women's movements, many second-wave feminists came to feminism through their bodies, challenging women's inability to control their reproduction, protesting their vulnerability to sexual assault and domestic violence, and objecting to the constraints of the sexual double standard." The first women's self-help health group in the United States emerged in 1970. This movement grew quickly so that by 1973, there were more than 1,200 women's self-help health groups across the country [Schneir (1994)].



Judith Houck's book *Looking Through the Speculum* retells the self-help movement of the 1970s.

Reshaping the Delivery of Care

Associated with this idea was the practice of opening clinics that specifically served women and were run by women who were familiar with the themes of the women's liberation movement.

Dudley-Shotwell (2010) and Houck (2024) note that this was particularly successful in California, where ideas from the liberation movement took firm hold. There were also highly successful movements built around women's clinics as both a source of care and meeting places where discourse and friendship could take place throughout the country. The movement prioritized self-care and bodily knowledge, most famously through practices such as vaginal self-examination workshops, collective discussions of menstruation and childbirth, and the dissemination of plain-language medical information.

These clinics and collectives often rejected traditional medical norms. Many were non-profit, community-run, and explicitly feminist, staffed by nurse-midwives, counselors, and physicians committed to shared decision-making.

The effects were meaningful as noted by Francine Nichols (2000): "Despite setbacks in the area of reproductive rights during the 1980s, the WHM made significant gains in women's health at the federal policy level during the 1980s and 1990s. The WHM became a powerful political force. The achievements of the movement in improving women's health during the 20th century were numerous and significant."

Nancy Miriam Hawley helped to reshape social conversations about women's health in the 1970s and 1980s along with many collaborators called the Boston Women's Health Collective including Joan Ditzion, Paula Doress-Worters, Judy Norsigian, Jane Pincus, Esther Rome, Wendy Sanford and Norma Swenson.

Challenging the Doctor-Patient Relationship

One of the most influential products of this era, *Our Bodies, Ourselves* (first published in 1971), exemplified the movement's ethos by providing accessible, woman-centered medical information and encouraging patients to question doctors and demand informed consent.

This book grew out of the efforts of Nancy Miriam Hawley and was originally published in 1970 with the title "Women and Their Bodies".

The movement also critiqued the traditional doctor–patient relationship, which often treated women as passive recipients of care. Feminists highlighted issues such as the overuse of hysterectomies, the dismissal of women's pain, and the pathologizing of normal female experiences like menstruation and menopause. Mental health diagnoses, including the overuse of tranquilizers prescribed to women, were similarly scrutinized.

The Women's Liberation Movement Shaped Attitudes Toward Key Topics Like Menstruation and Menopause

The long-term effects of the women's liberation movement on healthcare have been profound and enduring. Legally, many countries expanded access to contraception and abortion during and after the 1970s, fundamentally altering women's reproductive choices. Medical research gradually began to include women as subjects, leading to better understanding of sex-specific health issues.

Culturally, the movement normalized conversations about menstruation, sexuality, menopause, and reproductive health, reducing stigma and silence. The presence of women in the medical profession increased significantly, influencing research priorities and patient care practices.

Over time, however, the movement underwent institutionalization and fragmentation. Many women's health clinics professionalized, sought stable funding, and integrated into mainstream healthcare systems, especially as regulation, malpractice risk, and reimbursement requirements increased. While it is true that by the late 1980s and 1990s, the women's health movement no longer functioned in a unified way, partly due to social reform, many of the larger ambitions of the movement remain alive despite today's Trumpian moment.

Sarah Franklin's 2018 essay "Feminism and Reproduction" reviews the many living and vital threads of the Women's Liberation movement that are shaping our society today.

Women's activism in favor of their health and body autonomy has revived in recent years. The U.S. Supreme Court overturned the *Roe vs. Wade* decision in 2022 allowing many states to ban abortion. Levels of activism from a new generation of women have been high since then.

WOMEN
and
THEIR BODIES
a course

75¢

by
BOSTON WOMEN'S
HEALTH COLLECTIVE

The "Ground Zero" publication for the women's liberation movement in health

BOSTON WOMEN'S HEALTH COLLECTIVE

Women and Their Bodies

New England Free Press, Boston, 1970.

Our Bodies, Ourselves—first published in 1970 as "Women and Their Bodies" and updated repeatedly over the following decades—approached women's health as both a social and medical issue.

The women's health workshop that inspired this book was organized in spring of 1969 by Nancy Miriam Hawley. The workshop, titled "Women and Their Bodies", was part of a female liberation conference held at Boston's Emmanuel College. The material from the workshop was mimeographed and after becoming an underground sensation, was compiled on newsprint in a book entitled "Women and their Bodies". The early editions were groundbreaking by encouraging women to understand and celebrate their sexuality, with sections on reproductive rights, lesbianism, sexual independence, and masturbation.

In their 1973 Preface, the authors cited four lessons learned during their research: (1) that it was important to supplement medical facts with personal experiences, how the latter could enrich knowledge of women's bodies; (2) that possessing basic information was liberating; it meant women were "better prepared to evaluate the institutions that are supposed to meet our health needs"; (3) that they were combating an ignorance which plagued women for centuries and "had one major consequence—pregnancy. Until very recently pregnancies were all but inevitable, biology was our destiny"; (4) that "body education is core education. Our bodies are the physical bases from which we move out into the world; ignorance, uncertainty—even, at worst, shame—about our physical selves create in us an alienation from ourselves that keeps us from being the whole people that we could be."

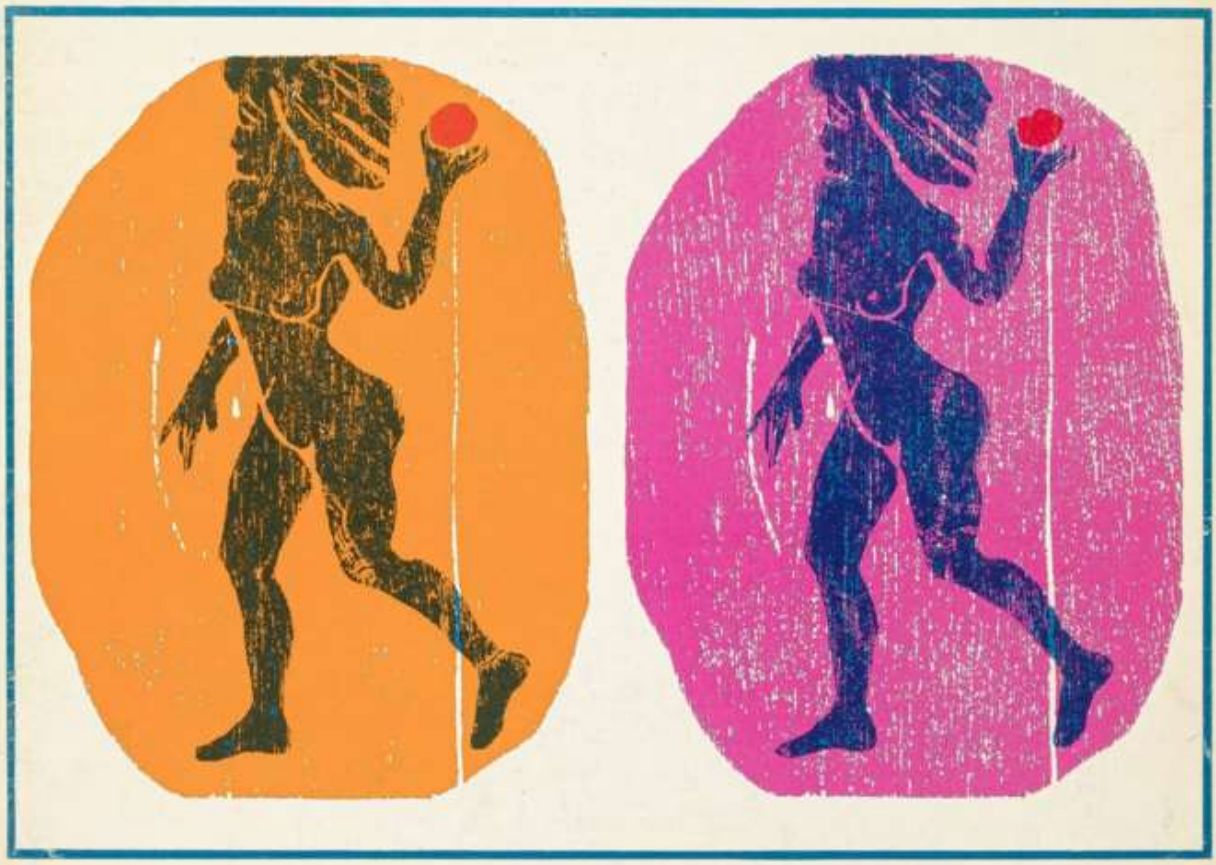
Book Notes: Bound in publisher's original side-stapled newsprint self-wrappers. 1-87, 89-193pp. The first edition of this title is scarce. While over 4 million copies of the title *Our Bodies, Ourselves* eventually sold, the first printing, *Women and Their Bodies* was issued on newsprint in five thousand copies. Today, only two copies can be found in a library (Boston Public Library & Harvard University). The files of Boston Women's Health Collective are at the Harvard/Radcliffe Schlesinger Library and the Countway Library.

