16/8

DISEASES AND DISCOURSE

Not Soldiers but fire fighters (Semino 2021)

Metaphors are used to think about things, perceive similarities and draw analogies between two ideas or things. Eg: 'I need some direction in life' comes from LIFE IS A JOURNEY.

War metaphors are commonly used when talking about COVID.

Metaphors are important devices in explaining & persuasion.

DIFFICULTIES ARE OPPONENTS — they can be fought with, struggled with, defeated or succumbed to. War is the most extreme form.

So, we use war metaphors — virus: enemy, doctors: army, dead people casualties

Such metaphorical descriptions can be useful in some contexts — can increase vaccination rates etc.

- presents problem as serious & urgent, & modify their behaviours
- framing (& effectiveness) of metaphor depended on 'resonance' and 'fit'.

Can also be counterproductive —

- increases fatalism, especially in long pandemic where a clear victory is not certain
- increase the attribution of guilt to a patient who does ~~cannot~~ recover
- people tend to support law enforcement over social reform

Perhaps this was useful in the beginning days, when extreme caution was necessary but not anymore

Fire metaphors work well for COVID. But Sports & Journey metaphors help to depict that it's going to be long & hard.

Specifically forest fire metaphors can be very useful —

virus : fire

victims / patients : trees

doctors / nurses : firefighters

Also, fire causes harm by 'spreading'. trees spread fire by spewing embers.

Fire metaphors can —

- convey danger and urgency
- distinguish b/w different phases of pandemic
- explain measures to reduce contagion
- portray a better role of healthcare workers
- outline post pandemic future.

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Lecture 3 - NM

Disease

Not at ease, lack of feeling healthy

Some things are called diseases. Some features —

- Discomfort & damage
- Deviation from normal
- There are a set of symptoms used to describe each disease
- prescriptive diagnosis.
- Prescribed treatment

Why are these things not disease?

Menopause - normal

Aging - normal

Osteoporosis - normal in old people
not so in young people

Until 1990s, osteoporosis was seen as a normal aging process in post menopausal women because it was recorded in 30-40% of women. Once it was defined as a disease, because it can be prevented and diagnosed,

Tumors - [illegible]

more women were treated for it.

So, the way disease is dependent on how we define / view a healthy person, which changes from time to time.

Homosexuality was only depathologised in late 1970s.

One of the bad things was that there were so-called treatments for homosexuality called conversion therapies that involved electric shocks, hormonal therapy and so on.

But removing the support of (v. powerful) medical institution was / is important.

ADHD — still up for debate, but tipping towards a disease. But we still don't know its pathology.

Once it's (or anything) accepted as disease, the patients get —

1) help & treatment
2) exceptions & benefits (financial)
3) to be a part of community
4) mental peace & ~~accept~~ alleviation
5) representation.

The moment industries (pharma & insurance) have a stake in how diseases are treated, this also affects what gets defined as disease.

Idea of disease can be thought at 3 levels —

1) Individual — for them, it's just the feeling of not well
2) Biomedical — this community is going to look at pathology, symptoms, treatment etc.
3) Sociological — the way a disease is viewed by society is not often shaped by the science

For COVID, pathology, aetiology, causative agent, treatment etc. was discovered and defined very quickly because we already had some understanding of similar diseases. But for others, this can take a long while.

More complex the disease (esp. mental health), the harder it is to define the normal, which makes it harder to define its pathology.
The society also affects the definition of 'normal'.

Other things in gray area – skin tone, infertility, indigestion, broken ankle etc?

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Lecture 4

Etiology - the discipline that deals with the cause of the disease

Etiological factors –

1. Genetic ~~diseases~~ causes
   Eg. Color blindness, Sickle cell Anaemia, Hemophilia, Huntington's, Cystic fibrosis
   They are heritable, but not always. Other than familial, it can also be due to sporadic mutations.
   The diseases are caused due to a particular mutation or allele present in the individual.
   These diseases can be mono-genic or polygenic.
   Cancer is often genetic, but a polygenic disease so it's hard to pin down the combination of genes that gives rise to the disease.
   Many diseases that have genetic predisposition - are often polygenic and harder to decipher.
   GWAS is often used to study this, but how effective is it?

Penetrance: the same mutation might not manifest the same symptoms with same severity.

2. Environmental / Lifestyle diseases

Eg. Diabetes, several cancer, PCOS, Hypertension, Silicosis, Chronic Obstructive Pulmonary Disorders (COPD) Obesity, Heart diseases, Atherosclerosis Vitamin deficiency diseases

These diseases are caused by environmental factors. The occurrence of these diseases are associated with certain places or behavioural factors.

Some diseases, like diabetes, hypertension etc. have lifestyle and genetic components, so it's hard to compartmentalise them.

BRCA1 - mutation associated with increased chances for breast and ovarian cancer.

