SEXUALLY TRANSMITTED DISEASES

INTRODUCTION AND HISTORY
Disease transmitted by sexual intercourse

☐ “Venereal Disease”

☐ Sexually transmitted infection
   more accurate, since not all infections cause overt disease but we usually can’t identify all infections
Origins

☐ Not only humans, of course
☐ Occur in all animals that reproduce sexually
☐ Magnitude varies with frequency of mating and number of different partners
☐ Causative organisms are all parasites
Parasites

A successful parasite doesn’t kill its host or make it awfully sick, at least not before it has been passed on to another host.
STD’s are really good at this!
Types of Parasites

Ectoparasites
   Lice, mites (scabies)

Metazoa (e.g. worms, flukes)
   not usually sexually transmitted

Fungi
Protozoa
Bacteria          Mycoplasma
Chlamydia         Viruses
Bacteria
Conjugation-Not really sexual reproduction, but allows exchanges

Figure 4.5. (a) Electron micrograph of a sporulating bacillus. The spore is the large, dark oval at one end of the cell; it is surrounded by a visible spore coat. (b) Under favorable conditions, a spore coat forms around the hereditary material of some species of bacilli. Once the spore has formed, the remaining portion of the cell disintegrates.

Figure 4.6. Conjugation in the bacterium Escherichia coli, as seen with the aid of an electron microscope. In this primitive type of sexual reproduction, a piece of hereditary information is transferred from a donor cell to a recipient cell, which may then incorporate this piece of information into its chromosomes; the result is a cell that possesses hereditary information from two different parent cells.

As you will read later in this chapter, conjugation resembles the sexual process of eukaryotic organisms in that it results in a recombination of hereditary material. But there are fundamental differences between conjugation and sex.
How far back in human history can we trace STD?

Archaeology

bones – typical lesions

Art - depictions of lesions - sometimes very recognizable

Written documents
Syphilis - Albrecht Durer - 1496
Great Pox
Origins of syphilis

Possibly introduced into Europe in 15th century

Records show big epidemic swept western Europe then

Skin ulcers and eruptions depicted as ugly spots

One explanation that makes a lot of sense- Columbus’ crew brought it back from America- the virulence of the epidemic made it look like a newly introduced disease. Other treponemal diseases – pinta, yaws, endemic syphilis not sexually transmitted.
Distinction between syphilis and gonorrhea

From 16\textsuperscript{th} to beginning of 19\textsuperscript{th} century mostly assumed to be one disease- only a few “dualists” thought they were two separate diseases.

Middle of 18\textsuperscript{th} century John Hunter, British surgeon and pathologist, inoculated himself with urethral pus from gonorrhea patient – and developed a syphilitic chancre.

Virchow, at turn of the century documented 2 etiologic agents
John Hunter
Origins – First Evidence

☐ Many ancient references to STDs

- Reference to “corroding ulcer” of genitals in men and women in Chinese medical writings from 2500 BC

- Hippocrates (c. 460-377 BC) describes disorders of urination, menstruation, pregnancy, and reference to “moist ulcers, particularly of the mouth and genital”

- Galen (AD 130-200) first to use the word *gonorrhea* and described as “unwanted excretion of semen” - although not the same as gonorrhea today
Origins – Middle Ages

- Gonorrhea thought to originate in middle ages probably as a result of mutation of non-virulent form
- Other potential STDs of middle ages include chancroid, genital herpes, and lymphogranuloma venereum
- Most treatments emphasized men (as women were regarded as impure) and involved different urethral injections.
  - “Take the milk of a women, a little sugar, oils of violet and barley water and administer it with a syringe” (John of Arderne 1306 – 1390; physician to Richard II)
15th Century

- Origins of syphilis thought to be in the 15th century
- Return of Columbus from the Americas in 1492 was followed by an epidemic of a new “French Disease”
- By 1495 syphilis raging throughout continental Europe
- Development of printing press and publications between 1450 – 1492 may have increased publicity on the epidemic (and therefore effected shape of the epidemic curve)
16th – 19th Century