References: Davis (2007), Ditzion (2014), Houck (2024), Nichols (2000).

$1.25

women

winter '70 A Journal of Liberation



What Is Liberation?

An ongoing publication that provided support to those in the women's liberation movement

BALTIMORE WOMEN'S COLLECTIVE

Women, A Journal of Liberation, Winter 1970 Issue

Self-Published, Baltimore, MD, 1970.

The journal was founded in Baltimore, MD, by four women - Dee Ann Mims, Donna Keck, Vicki Pollard, and Carmen Arbona - with the goal of providing a forum for opinions and expression that were essential to the burgeoning women's movement. The journal was managed by a collective, with each issue focusing on a different theme. The publication ran from 1969-1983.

Themes across issues of this publication included family life, revolution, and women in the arts. Titles include "A Shout on the Wall," "Primate Studies and Sex Differences," and "Divorce as Survival." Issues cover a range of topics both specific to the time and universally relevant but together create a vivid picture of the conversation about women's liberation during the early seventies.

Issues include editorial articles, interviews, reviews, poems and short stories with bold cover art showing female figures trapped in houses, breaking chains, and sitting with head in arms in a chair, also suggesting domestic life as a cage.

Themes in this publication also sought to link health issues and lack of access to abortion to radical politics.

Book Notes: Quarto (28cm); illustrated card wrappers, stapled; 80pp; illus. Light wear.

References: Rowbotham (1972).

EVERYWOMAN

Every woman is our sister VOL. 1, NO 2 ISSUE NO. 2 EVERYWOMAN COPYRIGHT 1970 MAY 29, 1970

IS YOUR MARRIAGE A ONESOME, TWOSOME, OR THREESOME? 'VALIUM' OF THE DOLLS WOULD YOU RATHER SWITCH THAN FIGHT? ANGRY OR MANGRY? 25¢ SPERM POWER

SEXISM IN MEDICINE

MALE CONTRACEPTION — MALE RESPONSIBILITY

THE UNKINDEST CUT OF ALL

FRANCES

Before the "pill" responsible men used condoms to prevent conception of unwanted babies and keep themselves and their sexual partners free from venereal disease.

[illegible] responsibility of contraception, so look to women upon them, by the "pill," unwanted babies were checked but not the spread of venereal diseases, which have reached epidemic proportions in California.

Taking the "pill" makes women guinea pigs, in that they risk serious side effects—they risk cancer later in life and they experience a costly drain on their body processes every day of pill-taking, since taking the "pill" keeps their bodies and minds in a state of pregnancy. Women wouldn't love to be guinea pigs, if the pills now being tested for men were put on the market; but the male decision-makers keep them off the market because many men still believe the myth that the male pills will destroy their libido—their precious machismo—although studies show that libido is not affected by male pills. The few minor side effects would be nothing as serious as the side effects from indulging in alcohol, tobacco, and mentally-diseased women.

The use of condoms would solve most of the above problems. Latex condoms are available at drugstores to married men 18 and older (although they should be available to boys as young as 12). Governor Reagan recently vetoed a bill that would have allowed males under 18 to buy condoms. Although plastic condoms are superior to latex—more reliable and less expensive—for some reason they are not yet available at drugstores in this country but are available to foreign

Please turn to page 4

EVERYWOMAN
6556 W 83rd ST.
LOS ANGELES,
CALIF. 90045

Case history*

This 32-year-old housewife is separated from her husband. She has two children, aged six and nine. She was seen in psychiatric consultation because of insomnia, tension, mild agitation and extreme fearfulness. Her marriage was stormy, replete with verbal and physical abuse. In the end, her husband left her for another woman. During the ensuing several weeks, she developed the above-mentioned symptoms, which had become almost incapacitating. Her nocturnal thoughts alternated between murderous anger at her husband (for deserting her) and fear of having to get up in the morning to face people. As usual in them, and as [illegible] her fantasies involved running away and hiding in some desolate spot. She felt both helpless in dealing with situations that had presented no problem to her prior to the departure of her husband and hopeless that anything could be done to help.

She was placed on a regimen of Valium 5 mg t.i.d. Treatment was continued for three months, her anxiety diminished to the point where she could communicate much more easily with the psychiatrist and could adequately care for her children and her home, her fearfulness diminished to the point of her being able to begin to examine both the reasons for her symptoms and the nature of her marital relationship.

*Data on file, Roche Laboratories, Division of Hoffmann-La Roche Inc., Nutley, N.J.

The Draw-a-Person Test, often useful as a psychiatric diagnostic tool, may reveal interesting cues and clues about your patient's inner and outer worlds.

PRINCESS VALIUM

Princess Valium meets shrink think

CASHING IN ON SEXISM IN PSYCHIATRY

SYLVIA HARTMAN

Valium is a tranquilizer. And what you see above is part of an expensive pamphlet, aimed at psychiatrists, advertising that drug. For all I know, every single one of the nation's fifteen to twenty thousand physician-psychiatrists has received a copy of this ad.

Frankly, I'd rather see matches given to toddlers.

This ad is "sexist" in the worst possible way. It plays into the notorious, but typical, Freudian-based, anti-woman, sex-stereotyped thinking that permeates the mental health profession at all levels. (I call it SHRINKTHINK). Furthermore, it capitalizes on the fact that most psychiatrists don't know beans about the horse-poop of psychological testing and interpretation, which forces them to take the "scientific" conclusions of the equally anti-female psychologist on blind faith. Thus, sexism is perpetuated.

But, maintaining this myth that psychological testing is "mysterious" is about the only power-weapon the psychologist has against the higher-status psychiatrist - just as being "mysterious" is often the only power a woman has over the higher - status male. (Translated, this means the woman keeps what she really thinks to herself. Similarly, psychologists don't let on how they really come to their biased conclusions.)