3. Infectious diseases

These diseases can spread from one person to another because it's caused by a pathogen.

Pathogens are largely microbial.

Communicable - diseases that can spread from one person to another directly

So, all communicable diseases are infectious but not vice versa.

Pathogens

Virus - Dengue virus
Bacteria - S. typhii
Fungus - Candida
Protozoans - P. falciparum
Worms - tape worm
Arthropods - ticks, lice
Prions - Mad cow

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Lecture 4

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Idea of infections diseases

Definitely by Louis Pasteur's time — described the Germ theory.
He disproved the spontaneous life theory using swan neck glass containers, showing that meat broth didn't spoil when sterilised.
The idea of disease transmission had already existed.
John Snow - cholera epidemic of London.

Robert Koch
- Main push behind germ theory
- He worked on two acute diseases — Anthrax & TB
- He was also a very successful microbiologist.
- Anthrax is primarily a cattle disease, and it manifests as respiratory disease or skin ulcerations.

Koch takes blood samples and detects bacterium in infected individuals. He cultures Bacillus anthracis and infects healthy animals with cultured bacteria and with blood of infected animals.
He establishes experimentally the causative patnogen, and formulates — Koch's Postulates

1. Patnogen should only be found in infected individuals and not healthy ones
2. The patnogen should be culturable outside the host
3. Cultured patnogen when introduced to a healthy individual should cause disease symptons in it
4. If the patnogen (bacteria) is continuously cultured in lab, then it should still be able to infect healthy individuals.

This formulation was possible because he worked on bacterial disease!
Discovering the cause of a TB was a major achievement for Koch.

Burst size -

Around this time, lot of bacteria were being discovered and bacteriological methods were being developed

Virus

- They cannot survive outside the host, because it needs host machinary to reproduce
- Submicron in size (~100 nm)
- Fast reproduction
- Diversity in genetic material : DNA or RNA
- Structure : it's just genetic material covered with protein coat called capsid
- They are very host-specific because they have very specific receptors.
- They evolve rapidly because of their low-fidelity genetic replication, especially when it comes to RNA viruses. (RNA polymerases are more error prone)

Bacteria

- They are few microns large
- They can be cultured outside the host (exception: Mycobacterium leprae)
- They are single-celled, but they can come together and form biofilms which could be important for causing diseases
- They don't have subcellular structure ie. prokaryotes
- They also come in different shapes
- Nucleoid — their circular DNA is compacted into a tight cluster
- Gram positive & Gram negative bacteria - distinguishes bacteria based on whether their cell wall can hold on to a stain or not.
- They have cilia & flagella which allows them to move, but their microstructure is different from that of eukaryotes.

(08) - They have plasmids — which allows them to share features
↓ (virulence factors, resistance)
extra nucleoid DNA

- Reproduction: mostly asexual by binary fission
also sexual: translation, transduction and

- CRISPR CAS was discovered in bacteria and it's now being used for gene editing

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Lecture

3. Protozoa

Eg. Plasmodium - P. vivax & P. falciparum are most common ones that cause malaria in humans

They're 10s of microns large, eukaryotic and single celled.

Eg. Trypanosoma, amoebae

Protozoa can form cysts, so they can transmit through unfavourable conditions and when conditions are favourable, they develop and cause disease.

These pathogen have particular developmental pathways, so in malaria you get periodical fever.

They don't have cell wall, but a covering called glycocalyx.

4. Prions

They are misfolded proteins. They're not a living entity.

Due to some reasons, some proteins of the body get misfolded which makes them aggregate and affect the nervous system.

They are infective because one copy of misfolded protein can cause other similar proteins to misfold

Eg. Mad cow disease

Kuru in humans - thought to have come ~~as~~ because of cannibalism

Methods of Transmission —

1. Air borne : COVID, cold, flu, TB, whooping cough
2. Water : Cholera, Typhoid, Jaundice, Hepatitis, Dysentery
3. Contact : STD, Chicken pox, Monkey pox, Small pox
4. Vector : Malaria, dengue, plague, ~~rab~~ lyme disease
5. Food : Food poisoning, Botulism, Helminthic diseases
6. Abiotic : Tetanus, hookworms, leptospirosis
7. Livestock / Zoonosis : Respiratory illness (H1N1, bird flu), anthrax, cow pox
8. Medical : ESKAPE bacteria

- Airborne diseases are caused by bacteria / virus in droplets which are 0.1 - ~100s microns, which can stay in air or otherwise they dessicate pretty fast
Masks keep droplets out
- In water borne also, bacteria form aggregates / biofilms which are most infective, as compared to single bacteria
Water bodies get contaminated through fecal matter
- Contact based diseases get transmitted through a cut in the skin or through mucus membranes.
Viruses get ~~infe~~ engulfed by immune cells in the mucosal membrane. This allows them to infect cells and ~~and~~ take over host machinary.
Fungal transmissions don't need either — the spores germinate & grow on the skin when it's moist. Eg. Athlete's foot.
Immunocomprimised & diabetic people are more susceptible.
- Vectors : non-human animals that transmit diseases but don't ~~cause~~ suffer themselves.
Eg. Mosquitoes, Tse-tse fly, ticks (lyme diseases), fleas
Vector vs Reservoir - if an animal is specific and needed for transmission of disease, then the animal is a vector.