- Between 16th and 18th century study of venereal diseases made slow progress
- Most doctors assumed gonorrhea and syphilis were manifestations of the same disease
- In 1837 French venerologist Phillipe Ricord established:
  - the specificity of the two diseases
  - first to differentiate the stages of syphilis – “primary, “ secondary,” and “tertiary”
16th – 19th Century

- Long after ravages of syphilis became clear, gonorrhea still considered a relatively minor disease
  - Doctors in mid-19th century believed it to be a result of excessive sexual intercourse and recommended marriage as a cure
  - Asymptomatic nature in women led to the idea that all women carried gonorrhea
  - French physician wrote of women “she is contagious without having been contagioned”

- In 1879 German dermatologist Alber Neisser identified gonococcus as the organism responsible for infection

- Subsequently shown that the bacteria could cause a number of ailments and gonorrhea now joined syphilis as a serious venereal malady
20th Century

- Although etiology and pathology relatively well understood by late 1800’s and early 1900’s treatments were limited
  - Syphilis treated with mercury, either orally, in vapor baths, or topically
  - Modern observers suggest that high doses of heavy metal therapy neared lethal rates and many symptoms attributed to syphilis likely the result of mercury intoxication
Origins – 20th century

- Limited therapeutics partly explains high rates of disease
  - No reporting but based on military data in 1909 the admission rate for VD was 200 per 1000 men and 1/3 of all days lost from duty resulted from these infections

- In 1911 under William Snow’s leadership, CA became first state to require anonymous reporting of cases

- By 1913 five states had regulations requiring venereal disease reporting

- Vermont had the most unusual plan, requiring all cases be reported and provided a 25 cent fee to physicians for each case
20th century

- Extensive “anti-venereal” crusade during WWI and WWII
  - “Fit to Fight” campaign during WWI – sought to dispel the notion that men must be sexually active to maintain health
    - “over-exercise or excitement of the sex gland may exhaust and weaken a man”

- Substantial amount of propaganda including films, lectures, pamphlets, and posters
Origins – 20th century

"Worst of the Three" U.S. World War Two poster comparing Hitler, Hirohito and VD, portrayed as the most serious threat of all
20th century

- U.S. Army poster circa 1940
20th century

VD can be cured

But there's no medicine for regret

What a sucker I've been!

I let 'em all down
20th century

- Marked decline in interest in the 30’s and 40’s but Thomas Parran (Surgeon General 1936 – 1948) brought issue to forefront, including:
  - Syphilis control program based on case-finding by the provision of free serology, prompt treatment, and examining contacts
  - Compulsory blood tests before marriage and during pregnancy
  - Sought funds for the Venereal Disease Control Act (1938) which authorized provision of federal funds for a comprehensive control program
20th century

- Treatment for gonorrhea and syphilis was revolutionized by the introduction of penicillin
- From 1946 there was significant reduction in the number of infections
- Mass testing policy for syphilis instituted in 1945 and by early 1950’s more than 2 million people had been treated
- By mid 1950s it seemed that venereal diseases, like other infectious diseases had yielded to the power of modern medicine
No Happy Ending

- Despite effective treatment venereal diseases became “problematic” again starting in the 1970s with reasons including:
  - Population movements, increasing affluence, promulgation of sex in popular culture → sexual revolution
  - Resistance to treatment, particularly in terms of gonorrhea
  - Increase in “second-generation” diseases including chlamydia, genital herpes, HPV, and HIV
PNEUMOCYSTIS PNEUMONIA IN HOMOSEXUAL MEN—LOS ANGELES

Since October 1980, physicians at 3 hospitals in Los Angeles treated 5 young Caucasian homosexual men for Pneumocystis carinii and mucosal Candida infections. The age range of the 5 patients was 29 to 36. Clinical cytomegalovirus (CMV) infections preceded the pneumonia in 4 of the 5 patients, and the 5th patient has grown CMV from an esophageal culture. Two patients died with persistent P. carinii and CMV pneumonia despite treatment with courses of Bactrim and pentamidine. Four of the 5 were previously healthy. The 6th patient (one of the 2 deceased) had Hodgkin's disease 3 years prior, was treated with radiotherapy alone and was considered in remission. He had no evidence of Hodgkin's disease on postmortem.