As an EX-psychologist (I lost The Faith) I warn any psychiatrists who might still be taking such tests as the Draw-A-Person seriously that they

Please turn to page 4

Highlighted the sexism of using tranquilizers to manage female moods

BY WOMEN FORFREEDOM, ANN HERSCHFANG AND VARDA MURRELL, EDS

Everywoman, Every woman is our sister; Vol. 1 no. 2, May 29, 1970

Self-Published, Los Angeles CA, 1970.

Everywoman, a newspaper published bimonthly in Los Angeles from May 1970 to April 1972, republished advertisements from other publications in order to expose expectations of patriarchal society.

This newspaper was written and produced by Ann Herschfang and Varda Murrell. Varda Murrell is best known as the person who first proposed gender-neutral pronouns.

This issue features an article highlighting sexism in medicine, noting that socially established gender roles at the time work against women's interest in seeking medical care.

A related article discusses the medicalization of women's moods with Valium.

The article, written by former psychologist Sylvia Hartman, entitled "Princess Valium Meets Shrink Think," defines Valium as both a tranquilizer and threat to individual freedom, and explains how psychiatrists arbitrarily prescribe the drugs to women through the sexist "Draw-a-Person" test.

The article discusses an ad for Valium that was used at the time. The ad includes six snapshots of a woman on vacation, accompanied by a story about an "unmarried with low self-esteem" woman named Jan who is in a "losing pattern" and is afraid she will never get married ("35, Single" 2).

This ad is strikingly misogynistic, as it is centered on the notion that women embody such a strong and innate desire to be married to a man that they enter depressive states as a result, which suggests that women are codependent to the point of needing treatment.

Book Notes: 12p., folded tabloid format newspaper, paper evenly toned, edges of front wrap foxed, otherwise very good condition.

References: Houck (2024).

9

Female-Predominant Disease

In 2021, the National Institutes of Health (NIH) began to discuss a shift in its research framework by discussing the concept of “Female-Predominant Disease."

Propagated largely through the Office of Research on Women’s Health (ORWH) this concept moves beyond just "female-specific" conditions (like pregnancy or cervical cancer) to address the vast spectrum of chronic illnesses that affect both sexes but occur far more frequently in women. The lead author on publications from ORWH was Sarah Temkin.

We like this classification, although one risks stretching the boundaries of women’s health as a concept too far if the bar is set too low on what might be female predominant.

The Future of Women’s Health Will Involve Doing a Better Job With Female-Predominant Diseases

Despite recent rollbacks that have, among other things, led to turnover at the NIH, including a number of people at ORWH, it seems rather obvious to us that our society globally will increasingly focus on the etiology of female-predominant diseases.

A particular priority is to understand what these diseases are and why they are female predominant. A consistent pattern evident throughout this report is that the more the science underlying a condition is understood, the better the treatment options for that condition become.

The NIH Began to Consider a New Framework for the Boundaries of Women's Health in 2021

Temkin *et al. BMC Women's Health* (2023) 23:162
https://doi.org/10.1186/s12905-023-02319-x

BMC Women's Health

REVIEW

Open Access

Chronic conditions in women: the development of a National Institutes of health framework

Sarah M. Temkin[1*], Elizabeth Barr[1], Holly Moore[2], Juliane P. Caviston[1], Judith G. Regensteiner[3] and Janine A. Clayton[1]

Abstract

Rising rates of chronic conditions were cited as one of the key public health concerns in the Fiscal Year (FY) 2021 U.S. Senate and House of Representatives appropriations bills, where a review of current National Institutes of Health (NIH) portfolios relevant to research on women's health was requested. Chronic conditions were last defined by the US Department of Health and Human Services (HHS) in 2010. However, existing definitions of chronic conditions do not incorporate sex or gender considerations. Sex and gender influence health, yet significant knowledge gaps exist in the evidence-base for prevention, diagnosis, and treatment of chronic diseases amongst women. The presentation, prevalence, and long-term effects of chronic conditions and multimorbidity differs in women from men. A clinical framework was developed to adequately assess the NIH investment in research related to chronic conditions in women. The public health needs and NIH investment related to conditions included in the framework were measured. By available measures, research within the NIH has not mapped to the burden of chronic conditions among women. Clinical research questions and endpoints centered around women can be developed and implemented; clinical trials networks with expanded or extended eligibility criteria can be created; and data science could be used to extrapolate the effects of overlapping or multiple morbidities on the health of women. Aligning NIH research priorities to address the specific needs of women with chronic diseases is critical to addressing women's health needs from a life course perspective.

Keywords Women's health, Chronic disease, Multimorbity, Sex differences, Gender

Background

Rising rates of "chronic debilitating conditions among women" were one of three key public health concerns cited in the Fiscal Year (FY) 2021 U.S. Senate and House of Representatives appropriations bills, where a review of current National Institutes of Health (NIH) portfolios and an expert convening related to women's health research was requested. The NIH's Office of Research on Women's Health (ORWH) responded to this congressional request by reviewing the current NIH activities on the priority topics, as well as collecting input on the priority areas from experts in women's health and members of the public. Members of the NIH Advisory

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The NIH defines this category as diseases that predominantly affect women, often with significantly higher prevalence, greater severity, or different clinical presentations compared to men. See Temkin et al. (2023)

The NIH initiative identifies three primary pillars within this framework:

1. **Autoimmune Diseases:** This is the flagship category of female prevalence. The NIH notes that nearly 80% of individuals living with autoimmune conditions—such as lupus, Sjögren's syndrome, and rheumatoid arthritis—are women.

2. **Chronic Debilitating Conditions:** Diseases like fibromyalgia, migraine and Chronic Fatigue Syndrome (ME/CFS), where women represent up to 90% of the patient population but have historically faced research gaps and stigma.

3. **Age-Related and Lifestyle Conditions:** This includes conditions like Alzheimer's disease and osteoporosis, which show a massive gender disparity in late-life prevalence and disability.

Sarah Temkin was Associate Director for Clinical Research within the Office of Research on Women's Health at the National Institutes of Health. She coordinated research on women's health across the agencies and provided clinical expertise on matters related to gynecologic cancer and cancer care for women. She currently works for the American Cancer Society.

If the literature is sparse on the history of traditional women's conditions like endometriosis and menopause, you won't be surprised to hear that it is particularly light in this expanded new territory of women's health.

In this section we delve a bit into the history of female-predominant PCOS, depression, autoimmunity, fibromyalgia and anorexia – highlighting some key research that noted the higher prevalence of these conditions in women for the first time.

However, the history is not as detailed as in other sections – in part, because there isn't as much history to report on.

It's quite clear, nonetheless, that as a society we have not spent nearly enough time sorting out the etiology, prevalence and therapeutic strategies for many of these disease states.

As Veronica Barcelona wrote in 2025 with respect to current NIH funding: "The [National Academies review] committee found that, from 2013 to 2023, only 8.8% of NIH research dollars focused on women's health research and that basic knowledge about women's physiological, hormonal fluctuations, and chromosomal differences is lacking. Data are also needed to better understand diseases that are female specific, are more common in women, or affect women differently."

Autoimmunity is Particularly Noteworthy

Autoimmune diseases are the fifth leading cause of death for women under 65 and one of the most common causes of suffering for women under 65 years of age.