- Food contamination usually occurs through food handling But could also happen through meat (undercooked).
- Soil : Clostridium tetanii - lives in the soil
- Livestock, pets - they are sources of diseases sometimes There are also reservois animals
- Medical : Some pneumonias are transmitted through ventilators Bacteria are circulating in hospitals. So the medical infrastructure is encouraging the spread of diseases.

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Lecture

Nosocomial - infections that are picked up from hospitals

Methods to stop spread of diseases

Hygeine	Vector control	Prophylaxis
Sanitation	Vaccination	Probiotics
Physical distancing	Education	Lifestyle changes
Culling animals	Chemotherapy	Surgical interventions

Most methods are preventative measures; the only effective modality to control diseases after its occurrence is by using chemotherapy which is a treatment measure.

Against microbes -

Antivirals : stop the infectious agent from multiplying or reinfecting the cells

So, most drugs stop the pathogen from multiplying to control the disease in an individual.

But there are some diseases for which there's no cure -

Prion diseases	Rabies	Tetanus
Dengue	Some hepatitis	Herpes.

So, we try to manage the symptoms instead of trying to cure them.

Pathogens need hosts and use them for protection, nutrition etc.

But why do pathogen cause harm?

Many microbes in our body are commensals. Some of them cause pathology (pathogenesis) and their main goal is to spread from one person to another. And they cause a lot of symptoms to make this happen —

eg. Cholera toxin - diarrhea : mangement - ORS (stay hydrated)
Virus/bacteria - respiratory symptoms : cough syrup, anticongestion meds

Pathogenesis due to — mechanisms for spread of pathogen
immune reaction of the body.

The inflammation / immune reaction of the body also causes a lot of pathology — fever, inflammation (heat, pain, swelling, colour), fibroids in lungs during TB.

To manage this, we use anti-histamines, anti-fever meds and steroids (immunosuppressants).

This manages the disease and it's not a cure because these interventions are not directly eliminating the pathogen.

Prophylaxis - the same chemicals used as cure are used as a preventative measure

Vaccines

Molecules that are used to generate an immune response against some pathogen before they can actually infect the person. They are a very specific form of preventative measure.

Types of vaccines —

- attenuated pathogen : weakened form of the pathogen
  eg: Polio, BCG
- Antigen : the antigen, a part of pathogen, is injected into the body to generate immune response.

Vaccines are also more expensive in terms of production, distribution and administration.

But vaccines can't be made for all diseases, and they're more invasive than other preventative measures.

When a medical practitioner comes across a new disease / symptom

- eliminate known etiologies
- give antibiotics & try to manage symptoms
- isolate person, grow bacterial culture
- environmental or family history?
- Could be viral — detect some virus (comparing against known virus)

All of this is an empirical process, relying heavily on known information.

This is what happened during COVID 19.
Within 6 weeks, we had the entire sequence of the corona virus (using lavage samples).

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Lecture

COVID was very similar to the SARS epidemic and the previous knowledge we had from dealing with that.

Discovery of pathogens that don't follow Koch's postulates —

1. Gastric ulcers
Wounds are caused by physical disruption whereas ulcers are caused by inflammatory response.

Symptoms
Severe pain, nausea, vomiting blood, acidity

Before 1970s, this was thought to be caused by bad eating habit, bad nutrition and stress.

But 80% of cases are caused by bacterial infection, Helicobacter pylori. Marshall & Warren (Australian physicians) discovered the bacteria, but no one believed them (beuz pH!)

So, Marshall drank a culture of this bacteria to prove it. He developed Gastritis and was cured by antibiotics.

They got a Nobel in mid-2000s, for discovering that such a common disease was infectious, and prevent gastric cancer (which is caused by chronic inflammation).

Why was the misconception around for so long?
- infectiousness is low, because transmission is less efficient
- it was strongly beleived that it's a lifestyle disease
- it's a chronic disease

Complication 1: 50% of people have Helicobacter in them, and don't have the disease. This violates Koch's postulates. Usually, they're a non-virulent strain, in a smaller quantity.

2: Removing Helicobacter from healthy individuals increases acidity and causes Gastro-oesophagal Reflux disease (GERD) which increases oesophagal cancer risk.
So seems like humans are at equilibrium with this bacteria.