The 5 patients described herein did not know one another and had no common contacts or knowledge of sexual partners who experienced similar illness. There was no consistent pattern with respect to previous sexually transmitted diseases or prior antimalarial therapy. Four of the 5 had serological evidence of remote hepatitis B infections without hepatitis B surface antigenemia. Two of the 5 frequented homosexual clubs or bathhouses and had multiple sexual partners. The 3 cases who were studied had reduced numbers of T-cells and diminished in vitro proliferative responses to mitogens and antigens.
PNEUMOCYSTIS PNEUMONIA IN HOMOSEXUAL MEN—LOS ANGELES

Since October 1980, physicians at 3 hospitals in Los Angeles treated 6 young Caucasian homosexual men for Pneumocystis carinii and mucosal Candida infections. The age range of the 6 patients was 23 to 38. Clinical cytomegalovirus (CMV) infections preceded the pneumonias in 4 of the 6 patients, and the 5th patient has grown CMV from an esophageal culture. Two patients died with persistent P. carinii and CMV pneumonia despite treatment with courses of Bactrim and pentamidine. Four of the 6 were previously healthy. The 5th patient (one of the 2 deceased) had Hodgkin's disease 3 years prior, was treated with radiation therapy alone and was considered in remission. He had no evidence of Hodgkin's disease on postmortem.

The 5 patients described herein did not know one another and had no common contacts or knowledge of sexual partners who experienced similar illness. There was no consistent pattern with respect to previous sexually transmitted diseases or prior antimicrobial therapy. Four of the 5 had serological evidence of remote hepatitis B infections without hepatitis B surface antigenemia. Two of the 6 frequented homosexual clubs or bathhouses and had multiple sexual partners. The 3 cases who were studied had reduced numbers of T-cells and diminished in vitro proliferative responses to mitogens and antigens.

DISCUSSION

This development of P. carinii pneumonia in apparently normal hosts is distinctly unusual. The occurrence of this syndrome in gay men suggests an association with sexually transmitted diseases since such diseases are highly prevalent in this population. One such prevalent sexually transmitted disease is CMV which can be shed in semen. In one recent study from San Francisco, 34 percent of exclusively homosexual men were seropositive to CMV compared to 54 percent of heterosexuals. Furthermore, CMV is known to induce transient abnormalities of in vitro cellular immune function in normal hosts. The possibility also exists that in these patients another common unrecognized exposure-induced cellular immune dysfunction which predisposes to opportunistic infection. Sexual transmission of P. carinii is unlikely, but also must be considered.

We suggest that P. carinii be suspected as a cause of dyspnea and pneumonia in young homosexual men despite good health. We urge that any such cases or cases of FUD (fever of unknown origin) in homosexuals be reported to Acute Communicable Disease Control at 974-7941.
Pneumocystis Pneumonia — Los Angeles

October 1980-May 1981. Six young men, all active in a health club, developed Pneumocystis carinii pneumonia at 3 different sites of the body. Two of the patients died. All 5 patients were infected with the cytomegalovirus (CMV), which was detected by fluorescent antibody tests on lung biopsy specimens.