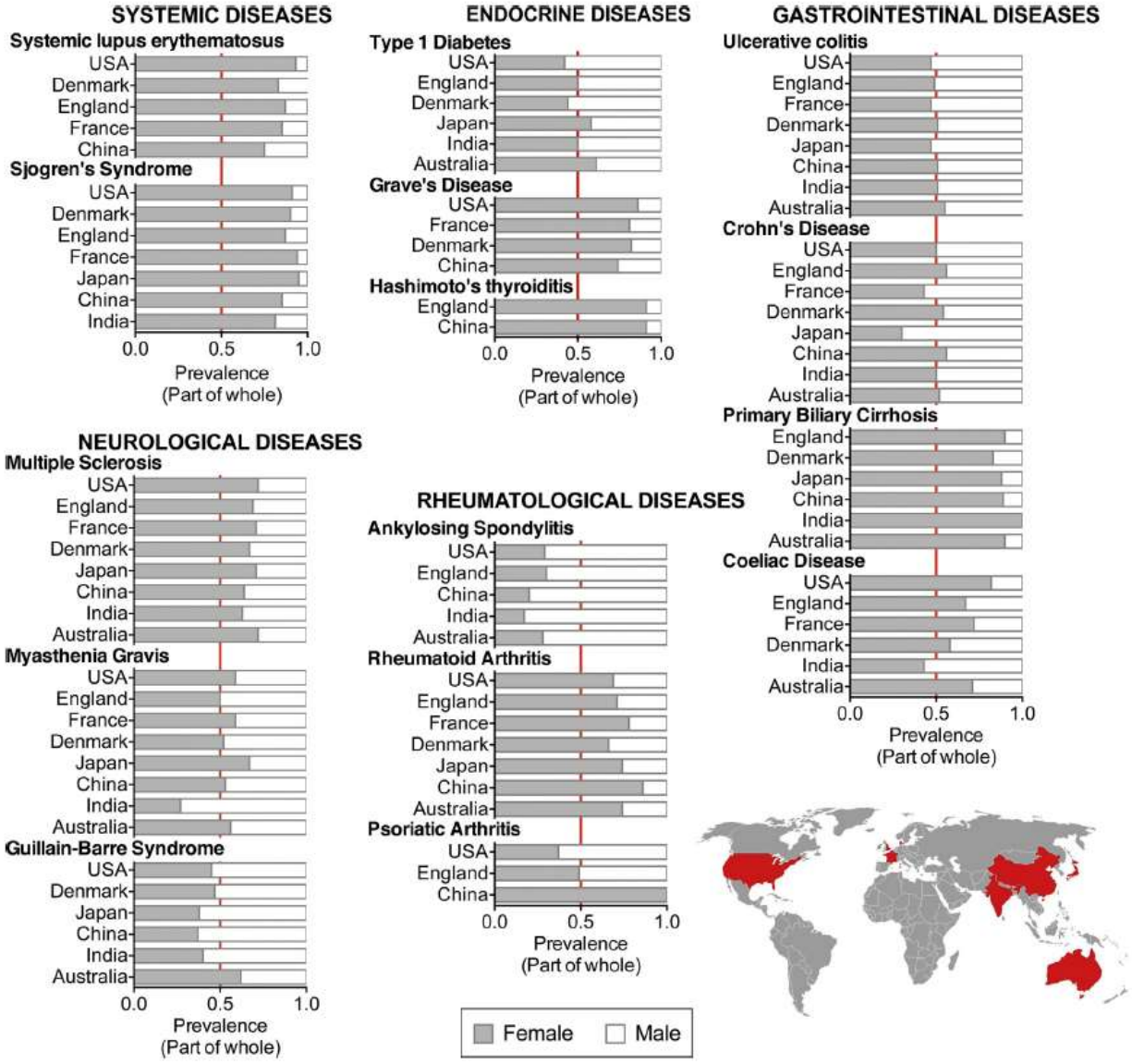


Figure 5. Prevalence of Autoimmunity by Disease and Country

The chart above taken from Ngo et al., (2014) shows that some autoimmune conditions like Sjögren's and lupus are female dominant while others such as ulcerative colitis are not. It's interesting also to note that, in general, these differentials are not dependent on the nation of the patient of interest.

There are a number of theories as to why women experience more autoimmunity:

1. **Hormonal Fluctuations**: Puberty, pregnancy, and menopause significantly alter hormones (estrogen, progesterone, etc.), influencing the immune system.
2. **Genetic Factors**: The X chromosome, which women have two of, carries genes related to immune function, with one gene (Xist) linked to autoimmunity.
3. **Immune Response**: Women naturally produce more vigorous immune responses and higher antibody levels, potentially an evolutionary advantage for pregnancy but a risk for autoimmunity.
4. **Viruses**: There is increasing evidence that some autoimmune conditions, particularly lupus and multiple sclerosis, have a viral origin. Not all persons with viral infections, however, get autoimmune disease. Somehow, gender might play a role.
5. **Microbiome & Environment**: Differences in gut bacteria and environmental factors may also contribute.

Sorting out these theories is a high priority for researchers today. We would note that hormonal stories are hard to make sense of. Women, on average, have higher levels of estrogen than men. But, in menopause, their levels of estrogen go down substantially.

Nonetheless, autoimmune conditions like RA, tend to get worse in menopause. Similarly, pregnancy is a high estrogen state, but autoimmune conditions often subside in pregnancy and resume in the post-partum state.

Our read of the literature tends to support the two X chromosome theory that was recently outlined by Diana Dou and Howard Chang in their Feb 2024 article in *Cell*.

Diana Dou of Duke has discovered a novel role for the Xist ribonucleoprotein (RNP) as a driver for autoimmunity underlying the sex-biased female preponderance for developing autoimmune diseases. Our read of the literature supports the theory that she developed with Howard Chang (now at Amgen) and others. See Dou et al. "Xist ribonucleoproteins promote female sex-biased autoimmunity," *Cell* Feb 1, 2024, 187(3):733-749

CNS Conditions are Highly Prevalent in Women

The consistent higher levels of depression in women are noteworthy as are differences in other conditions like migraine, anorexia and fibromyalgia. Like autoimmunity, most researchers tend to attribute these differences to hormones. Here the evidence would seem, somehow, to point to a binding receptor for estrogen that regulates neuroreceptors. We say this because depression rates are not high in menopause but tend to be high in perimenopause when estrogen levels are dropping. Similarly, one sees depression after pregnancy when estrogen drops but this is short-lived.

It seems that the relevant receptor changes its density when ligand density drops.

PHTHISIOLOGIA

John SEU Crusoe

EXERCITATIONES

DE

PHTHISI

Tribus Libris comprehensæ.

Totumque Opus variis Historiis illustratum.

AUTHORE

RICHARDO MORTON, Med. D.
& Regii Collegii Medicor. Lond. Socio.

Οὐδὲν εἰκῇ, ἐδὲν περωφᾷν. Hippocr.

LONDINI:
Impensis *Samuelis Smith*, ad insignia Principis in Cœmeterio Divi Pauli.
MDCLXXXIX.

RICHARD MORTON (1637 - 1698)

Phthisiologia seu exercitationes de phthisi tribus libnis

London: Samuel Smith. 1689.

"Richard Morton made the first reference to anorexia nervosa, a serious eating disorder "... the first chapter contains the first description of anorexia nervosa"--Norman 1555.

In a celebrated case history, he described a young woman with profound weight loss, amenorrhea, and loss of appetite who lacked cough, fever, pulmonary lesions, or other signs of phthisis. Morton explicitly rejected tuberculosis as the cause and instead attributed the condition to a disorder of the "nerves" and passions, describing it as a form of nervous wasting rather than organic lung disease.

This distinction is historically crucial: by separating severe emaciation caused by appetite loss from physical wasting, Morton laid the conceptual groundwork for what would later be recognized as anorexia nervosa.

After Morton it was not until 1859 that the French physician Louis-Victor Marcé published a case study of a patient with symptoms of anorexia emphasizing the patient's "obstinate refusal of food".