2. Clostridium difficile [Cdiff]

It causes chronic diarrhea, unlike Salmonella, shigella, E.coli, amoeba etc. which causes acute diarrhea.
This is also called hospital-associated or antibiotic-associated diarrhea. Cdiff is found in large intestine. When you take large doses of antibiotics, it kills E-coli and Bacteriodetes in the colon, and Cdiff (which is Gram +ve ⇒ forms spores) hyperproliferates in the colon and causes inflammation (colitis).
So, the normal flora of the body compete with harmful pathogen and keep them from causing harm.
Cdiff is very resistant to most antibiotics.
Probiotics are commensal bacteria which prevent growth of pathogen. so they're adminstered with antibiotics.

Faecal microbiome transplant — an experimental approach to deal with diseases where we're not trying to kill pathogen anymore, but instead introduce more bacteria instead of sticking to chemotherapy.

Opportunistic infections

Diseases caused by certain microbes that affect only when the immune system is compromised. There also violate Koch's postulates.

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Lecture

Scientist biographies

Knowledge is not final or definitive, it's evolving

Discourse — general idea : discussion or conversation
also a collection of

Why colonialism and medicine?

- Colonialism created conflicts between important ideologies that differed significantly
- Modern medicine was spreading with colonialism
- We are a post-colonial country.

Terminology

1. Colony : a land controlled or politically governed by a more powerful country often far away
   - Metropolis vs Periphery
   - There has been a long history of trade, travel and expansion of empires. The colonialism we're discussing came with rise of capitalism and the movement of goods, capital and people moved from periphery to the metropol.
   - The colonies suffer and the metropol gets richer and bigger.

Types of Colonies

- Settler colonies : people from metropol settle in the colony & take over. Eg. Canada
- Administrative colonies : colonists only administered the land Eg: India
- Hybrid : a mid-point between the two Eg: South America

→ Harrison's essay :

Difference between East and West Indies : colonisers were ready to accept that India might have had some knowledge in the past, so they could adopt some things. They were not even ready to consider that African slaves might have had any medical knowledge.

→ The Othering :

Colonisers differentiated between an 'us' and 'them' to justify their actions of colonising.

Macaulay - wanted a class of Indians who had English tastes but still inferior to Europeans.

William Jones - Orientalist

→ Hegemony : Gramsci's idea : cultural idea / domination through which people impose their own worldview on others because they think it's beneficial to all.

→ Post-colonial (temporal) vs Post-colonial (contextual)

Colonies were not equal, neither were the colonised people at all times. People have been oppressed by the state during and after colonialism

→ Is there a golden age we can aspire to go back to?

→ Neo-imperialism

Vespucci & America : 1580 Engraving

Biomedical health

- Humoral health
- Miasma theory
- Contagion theory
- Germ theory
- Acclimatization theory: by spending enough time in a colony, your coloniser will become immune, but lose their morality in turn.
- Nosology

Colonialism and Medicine

- Uneven "modernity" and tradition; subject & citizen
- Colonialism was not one way — there was assimilation, oppression, resistance & negotiation
- Tropical medicine: epistemology of western medicine & influence on colonial policies.
- Colonialism also caused epidemics — small pox and syphilis exchanged b/w South America & Europe

History is tentative, not absolute

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Lecture

- Anxieties of the colonisers
  - anxeity that they will lose their morals and become weak or 'go native' / moral degradation
  - anxeity of colonised - loss of identity
- Vaccines are more invasive than other measures
  Invasive procedures made the people reluctant to accept medical help.

Chapekar brothers: very strict quarantine measures against the plague, homes burned, bad treatment in hospitals, not segregation etc
Brothers assassinated the plague commissioner.

Ballingan : Hysteria

* Deepak Kumar essay

- How 3 natives reacted to western (Maratha Prince, Math Prof, Medic)
- Chronological development of conflict & contact of systems
- Institutionalisation and codification — doctor registration, selling medicines at fixed price.
- Upper caste / Urban - Rural divide when it comes to accepting Western medicine
- Revival of native medicinal systems along with resistance to the colonisers
- Ayurveda & Unani practices were forced to accept medical practices, but not the other way around.
- Census is a way of state control, which was widespread along with vaccination etc.
- Rural masses continued to rely on indigenous treatments because the state didn't have enough resources.
- Proposition to train hakims and vaids, but allopathy doctors protest strongly.

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Lecture

Mark Harrison's essay

- Relationship between race and disease
- Acclimatization (Enlightenment philosophy)
- Anxiety of the colonisers and hardening race boundaries.

He analysed medical texts by European medical men situated in India & West Indies [different types of colonies].

Curtis: European classification doesn't make sense to Indian diseases
Different hepatitis

Paisley: Cholera presents differently in Madras as compared to Europe

Ballingall: Dysentery

Lecture 15/9

- Racial pathology : different races get different kinds of diseases and symptoms
- climates makes people slothful
  no appreciation of sanitation & cleanliness
- Armstrong : acclimatization is possible
- Knox : acclimatization is not possible
  races are basically different species
  settler colonies not possible
- Muting happened in the hot season
- Pessimimism ↑ Acclimatization ↓

Notion of deities eradicating diseases.

