The 19th Century

Medical Revolutions

Overview

❖ The 19th century saw a number of trends converge which brought forth the first appearance of what we might call “modern medicine.”
❖ Here we see the rise of research hospitals, along with an empirical approach to medical research in the laboratory. (Medicine begins to be a science.)
❖ The wars of Napoleon spread typhus, but they also provided plenty of opportunities for the medical community to hone its skills and compare notes on surgery and disease.
❖ A host of new developments constituted a legitimate revolution in medicine:
  ❖ The stethoscope
  ❖ Hands-on physical examination for diagnosis (patients took some time to accept this).
  ❖ Powerful microscopes, microscopic anatomy, and “histology”
  ❖ Cell theory
  ❖ Germ theory
  ❖ Many benefits from the experiments of chemists.
  ❖ Increased popular respect for the professional physician.

The Three “A’s”

❖ Roy Porter, among others has observed that three developments, more than all others, made the modern approach to medicine possible:
  ❖ Anaesthesia
  ❖ Antiseptics (and antisepsis)
  ❖ Antibiotics (ultimately)
❖ The first two were the key to the 19th century rise of the surgeon as something more than a “last resort.”
❖ The last is essentially a 20th century phenomenon, but it required the advances in cell and germ theory which were the achievement of the 19th century.
❖ (These three are useful for organizing the final topics of this course.)
❖ Other developments (in instruments, method, etc.) were occurring right alongside these, and should not be discounted.
❖ Taken together, the changes of the 19th century produced a rather justified optimism about the potential of medicine.
❖ The idea that, with time, more and more cures will be found caught in the popular imagination.
Anaesthesia

- Attempts to operate under the influence of opium or other “sleep inducing” drugs had proven inferior to sheer speed on the part of the physician.
- Opium itself was not sufficient (particularly because the patient could move or behave erratically), so attempts were made to mix it with more powerful drugs (hemlock was common).
- As Gabriel Fallopia lamented, “When soporifics are weak they are useless, and when they are strong they kill.”
- Potency and accurate dosing required an understanding of chemistry which was not available in premodern medicine.
- Practicality always ruled, and patient survival was greater with a surgeon who was simply fast.
- The first step toward modern anaesthesia was the discovery of the properties of nitrous oxide.

Nitrous Oxide

- The English chemist Joseph Priestly first discovered “dephlogisated nitrous air” late in the eighteenth century.
- 1795: the apprentice chemist Humphrey Davy (1778-1829) found a use for it.
- Davy was working on the possible medical applications of gases (or was supposed to be working on this) at Thomas Beddoes’ “Pneumatic Medicine Institute” in Bristol.
- He applied Nitrous Oxide to his favorite test subject (himself) and got quite “intoxicated” after 7 minutes and 16 quarts.
- From this point on in his life Davy used Nitrous Oxide frequently, especially before the public lectures for which he was famous.
- (Possibly with help from the gas, he was considered quite the showman.)
- Davy contributed many discoveries to chemistry, and died rather young (possibly as a side effect of his prolonged habit of self experimentation.)
- Davy was far more interested in chemistry than medicine.
- The great value of Nitrous Oxide, as he saw it, was that it imparted all the pleasant effects of alcohol without the negatives.
- Medical application would have to wait.
A Public Lecture (Davy is at the bellows)

Nitrous Oxide and Dentistry

❖ 1844: Watching a public lecture (in America) by Gardner Colton, Horace Wells, a dentist, observed the effects of nitrous oxide deadening sensation.
❖ (Colton had volunteers inhale then demonstrated that they could feel no pain -- until the effects wore off and the bruises started to swell anyway. Fun, 19th century style.)
❖ Wells had Colton administer nitrous oxide to him and then his partner, John Riggs, extracted a wisdom tooth.
❖ Dosing was a problem yet to be solved, and there was a tendency to use too little gas (out of caution).
❖ The gas was entirely unsuitable for major surgery in the amount in which it could be produced.
❖ (This was discovered in another, less happy public demonstration. See Kennedy, p. 131.)
❖ Kennedy observes that Wells later became addicted to chloroform and committed suicide. He neglects to mention that the suicide followed on some unfortunate legal trouble involving sulphuric acid and a prostitute. (!)
❖ (I don't suppose that's absolutely relevant.)
Ether

Originally a byproduct of alchemy, discovered by Ramon Lull, 1275.