The New England Journal of Medicine

December 11, 1981

Original Articles

Pneumocystis carinii Pneumonia and Mucosal Candidiasis in Previously Healthy Immune Deficient Men: Evidence of a New Acquired Cell-mediated Immune Deficiency

Michael S. Gottlieb, John D. Weisman, Bruce S. Schectman, Philip S. Orenstein, and Andrew B. Sonne
The Tuskegee Syphilis Study

Brief Overview

Official Study Name: The Effects of Untreated Syphilis in the Negro Male

Purpose

To study the natural history of rural syphilis in the Black male

Study Population

Total: 600 Black men from Tuskegee, Macon County, Alabama
  399 positive for syphilis
  201 negative for syphilis (controls)

Timeline

Study occurred between 1932 – 1972 (40 years)
1929  Mercury and Bismuth are used as treatment options
  Cure Rate is <30%, toxic side effects, outcome can be fatal
1945  Penicillin becomes accepted treatment for Syphilis
1964  Declaration of Helsinki
The Tuskegee Study
Background - 1929

- Rosenwald fund conducted a pilot study looking at the diagnosis and treatment of syphilis in Black males
  - In 1900, Julius Rosenwald created the Rosenwald fund to supply monetary support in the development of schools, businesses, factories, and agriculture.

- 36% of the 27,000 residents of Tuskegee, Macon County, Alabama were infected with syphilis
  - One of the highest in the United States

- 82% of the county residents were of African American descent.
The Tuskegee Study
Background – 1929 (continued)

Dr. Taliaferro Clark decides to follow the men who were left untreated at the end of the pilot - it would be “valuable” to observe the consequences of no treatment.
- Dr. Clark was a well respected venereologist and chief of the United States Public Health Service (USPHS) Venereal Disease Division.

One of Dr. Clark’s objectives was to compare the findings of the prospective cohort to a retrospective cohort that had been done earlier in Norway with white men and women during a time when little treatment was available.
- The Oslo Study of untreated syphilis estimated that 70% of syphilitics went through life without any inconvenience of disease.
- But, the study did also show that there were acknowledged dangers of untreated syphilis in the remaining 30%.
- The study ended when arsenic therapy became available.
The Tuskegee Syphilis Study

Subject Selection and Maintenance

- In order to get potential subjects to participate, Dr. Vonderlerhr told the men they were ill and would be receiving free care for their “bad blood”.

- They were not told they were part of an experiment.

- The Tuskegee residents thought they were participating in a study similar to the pilot conducted by the Rosenwald Fund several years earlier.

- Incentives: transportation, free lunches, medical care

- Obtaining informed consent was not a required standard at this time
The Tuskegee Syphilis Study

Key aspects of Study Design

- 4000 men screened for tertiary syphilis – 399 men were enrolled.

- Tests performed on the subjects:
  - physical examinations
  - blood tests
  - lumbar punctures

- Vitamins, tonics, and aspirins were given as “treatment” for “bad blood”

- First years of the study – a few men received sporadic treatment with arsenic and bismuth

- The study was extended beyond the original 6-8 months in order for the investigators to observe the deterioration over time that results from untreated syphilis
  - Each participant was followed until his death; postmortem examinations were the endpoint
The Tuskegee Syphilis Study

Key aspects of Study Design

- Later on, a control group of 201 nonsyphilitic men were included.

- To increase recruitment, $50 burial stipends were added as incentives and each year that the men participated in the trial they received $25.

- Extreme measures to maintain participants
  - WWII: USPHS convinced Macon County draft board not to draft the men who were participating in the study.
  - Penicillin had become the widely accepted therapy and was being offered to other syphilitic men in Macon County; investigators rationalized that penicillin could be harmful for men who have syphilis for a long time.
The Tuskegee Syphilis Study
Stopping Tuskegee

- Peter Buxton wrote to the CDC concerned about the appropriateness of the study.
  - Peter Buxton was a venereal disease investigator for USPHS

- CDC did not respond to his concerns

- 1972: Failure of CDC to respond prompted Buxton to contact Jean Heller, reporter. She published an article regarding Tuskegee on July 26, 1972

- As a result of her article, the public was enraged and a committee was formed by the Department of Health, Education, and Welfare to investigate
  - The panel focused on 2 issues: no penicillin, no informed consent

- March 1973 – study ended when the men were given treatment