Eg. Manasa devi — snake bites
Shitala - pox goddess - broom + pot of water - vindictive.
Mari-aai - plague goddess
Khem-Adkhal - water borne epidemics
Khokla-ai - cough diseases.

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Lecture

Epidemiology

It's the study of -

- spread
- distribution (geography & demography)
- temporal dynamics of diseases,

and how these patterns can be used for interventions to control the disease.

They look at observational and experimental data, and the approach could be analytical or descriptive.

Three terms often used in epidemiology -

Endemic Epidemic Pandemic

There's no fixed category. they're described relatively.

Endemic : fixed rate of occurrence in an area, over time.

Epidemic : In an area, when there's an outbreak or, sudden surge of cases

So, even an endemic disease can become an epidemic.

Pandemic : when outbreak in one region leads to an outbreak in another region, that's significantly disconnected, then it's a pandemic

With increasing globalisation, there's increasing risk of pandemic.

Epidemiology through the lens of Cholera

→ Caused by : Vibrio cholerae

comma-shaped, motile (with flagella)

Naturally found in warm, marine water

Abiotic reservoirs — so it's harder to control

2 circular chromosomes : not diploid ; one of the chromosomes has the toxin that causes the disease

Over 200 serogroups (strains that elicit a particular antibody response), and only 2 cause disease, because they're toxigenic.

→ Symptoms

Watery diarrhea

Nausea / vomiting

Dehydration

There are 10^9 bacteria per ml

→ Etiology

The bacteria secretes cholera toxin which hyperactivates CFTR (Cl^- ion channel), so in the digestive system, the ~~water~~ body starts throwing out a lot of water.

This is pathogenesis caused by the spread of the pathogen.

(20) →

Cholera shows endemic, epidemic and pandemic patterns

There have been 7 known cholera pandemics

Recent pandemic caused by 'El tor' strain, and before that by 'classical' strains.

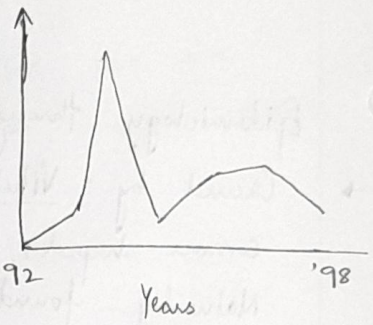
John Snow : epidemiologist who did contact tracing in London, and localised the cause to a single hand pump.

↓

This was caused by the 3rd Cholera pandemic, which was spread through ships carrying carriers.

→ Cholera epidemic in Argentina (1992 - 1998)

This epidemic was caused by strains foreign to Argentina that was introduced. The population equilibrates with the endemic strain. This is a big economic burden.



→ Cholera as an Endemic

It's endemic to Bengal & Tamil Nadu, which have a lot of rivers / marine environment, reservoirs for cholera bacteria. Adults have developed immunity, but children are very vulnerable, & child mortality due to cholera is still quite high.

Increased cases during monsoon — because of more mixing, worse sanitation & lots of water.

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Lecture

SIR Model

To predict whether a disease is going to become an epidemic or not.

This is a kind of compartmental model

A population of N individuals is divided into 3 compartments — Susceptible, Infected/Infective & Recovered/Removed

Over time, we want to track changes in the number of S, I & R people, so we come up with mathematical expressions to do so.

Assumptions:

1. $S + I + R = N$

It's a closed population (no migration) and we assume there's no birth or death during this period.

$\Rightarrow s + i + r = 1$ where $s = \frac{S}{N}$

2. Susceptible can catch disease, infected can give disease to others and recovered/removed people can't give disease to anyone

3. All interactions are random and interaction rate is constant. Recovery rate is also constant.

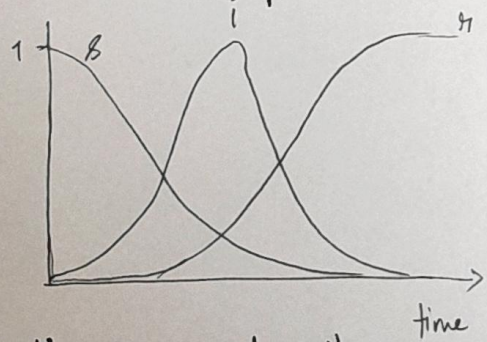
Consider b: per day interactions made by 1 'I'

$$\frac{ds}{dt} = -b \cdot i \cdot s$$

$$\frac{dr}{dt} = k \cdot i$$

$$\frac{di}{dt} = bis - ki$$

At the start of an potential epidemic, $I \ll N$ & $S \sim N$.