(See, I told you alchemy mattered.)

1842: William Clarke (physician and dentist) recommends it for dentistry. It worked.

Prior to this it had been used as an expectorant and for recreation.

Crawford Long, a fan of ether at parties and a Georgia surgeon, performed the first surgery on the (possibly unsuspecting) boy, James Venable, at an “ether frolic.”

James was not a fan of pain and had avoided surgery on two cysts because of it.

It worked, and the news spread.

Long continued using ether for surgery and childbirth (built him quite a local reputation).

(Along with the parties.)

William T. Morton tried it at a public demonstration in New England in 1846. Ether worked where Nitrous Oxide had not, and it was well on its way to becoming standard for operations.

(Note Kennedy's discussion of the debate over who “discovered” ether: pp. 133-34. Fights over “credit” became part of science with the Sci. Revolution.)

Chloroform

Ether received some strong competition from another candidate (which also began as a recreational-drug).

1831: American chemist Samuel Guthrie discovered the “spirituous solution of chloric ether” (note how scientific language has changed).

Again, it was mostly an interesting curiosity at parties until 1847 when James Young Simpson learned of its sleep inducing, and pain killing, properties.

The story in Kennedy may be balanced against other stories which involved “tumblers” of chloroform “served” to the friends at the table.

(Some tidying of the details may have been done for posterity.

The chief interest of Simpson was in relieving the pain of childbirth (1853: Queen Victoria is a patient under John Snow), but it soon displaced ether for a time in surgery.

Ether won out in the end, when carefully kept statistics showed a lower mortality rate (irritation of the lungs was a factor in ether’s favor).

Note, finally, the rise of local anaesthetics based upon cocaine, in Kennedy.

The first great “advance” in surgery was in place, but it also had a down side:

With surgeries more frequent, but no understanding of germs or sterilization, mortality actually increased overall in the wards.

The second great ‘N’ followed about a decade behind...
Antisepsis (and hygiene)

- We have already seen the unfortunate case of Ignac Semmelweiss in regard to the reception (or lack thereof) of hospital antisepsis.
- Doctors everywhere were reluctant to adopt it, partly because of pride, perhaps, and partly because of horror at the implication that they had been the cause of very preventable deaths.
- The French Chemist Louis Pasteur (who does not get enough pages in Kennedy's book) pioneered the "germ theory" of disease.
- The real changes, however, were to be championed (and in many places established) before Pasteur's theory would be widely accepted.
- Practicality (again) led the way.
- Kennedy uses three fine examples:
  - Florence Nightingale,
  - John Snow (same as three slides ago),
  - and Joseph Lister.
- Kennedy's coverage is fairly accurate, here, though he leans toward a 'hero worship' style excess in his language and conclusions (especially about Nightingale).
Florence Nightingale

- Felt a "calling from God" to work with the suffering.
- Among other advances which may be attributed to her:
  - Keeping statistics on patients in hospitals.
  - Trained (and respectable) nurses, and the concern that regular patient care was critical for recovery.
  - A concern for the mental well-being of those in hospitals.
  - A sense, that, for whatever reasons, crowded wards, and filth, were harmful for recovery.
- Her work at the hospital in Scutari during the Crimean war (1854) was pivotal in the British understanding of the need for clean wards (this spread to other countries at different rates.)
- Even after surgery the patients, in Nightingale's account, were lying about the floors covered in their own blood, still in the uniforms in which they had received their wounds, rats and other vermin were crawling everywhere.
- (Then of course there was the dead horse clogging the water system.)
- With her war department mandated reforms death rates post-op plummeted.
- A real watershed came in 1855: an outbreak of typhus and cholera at Scutari prompted further reforms of sanitation led by Nightingale.
- February death rate: 42%.
- June: 2%. (The British came to very practical conclusions.)
London Sanitation