Later, In 1873, William Gull, Queen Victoria's personal physician, established the name "anorexia nervosa". He argued that the condition was a "nervous" (mental) disease rather than an "hysteric" one, noting it could affect both sexes.

Broad public awareness of this disease did not occur until the 1970s. This was driven by psychoanalyst Hilde Bruch's work, increasing media coverage of the "starving disease," and the high-profile death of singer Karen Carpenter in 1983. Among young adults, between 5.5% and 17.9% of women and 0.6% to 2.4% of men are diagnosed with a clinically significant eating disorder. The proportion of patients that are female is roughly ten times higher than that of men.

References: GMN 3216; Norman 1555; Osler 3459.

English physician Richard Morton is credited with the earliest medical descriptions of the anorexic condition in this 1689 book.

ARCHIVES GÉNÉRALES
DE MÉDECINE

AVRIL 1873.

MÉMOIRES ORIGINAUX

DE L'ANOREXIE HYSTÉRIQUE.

Par le Dr Ch. LASÈGUE.

Mon sentiment est qu'on ne parviendra à constituer l'histoire des affections hystériques qu'en étudiant isolément chacun des groupes symptomatiques; après ce travail préalable d'analyse, on réunira les fragments et on en recomposera le tout de la maladie. Envisagée dans son ensemble, l'hystérie a trop de phénomènes individuels, d'incidents hasardeux, pour qu'on arrive à saisir le particulier dans le général.

Ce procédé, plus que discutable si on l'applique à des maladies limitées quant au temps, quant à l'espace et aux localisations, quant à la modalité des phénomènes, trouve ici son emploi légitime. J'ai déjà cherché à donner la caractéristique de la toux et de la catalepsie passagère de nature hystérique; d'autres ont consacré de précieuses monographies aux hémiplégies, aux contractures transitoires ou durables, à l'anesthésie, etc. J'ai en vue de traiter aujourd'hui d'un complexus symptomatique trop souvent observé pour qu'il soit un accident exceptionnel et qui, de plus, a l'avantage de nous faire pénétrer dans l'intimité des dispositions mentales des hystériques.

Les troubles digestifs qui surviennent au cours de l'hystérie sont nombreux. Ils consistent dans des vomissements répétés et

Described anorexia as a form of hysteria resulting from family pressures

CHARLES LASÈGUE (1816 - 1883)

De l'anorexie hystérique

Archives générales de médecine, 7e série, tome 1, 1873, pp. 385–403.

Charles Lasègue

Charles Lasègue provided one of the first systematic clinical descriptions of what we now call anorexia nervosa. Working within the Parisian tradition of clinical observation, Lasègue framed the disorder as a form of hysteria, emphasizing its psychological and social dimensions rather than organic disease. He described young women who progressively restricted food intake despite preserved appetite, marked weight loss, hyperactivity, and denial of illness. Crucially, Lasègue focused on the family environment, noting how parental anxiety, coercive feeding attempts, and emotional dynamics could reinforce the illness. His account is notable for recognizing anorexia as a self-sustaining behavioral and relational syndrome, not merely a symptom of another disease such as tuberculosis or gastrointestinal pathology. In the same year, William Gull independently described the condition in England and soon after coined the term "anorexia nervosa" (1873–1874). Gull's approach was more explicitly medical and nosological. He emphasized the absence of organic disease, the paradoxical preservation of energy despite starvation, and the importance of firm but compassionate nutritional rehabilitation. While Gull acknowledged psychological factors, he did not embed the illness as deeply within family or social dynamics as Lasègue did.

Instead, Gull sought to define anorexia as a distinct clinical entity, separating it from hysteria, phthisis, and other wasting disorders. His framing made the condition legible within emerging internal medicine and psychiatry. Comparatively, Lasègue and Gull described the same syndrome through different lenses. Lasègue highlighted psychological mechanisms and interpersonal context, anticipating later family-systems and psychodynamic interpretations of eating disorders. Gull, by contrast, provided the diagnostic clarity and terminology that allowed anorexia nervosa to enter mainstream medical classification.

References: Brumberg (2000); Nerissa Soh et al., "Charles Lasegue (1816–1883): beyond anorexie hysterique," *Acta Neuropsychiatrica*, 2010, 22: 300-301.

Sir William Gull

Named anorexia nervosa and provided a clinical profile of the disease which afflicts young women

WILLIAM GULL (1816 - 1890)

Anorexia Nervosa (Apepsia Hysterica, Anorexia Hysterica)

Transactions of the Clinical Society of London Volume VII, pp. 22-28, 1874.

William Gull published "Anorexia Nervosa (Apepsia Hysterica, Anorexia Hysterica)" in 1874. While Gull had briefly mentioned the condition in a 1868 lecture at Oxford, this 1874 paper provided the formal clinical framework and named the condition "Anorexia Nervosa“ for the first time.

Gull, a prominent English physician and Physician-in-Ordinary to Queen Victoria, sought to move the medical understanding of extreme self-starvation away from physical "wasting" diseases like tuberculosis and into the realm of the nervous system.

In the article, Gull described several case studies of young women, most notably a 17-year-old patient, Miss A., who exhibited a total "want of appetite" and extreme emaciation without any detectable organic disease. He meticulously documented their symptoms, noting that despite their skeletal appearance, these patients often displayed a strange "restlessness" and a tendency to be "brisk and active". Crucially, Gull argued that the root of the malady was a "perversion of the ego" or a mental state that led to the physical refusal of food. His treatment regimen was notably modern, emphasizing the importance of removing the patient from the family environment, establishing a strict nursing schedule, and implementing regular, forced feedings.

The impact of Gull’s 1874 article was profound, as it effectively medicalized a phenomenon that had previously been viewed through the lens of religious "fasting" or "hysteria".

By providing a specific name and diagnostic criteria, Gull allowed physicians to categorize and treat the disorder as a distinct psychiatric entity. His work, published almost simultaneously with Charles Lasègue’s research in France, sparked a "priority dispute" over the discovery of the disease, but Gull's terminology ultimately became the global standard.

References: Bell (1985); Brumberg (2000); GMN 4845; Smith (1998).

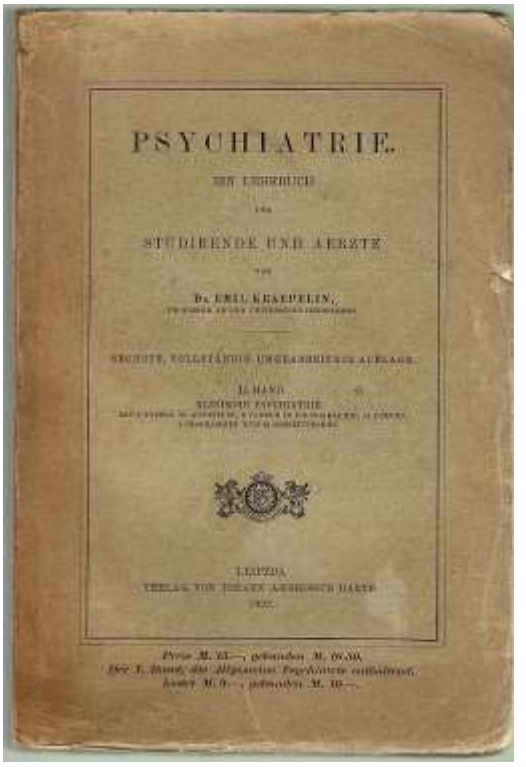
Emil Kraepelin

The first to report statistical evidence that depression is much more common in women than men

EMIL KRAEPELIN (1856 - 1926)

Psychiatrie. Ein Lehrbuch für Studirende und Ärzte

Leipzig: Verlag Von Johann Ambrosius Barth, 1899.