The shape of the curves is determined by values of b and k, which is determined by looking at real world data.

If $\frac{di}{dt} > 0$: epidemicity

$\frac{di}{dt} = 0$: endemicity

$\frac{di}{dt} < 0$: infections going down.

$$\frac{di}{dt} > 0 \quad \Rightarrow \quad \underbrace{(bs - k)}i > 0$$

$R_0 = bs - k$

Reproduction value (R_0) : no. of people an infected person can infect.

So, we want to reduce b (isolation, barriers), increase k (better healthcare) and reduce s (vaccination). These interventions would reduce the epidemic

Limitations

- Assumption that rate is constant, particularly b
- R → S is also possible
- I pool is v. small, so changing initial N might change I.
- No spatial heterogeneity, probability of infecting other people
- Not including abiotic / biotic reservoirs or vectors
- Different susceptibilities
- This model rests on the reliability of data

6/10

23A

Lecture

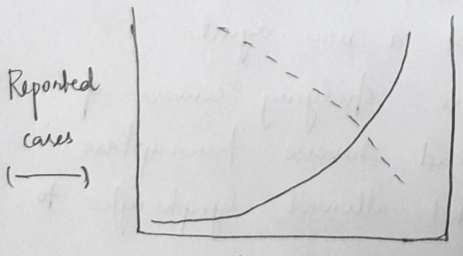
Early days and discovery

- First reported case: Los Angeles published case study in a journal in 1981
- Five homosexual men who were "healthy" came down with a series of infections.
  - Pneumonia caused by pneumocystis fungus – colonizes the lungs and earlier reported only in immunocompromised people or those who were on immunosuppressants
  - Mucosal candidiasis: Candida is part of normal flora, but can overgrow to form thrush
  - Cytomegalovirus (CMV) – infects eye & causes blindness. Also only affects immunocompromised people.
  - Kaposi's sarcoma (skin cancer) – caused by a virus here

Only common factor among the patients was that they were homosexual

Other such cases were reported in coastal cities & economic hubs. Some of these are also seen in auto-immune diseases because T_H cells are regulate & suppress other immunocytes.

It was called 'gay disease' – narrative built by religious institutions in reaction to Stonewall riots



Very alarming to the medical community due to high mortality rates

Puzzle: why were only men catching the infection?

What did medical professionals do?

→ Studied immune system of individuals — all had low counts of T_H CD4 cells. T & B cells are part of adaptive immunity. T_H cells secrete cytokines and alter activity of other immune cells.

22B Certain groups of people were reporting high frequencies of AIDS-like symptoms –

- homosexuals
- intravenous drug users
- people from Haiti
- Mothers → foetus

AIDS was an almost certain death sentence.

Due to high numbers of infected homosexual men, a commentary started on it.

AIDS was named before HIV was discovered.

Syndrome: complex set of symptoms that tend to co-occur without a cause.

acquired: individuals in the near past were healthy, not symptomatic

Thought to be an infectious disease due to –

- sperm in human blood: didn't explain disease in heterosexuals and IV drug users.
- drug use: inhalant drugs were predominantly used by gay men symptoms caused by lifestyle choice (inhalant drugs) correlated to risky sex.
- infectious agent: due to localised pockets of infection (coastal cities) + demographic affected. Hepatitis epidemic had just settled down in the US. Similar demographic → new agent!
- an already classified disease (like CMV) that could be causing new symptoms, not a new agent.

Luke Montagnier and Robert Gallo were studying cancers of lymphocyte. David Baltimore discovered reverse transcriptase

Gallo came up with a technique that allowed lymphocytes to proliferate outside the body.

↓

Lymphocytes from AIDS patients had RT ⇒ definitely caused by RNA virus / Retrovirus.

↓

Ruled out previously discovered retroviruses, discovered a new virus → HIV.

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(23)

HIV - Viral structure, Infection and Pathogenesis

Mortality - nearly 100%

HIV - lentivirus : family of virus that have evolved to inject their genome into the nucleus directly.

HIV - positive ss RNA genome
i.e it can be directly read by the translation machinary to produce proteins.

It has 2 copies of the same RNA strand.

The RNA and proteins are covered by capsid and in turn covered by matrix protein and host lipid membrane.

The virus also inserts specific proteins - gp120 - gp41 - on the outermost lipid membrane.

Matrix ~~protein~~ layer is important for information transfer.
There's protease outside the capsid, inside the matrix which processes HIV proteins into their mature forms.

RNA strands, Reverse Transcriptase, Integrase and some other proteins are bound up into the capsid.

Viral genome
It's very small and concise so it can be packed into a small space It has multiple reading frames and takes advantage of host splice machinery.
The translation results in a few large proteins which are then chopped up by protease to produce active proteins.

Gag - matrix proteins

Pol - RT, integrase.