- In 1750, 35% of the English population lived in urban areas.
- In 1850, 87% lived in industrial cities.
- The rapid growth of the cities (London, Birmingham, Manchester, etc.) occurred without any particular concern for sewage or water sources.
- Frequently those who rose into the middle class would move to houses on higher ground in the cities, leaving the poor living, literally, “downstream.”
- Draw your own conclusions about raw sewage and a good London rain.
- The Thames was recognized as filthy, and the filth was considered to relate to the cause of diseases (such as the Cholera epidemic discussed by Kennedy).
- This produced a somewhat pointless fleeing of the central city for the expanding suburbs (by those who could afford it).
- The general assumption was that the “vapors” or “miasmas” of the river (associated with its tremendous stink) were responsible.
- Some, such as John Snow, observed that the citywide pattern of Cholera did not match this theory.
- Solutions put in place by Snow included a return to the practice of carting away raw sewage and the closure of certain wells. (See Kennedy’s discussion of the “Broad Street Pump.”)

Reforms were occurring before germ theory was in place.

- Even with Pasteur’s discoveries, resistance was strong.
- Early in the development of germ theory, however, Joseph Lister was applying the idea to the cause of wound infection.
- His answer? That of Semmelweis: Carbolic acid.
- Everywhere.
- Note the case of James Greenlee on page 145.
- His publication in *Lancet*, 1867, relating to the healing of compound fractures, caused quite a debate.
- In spite of obvious success rates, adoption of “Listerism” was slow, though much faster in Britain and Germany than elsewhere.
- Combining Lister’s methods with Nightingale’s new statistical records made a difference in adoption:
  - In British hospitals post-op death rates between 1859 and 1870 were at 45.3%.
  - Between 1886 and 1890: 7.5%.
- Particularly in Germany, the race was on to find ever more effective methods of Antisepsis. (See pp. 154-56.)
Antibiotics

❖ At the dawn of the 20th century:
❖ "Aside from quinine, digitalis, vaccination, and morphine, there was no effective, non-surgical treatment of disease." (Kennedy, p. 178.)
❖ We should add arsenic, more generally.
❖ Surgery had become much more effective through anaesthesia and antisepsis, but post-operative infection was still mostly a "waiting game."
❖ Paul Erlich's development of drug treatments for Malaria and Syphilis gave hope on the front of using chemical drugs for specific diseases, but general infections seemed to be far too common, and caused by too many different bacteria for an easy solution.
❖ This would change with two developments: the Sulfa drugs and (most significantly) penicillin.
❖ Penicillin would have an advantage over the Sulfa drugs (and most other options) in that it was far less toxic.
❖ The problem was coming to the conclusion that it would work at all...

Tyndall:

❖ 1875: Physicist John Tyndall (inventor of an early gas mask, among other things) observed that Penicillin mold on broth cultures killed bacteria (the bacteria formed a brown silt at the bottom of his broth vials).
❖ Tyndall was working on the distribution of bacteria in the air, not on how to kill them. The medical application would have to wait.
❖ Note: always consider historical context: this discovery was made during the ascendancy of germ theory, and the expansion of Listerism.
❖ Neither did Tyndall keep it quiet: he presented his observations to the Royal Society.
❖ His book, *Floating Matter in the Air in Relation to Putrefaction and Infection*, was counter to Kennedy clearly concerned with medical implications of airborne bacteria.
❖ (At least he had discovered another potential antiseptic.)
A.E. (Ernest) Duchesne