In 1886, young German psychiatrist Emil Kraepelin held the inaugural lecture for his first lecture chair in psychiatry at the University of Dorpat/Tartu outlining his vision for the future of psychiatric research and clinical care. This lecture marked a turning point in the history of psychiatry.

Kraepelin noticed that the predominant approach to psychiatry, which at that time focused on neuroanatomy and neuropathology, reached its dead end. Despite decades of slicing brains from dead corpses, there had been no achievements in explaining the nature of psychiatric illnesses.

Kraepelin's 1899 psychiatry textbook was considerably expanded and contained a section in Volume 2 that discusses clinical depression in some detail – with substantial statistical depth.

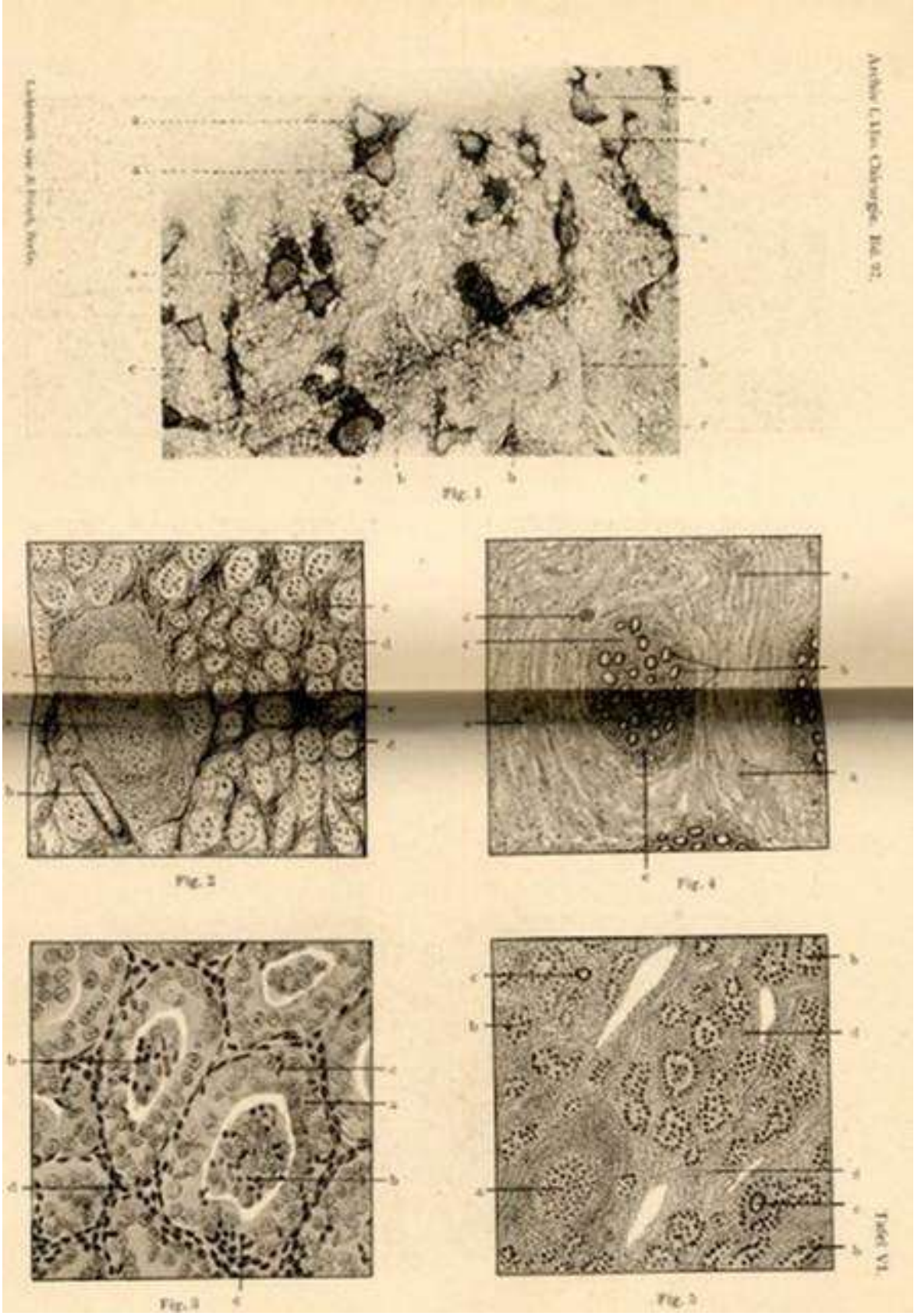
For the first time Kraepelin noted that his patients were roughly twice as likely to be women than men. This was in Vol 2 of the 1899 edition.

Kraepelin explicitly observed that the imbalance of women versus men with depressive illnesses (what he classified under manic-depressive insanity) was as a population-level clinical regularity, based on large asylum cohorts.

This 2:1 ratio was later confirmed by Myrna Weissman in her 1977 paper on sex differences and the epidemiology of depression (*Archives of General Psychiatry*).

Book Notes: (two volumes). 24 x 16.5 cm, original wrappers, uncut edges; XIII, 362 pp.; X, 607 pp., 6 autotype plates, 3 photographic plates, 16 curves, 3 diagrams, and 13 type specimens; in volume 2, some pages with numerous pencil annotations. Volume I: General Psychiatry; Volume II: Clinical Psychiatry

References: GMN 4941; Porter p. 184; Scull p. 302; Shorter p. 106.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Perhaps the first pathological description of an archetypal autoimmune disease: Hashimoto's Disease

HAKARU HASHIMOTO (1881 - 1934)

Zur Kenntniss der lymphomatösen Veränderung der Schilddrüse (Struma lymphomatosa)

Archiv fur Klinische Chirurgie 97. Berlin: Verlag von August Hirschwald, VI, pp. 219-248, 1912.

This is one of the most important landmark publications in the history of endocrine pathology and autoimmune disease of the 20th century, though its significance was not immediately recognized.

Hashimoto's work was based on careful histologic study of thyroid specimens from four women who had undergone surgery for goiter. Hashimoto described a distinctive pattern characterized by dense lymphocytic infiltration, formation of lymphoid follicles with germinal centers, destruction of normal thyroid architecture, and fibrosis—features that clearly distinguished this condition from simple goiter, thyroiditis of infectious origin, or neoplastic disease. His meticulous microscopic observations reflected the strong influence of German pathological traditions under which he had trained.

Conceptually, Hashimoto interpreted these findings as a form of chronic inflammatory enlargement of the thyroid, which he termed struma lymphomatosa. He did not frame the condition in immunologic terms—autoimmunity as a concept lay decades in the future—but he emphasized that the process was neither malignant nor suppurative. Instead, he proposed that it represented a unique pathological entity, marked by progressive glandular destruction accompanied by lymphoid proliferation.

The paper's historical importance became apparent only later. For several decades it remained obscure, cited infrequently. In 1931, Graham and McCullagh used the term "Hashimoto" for the first time in the title of an article, strongly arguing that struma lymphomatosa was indeed distinct from Riedel's thyroiditis. In 1939, the prominent British thyroid surgeon Cecil Joll coined the term "Hashimoto's disease" and used it in the title of a review about this condition. Since then, Hashimoto's thyroiditis has gone from being a rarity to one of the most common autoimmune diseases, as well as the most common endocrine disease. This 1912 paper is, in retrospect, one of the earliest descriptions of what would later be understood as an autoimmune disorder.

Hashimoto was a Japanese pathologist but himself never lived to see the significance of his discovery recognized. He studied medicine at Kyoto Imperial University and then did his postgraduate training in Germany – which is where this paper was written. After returning to Japan he entered clinical practice.