Env - gp120, gp41

Other polypeptides - tat protein : decides when the virus becomes active

(28) Replication cycle

If HIV cell doesn't find its host cell (CD4), then it'll get cleared from blood stream in ~30 mins.

gp120 protein recognises CD4 receptors on T-helper cell.

gp120 - CD4 is a weak interaction, so it needs to bind to co-receptors on T-helper cells (CCR5 & CXCR4) to clamp down and enter the cell. ↳ chemokine receptors

It may also bind to other receptors such as lectins

When the virus enters the cell, it has lost its lipid layer and matrix proteins are disturbed, which signals the same to the capsid.

RT gets activated inside the capsid † so that RNA → ds DNA

Then the capsid interacts with nucleopore complex, so integrase and viral DNA enters the nucleus and viral DNA is integrated into host DNA.

This can lie dormant for years, while the T cell replicates and each T cell has a dormant copy.

Viral transcription is inefficient, but transcription factors (like NF-kb) which are secreted when T cell is activated, these Tx factors increase viral transcription.

Once activated, viral DNA is transcribed & its proteins are synthesized and packed into capsid.

Then these virions bud out of the cell as a mature HIV virus.

1 T cell can produce 10,000 virus.

We've found inhibitors for almost every single step in the replication process. These inhibitors are given in combination during Anti Retroviral Therapy (ART).

This is because certain parts can mutate very quickly.

ART only acts on replicative part — so it can't do anything to dormant virus, i.e. not curative.

Also, since HIV mutates very fast ⇒ over the lifetime of an individual, they might develop a resistant virus.

Cutting edge treatment
- Modify CCR5 co receptor using gene therapy or stem cell transplantation.

13/10/22

Lecture

Real people, complex characters

Heteroglossia (Bhakhtin) – allows for different perspectives to come together : medical technical & rural Tennessee

Author's perspective
- unsure about his status
- perceptive
- empathetic
- internal struggle

Memoir : a part of one's life, or experiences regarding a field of experience

Genre

Story – events that occured
Plot – the way that those events are put together

The novel is a memoir, but definitely fictional.

The novel has characters – their story – not just data narratives that makes you want to read

The place is also very important – nature, veterans, tobacco, mines, trailer parks etc

Author vs Narrator
↓ ↓
Real world person Storyteller – exists only in fiction.

This novel is a first-person narrator – perhaps more personal, but colours our perception and its only limited to his/her experience, as compared to a third person narrative

(26) What constitutes the narrator?
- set in rural America in 1980s
- medical speciality
- heterosexual man
- race (foreigner)
- motivation and preferences

focalisation — saying other people's story through someone else
first patient — not even named

19/10

Lecture

Red Cross — produced an informational

The novel individualises all the patients, brings out their personalities and tells their stories.

THE CONNECTION: barely tolerant, people break windows & slash tires
media always reports incidents & people at connection

Author: admits prejudices.
J-eleven employee — uncomfortable everywhere
Narrator: uncomfortable while entering, but ~~also~~ not when answering questions, but again when he's on the floor.
Connection: people could be out in the clubs, but not a natural setting by any account

The 'othering' of homosexual people homogenises them, but this episode brings out the differences.

Gordon: support from family, community (father in denial)
more than just the label — gifted, ambitions
sees Jesus, gets baptized
orchestra metaphor
his death episode
whole story is from Essie's perspective — we don't know what Gordon is feeling

Lecture

Ways of thinking about diseases –
- media representation
- public attitude (stigma)
- impact on caregivers
- religion
- epistemology of disease
- demographics of patients
- activism

Ethical perspective — discrimination between differently diseased people.

Scotty Dows – AIDS dementia.
ICU faculty recent treating a DNR, demented patient
Nurse: "why are we going on?" – first time people are taking out their resentment on him.

family's reaction to his work – AIDS as his mistress.
Look up: Dominique D'souza, Sunidhi Solomon

Johnson's case
Similarities w/ Gordon –
- support from community
- vision of Jesus
- referred to by other people.

Differences – Gordon was passive, Johnson very active
Desperate to keep it a secret – for the fear of being secret
Denial (G), Johnsons are okay with it
'Guilty' ~~and~~ v/s 'Innocent' victims
Difference in how Abraham treats them.
↓ pg. 250 – introspecting his own biases for treating the Johnsons better

Doctors → Saviour complex
Narrator: not very comfortable with deathbed conversations. Always talks about how his patients die. Wants to understand death.

(28) Lecture — 26/10/22

UNAIDS — funds research, outreach programmes, on the ground work and collects data

Epidemiology

In South Africa, Zimbabwe: proportion of HIV infected individuals is quite high.

HIV is a chronic infection

They have several new infections in a year — countries have not been able to control spread, because they're not getting the antiretroviral drugs they need.

Number of deaths (transition to AIDS) are also looked at.