- 1896: Duchesne, a French medical student went so far as to inject penicillin into mice along with bacteria.
- The mice receiving both fared far better than those which did not.
- Again, the findings were presented to the scientific (this time, specifically medical) community. Duchesne reported them in his dissertation the next year.
- It's hard to say why this went unnoticed, but Duchesne's youth may have been a factor (he was 23).
- More likely, the sloppiness of the experiment was a consideration, along with the seeming impossibility of a miracle drug which could cure many diseases.
- One more factor must be considered: only one strain of the *Penicillium notatum* mold has the properties observed by Fleming, and Duchesne's appears to have been a different strain.
- Whatever Duchesne was using, it had some antibacterial effect, but it could have come up far short of Fleming's mold.

Andre Gratia

- 1925: Andre Gratia, a bacteriologist working at the university of Liege, Belgium, noted that a substance coming from a *Penicillium* mold killed anthrax bacteria.
- Ironically, he was working on methods of killing or controlling bacteria.
- Why did nothing come of this?
- No good answer.
- After 1928, and Fleming's publication of his findings, Gratia recalled his observation.
- It is easy for us to be amazed at what was missed.
- What these "missed opportunities" remind us, however, is that we live in a very different world from that of Tyndall, Duchesne, Gratia, and even Fleming.
- A certain skepticism about what might appear to be a "miracle cure" was healthy, especially for those researchers who also had practices on the side.

Alexander Fleming

- 1928-32: Fleming works on penicillin.
- (Kennedy is very good in his account, here.)
- Note, among the coincidences:
  - He leaves a petri dish out while on vacation.
  - The lab below is working with *Penicillium*.
  - It is exactly the right strain.
  - The weather cooperates.
  - Fleming is unaware of Duchesne's injections.
  - Or anyone else's discoveries (specialization can be a problem, at times.)
- Fleming saw it as an antiseptic and topical therapy.
- There it was left when Fleming moved on to other studies in 1932.
- Fleming must be given credit for two things particularly:
  - He gave penicillin a far more careful consideration than those before (and gave it its name.)
  - He maintained his particular strain of the *Penicillium* mold and distributed it for use by others.
Gerhard Domagk

- 1935: Domagk, a German physician and bacteriologist, announces the effective use of Protonsil, the first of the "sulfa drugs" (based upon aniline dyes, again, as per Erlich.)
- The first human test patient had been his daughter, who was gravely ill.
- The various sulfa drugs worked, but with potentially serious, or even fatal, side effects.
- (Toxicity actually appeared worse than it was, since a number of deaths were the result of contamination in the production process – led to federal regulation of drug production in a number of countries.)
- Domagk was awarded the Nobel Prize in medicine, but could not accept it according to the war policy of Nazi Germany.
- The effect:
  - Sulfa drugs gave the medical community a sense that a general antibiotic was possible.
  - However, their notable success (particularly in high profile cases: Churchill and Roosevelt) also mean that they eclipsed alternatives.

Howard Florey and Ernst Chain

- Florey had been informed that eye infections had successfully been treated by a bacteriologist named Paine.
- Various tests with Penicillin worldwide had proved to be inconclusive in establishing its medical value.
- A number of researchers were dissuaded from following up on promising tests. (R.D. Reid, for example, p. 278.)
- When Florey moved from Sheffield to Oxford he inherited a strain of Penicillin, which had been obtained by his predecessor, George Dreyer.
- Ernst Chain (a fugitive from Nazi Germany) also worked in the lab and approached Florey with the suggestion of intensive research based upon Fleming's findings.
- With the resources of Oxford at their disposal, and war looming, Florey and Chain headed a team which studied every aspect of penicillin in application.
- Including the internal use through the injection of mice (again.)
- Everyone in the department was injected for the first human test.
- Ironically, given the number of potential "discoverers," a controversy ensued between Florey and Fleming over the discovery of penicillin.