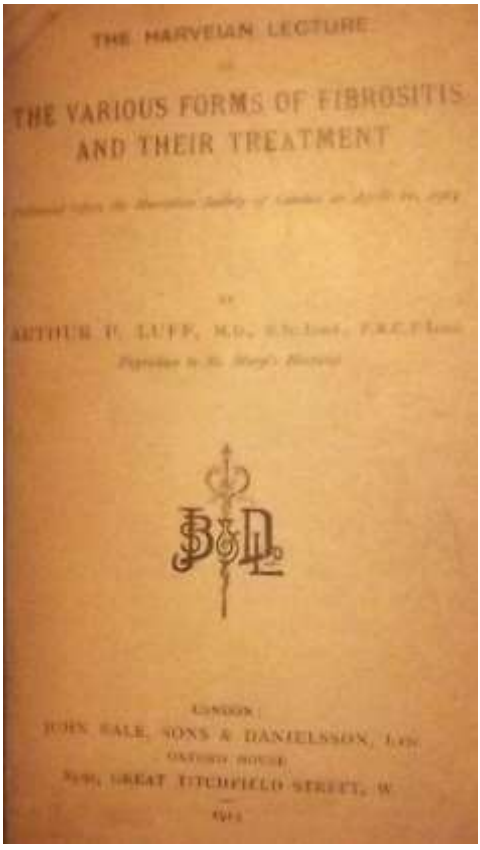
References: GMN 3845.

Arthur Pearson Luff

The first to identify fibromyalgia as a systemic disease associated with internal and external stressors

ARTHUR PEARSON LUFF (1855 - 1938)

The Harveian Lecture On The Various Forms Of Fibrositis And Their Treatment



London: John Bale, Sons & Danielsson, 1913.

Arthur P. Luff's 1913 Harveian Lecture expanded the clinical understanding of "fibrositis" (now known as fibromyalgia) from its original definition given by William Gowers in 1904. For the first time, Luff shifted the focus from localized muscle pain to a systemic, widespread condition (as fibromyalgia is now known). This was the first time that the condition now called fibromyalgia was described in a manner that resembles its current description.

Luff provided meticulous descriptions of "indurated nodules" or sensitive areas in the muscles that were painful to the touch, which served as the historical precursors to the "tender points" used in later 20th-century diagnoses. Furthermore, Luff recognized the influence of external and internal stressors, noting that symptoms were often exacerbated by "mental strain," weather changes, and gastrointestinal issues.

Both Luff and Gowers were ultimately limited by the technology of their time, as they incorrectly identified the root cause as peripheral inflammation—a theory that would not be debunked until modern research shifted the focus toward the central nervous system.

The transition to Yunus' landmark 1981 description of fibromyalgia represented a paradigm shift from anecdotal observation to rigorous, evidence-based science. While Luff identified "nodules" and associated symptoms like "mental strain," Yunus provided the first controlled clinical study to validate these findings. Yunus replaced the "inflammatory" label with a sophisticated "clinical syndrome" model, documenting the definitive association between widespread pain and non-muscular issues like non-restorative sleep, fatigue, and irritable bowel syndrome.

Most notably, while Luff's era spoke vaguely of a "change of life" or "climacteric" link, Yunus established the modern demographic profile of the disease, confirming the overwhelming female predominance and laying the groundwork for the 1990 ACR criteria that finally retired the term "fibrositis" in favor of "fibromyalgia".

References: Inanici and Yunus (2004); Smith (2010).

Noel Rose and Ernest Witebsky

(University of Buffalo, 1950s)

NOEL ROSE (1927 - 2020) AND ERNEST WITEBSKY (1901 – 1969)

Studies on organ specificity. V. Changes in the thyroid glands of rabbits following active immunization with rabbit thyroid extracts

Journal of Immunology, 76(6):417-27, June 1956.

In 1900 Paul Ehrlich and Julius Morgenroth famously coined the term "Horror Autotoxicus," arguing that while the body could theoretically produce antibodies against its own tissues, it possessed internal regulatory mechanisms to prevent this, as such self-destruction would be biologically "monstrous." This set the "pro-self" dogma that dominated the field for 50 years.

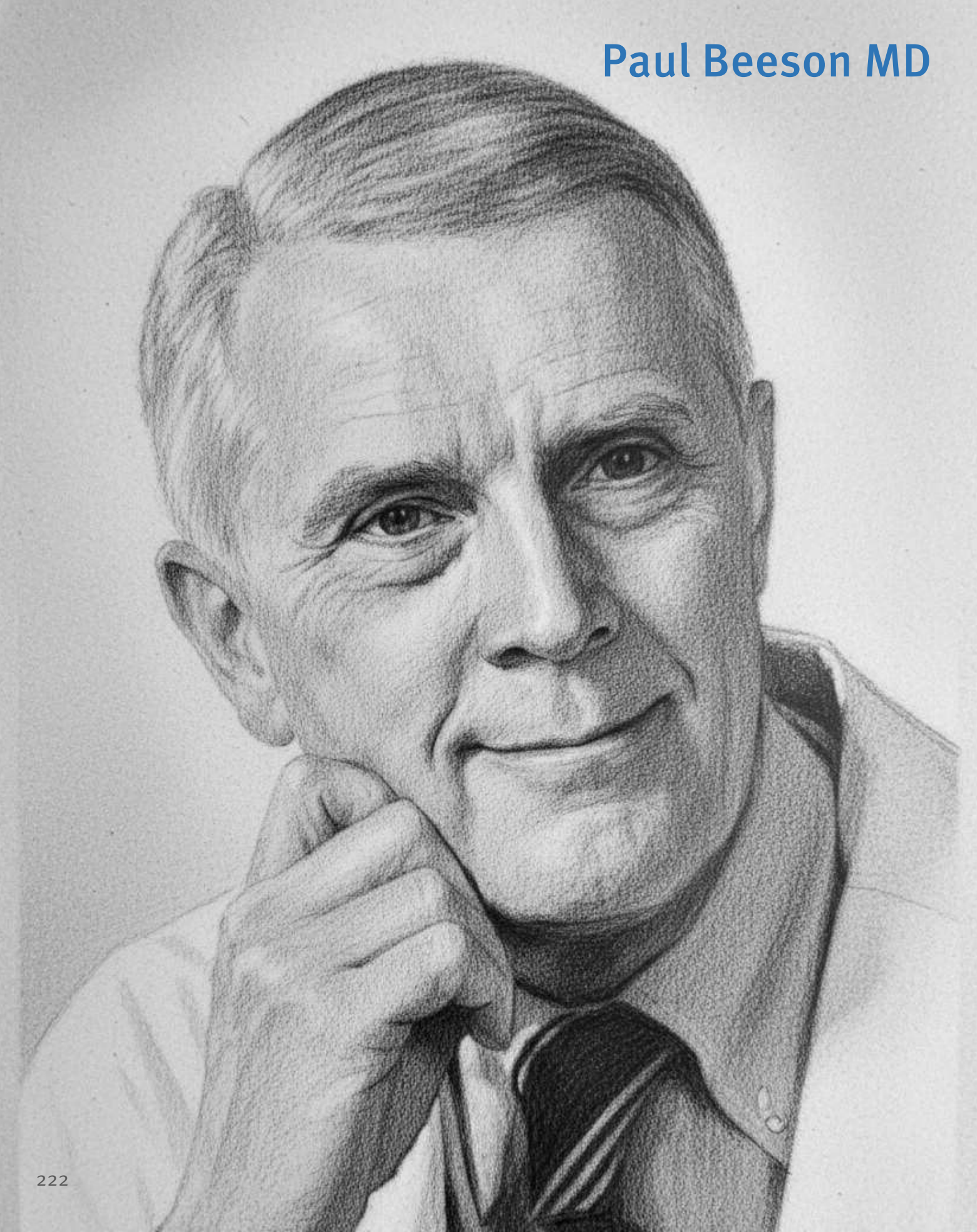
In their 1956 paper Witebsky and Rose delivered the experimental "death blow" to Horror Autotoxicus. The authors injected rabbits with extracts of their own thyroid glands or thyroid glands from other rabbits to stimulate a strong immune response. They observed that these rabbits developed specific antibodies that reacted exclusively with thyroid tissue, proving that the immune system could, in fact, be tricked into targeting "self". Today, Noel Rose is called the “father of autoimmunity” for this work.

The researchers further demonstrated that this immune response led to actual physical damage, a condition they termed experimental autoimmune thyroiditis. Upon examining the thyroid glands of the treated rabbits under a microscope, they found massive infiltration of white blood cells and the destruction of the normal follicular structure of the gland. This mirrored the pathology seen in humans with Hashimoto’s thyroiditis, providing the first reproducible animal model for a human autoimmune disease.

There are technically two papers (in succession in the June 1956 issue of the *Journal of Immunology*). The first paper (IV) showed the effect of immunization on antibody production while the second showed the physical effects of the antibodies (V). It is the second paper that is the more important one as antibody in the blood does not always equal a disease. By showing that these autoantibodies led to functional organ damage in Paper V, Rose and Witebsky proved that the immune system was not just "confused," but was actively pathogenic. This paper also laid the foundation for Witebsky’s Postulates, a set of criteria designed to determine if a disease is truly autoimmune.

References: GMN 2578.20 (for the paper showing the effect on autoantibody production – “Studies on organ specificity. IV”); Mackay (1995); Nakazawa (2009, p. 33); Silverstein (2006).

Paul Beeson MD



First to systematically document female predominance of autoimmune conditions

PAUL BEESON (1908 - 2006)

Age and sex associations of 40 autoimmune diseases

American Journal of Medicine, 96(5):457-62, May 1994.

Paul Beeson's 1994 paper, "Age and sex associations of 40 autoimmune diseases," for the first time provided broad quantitative evidence of the disproportionate burden of autoimmune diseases on women.

Before this paper, the female bias in autoimmunity was recognized as an "anecdotal" truth in medicine, but Beeson was among the first to systematically catalog these disparities across nearly every known autoimmune condition of the time.

By cataloging 40 distinct autoimmune diseases, Beeson provided the first comprehensive epidemiological evidence that the vast majority of these autoimmune conditions disproportionately affect women. He famously documented extreme female-to-male ratios in diseases like Sjögren's syndrome (up to 19:1) and Systemic Lupus Erythematosus (9:1), establishing a definitive statistical baseline that moved the observation from clinical anecdote to scientific fact.

Beyond merely listing ratios, Beeson examined the relationship between the age of onset and disease prevalence. He observed that the most pronounced sex disparities typically occur during the reproductive years—between puberty and menopause—while childhood and geriatric onset often showed more balanced ratios. This observation bolstered the theory that sex hormones play a "permissive" role in triggering these diseases, though Beeson was careful to point out exceptions, such as ankylosing spondylitis, which skew male, suggesting that the biological drivers of autoimmunity are more complex than a simple "estrogen-only" model.

By highlighting the consistency of the female preponderance across diverse organ systems, Beeson helped define "autoimmune disease" as a unified field of study rather than a fragmented list of unrelated conditions.

His work forced his scientific colleagues to look beyond superficial hormonal explanations and paved the way for current breakthroughs in X-chromosome genetics and sexual dimorphism in the innate immune system.

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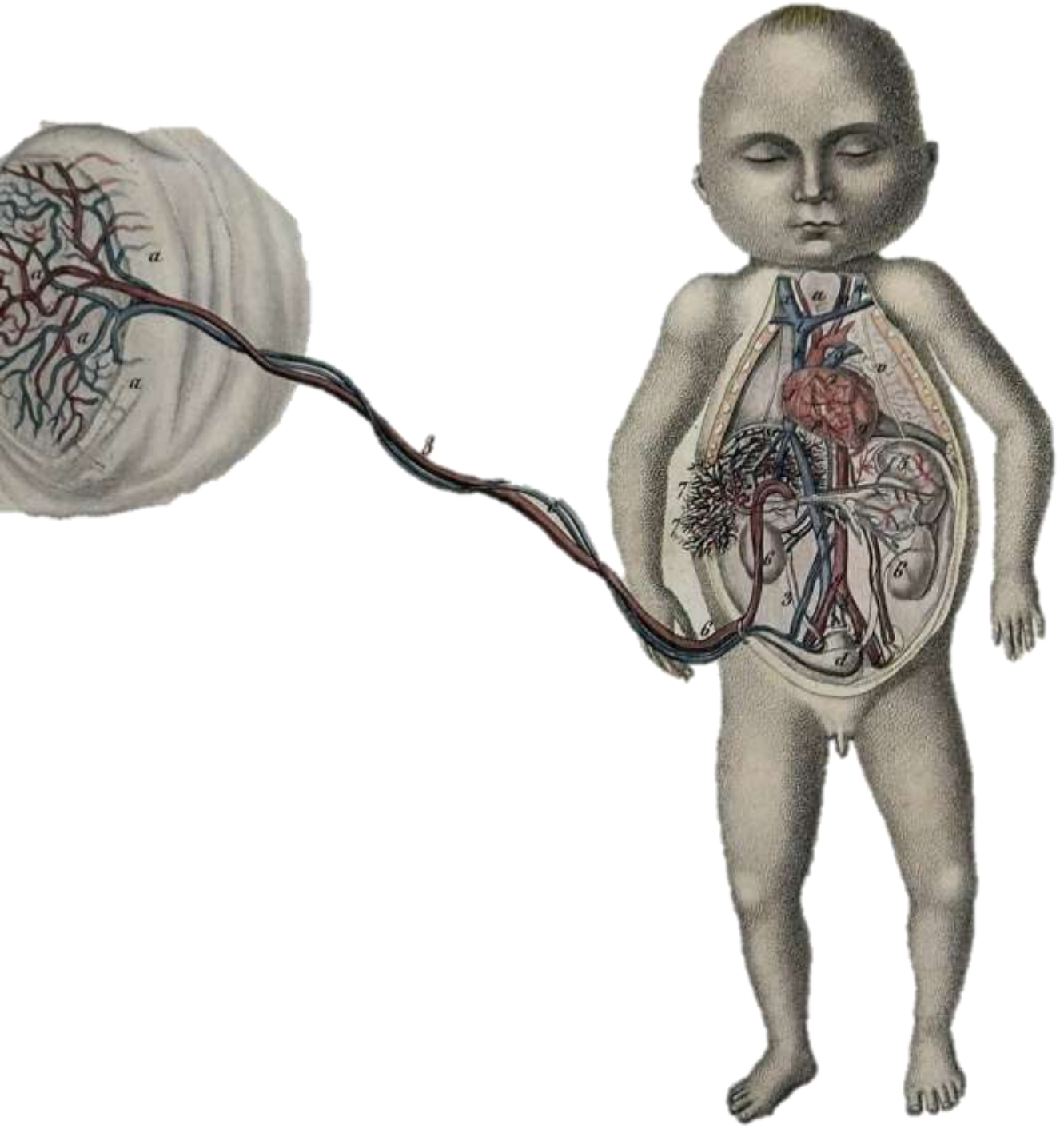

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