HIV is not a single pandemic — different countries are troubled with local problems, have different rates of spread, control measures etc. ← mainly based on availability of antiretrovirals

Demographic affected —

- More women in Africa suffer from HIV

Gay population in the US had already been through hepatitis epidemic. So, mechanism of corrective action was already established for this demographic. So numbers decreased in this demography.

Number of HIV cases were high in Haitian immigrants

In Africa, women were also affected because of high heterosexual spread

Spread and demography is based on movement

HIV — came from Simian Immunodeficiency Virus (SIV).

SIV infected chimps, gorillas, monkeys etc.

Found in Africa, yet reported in the USA first.

Why was it not reported in Africa?

In 1950s, it was just emerging from the clutches of colonialism
↳ routine blood collection to detect malaria showed antibodies against HIV, but this went undocumented

Transmission:

- Blood to blood contact : >50% chance of transmission
- semen
- breast milk
- woman → man transmission is lower; man → woman is higher.

Polygamy was a practice in Africa, so high spread to women
Prevelance of other venereal diseases (Herpes etc) increased the chances of getting HIV, because open sores and cankeroids would get in contact with infected semen

In 1950s in Africa, sublineages of HIV already existed. Meant that it had been circulating in Africa for a while
Transmission might have occurred in 1920s in across the world.
Africa — only continent with generalized transmission
cannot trace who you got the infection from

SIV. causes AIDS in mongabeys and other monkey species.
from Chimpanzee
Lentivirus has not equilibrated with human population, but manages to spread due to incubation period.

1. Lentiviruses in circulation in wild apes transmit like HIV but do not cause symptoms / AIDS in humans.
2. Hunters coming in contact with blood while cutting raw meat?
Need multiple succesful contacts for zoonosis to occur.
Chimpanzee were normally not consumed, since they were gamey, but people were forced to hunt them when driven to starvation by the colonizers.

3. Human to human spread – around 1% chance of transmission through heterosexual sex

4. Colonizers were vaccinating people, but <u>did not change needles</u> : acted as an amplifying event for HIV.

5. Movement of people : through railways, along the congo river → pockets of HIV due to river movement and transport

6. Commercial sex trade and establishment of brothels due to ~~gro~~ more money (via trade).

7. It was not caught early on as an epidemic due to lack of communication b/w hospitals

8. After independence from colonizers, Congo has no doctors. So they reach out to French speaking doctors in countries like Haiti — doctors bring it back to Haiti

9. Americans travel to Haiti to party, especially gay men, bring it back to America

Prev class: HIV in Africa

Epidemiology: skewed sex ratio, no. of cases, mortality rate
patterns of spread

1920s - first crossover
1950s - first antibodies discovered

The virus has crossed over twice from simians to humans in Africa -

HIV 1 - from Chimpanzee, Sub-Saharan Africa
HIV 2 - from Mongabeys, mostly occurs in Western Africa
much less transmission rate

There have been potentially 7 crossover events from monkeys to humans. Because HIV has high mutation rate, different strains have recombined.

Challenges in Policy-level intervention in South Africa

1990 - discovered Azidothymidine (AZT), the first effective antiretroviral against HIV virus. It binds to reverse transcriptase competetively.

AZT should've prevented HIV +ve patients from developing AIDS and kept infection level low. Highly Active Anti Retroviral Therapy (HAART) did this for people in the west, but not in Africa.

Hinderance to access — cost of the drug (because of patents)
But when there's an epidemic, the govt. provides medicines at subsidized rate or for free.

In 1990s in South Africa, Mandela's govt. passed the Medicines Act to face the burden of very high cost of ART meds.
This allows them to import medicine parallely — buy medicine from poorer countries at a price cheaper than the company. But this was in violation of world trade org.

rules, even though it helped suffering people. US lobby got pissed off and put an embargo on SA.
In 2000s, Clinton lifted embargo, but pharma companies sued the government, but didn't win the suit.
Then they also started producing generic meds. So, it was only in early 2000s that South Africa got medicines in the first place.

SA govt should have regulated who gets medicine. But the next president, Mbeki was an AIDS denier (AIDS denialism — AIDS is not caused by HIV because it stays dormant for so long). So he didn't institutionalize giving medicine to HIV+ pregnant women.
But ultimately did it because of public pressure.
3 lakh people could have been saved had he implemented this better.

Just the presence of a medicine doesn't ensure that the disease goes away — policy is important.

Things are much better now, in India as well — making sure people get ART meds regularly. There was an Act passed in 2017. [HIV-AIDS Act].
This also criminalises discrimination against HIV+ people.
There's also policy for preventing AIDS — targeting sex workers and gay men (after decriminalisation of 377).

Treatments

- Behavioural interventions — hard to implement quickly
- ART — prophylaxis, keep viral load below transmission levels
- Screen blood, sterilise needles / disposable needles
- Vaccination: we don't have a vaccine because
  - high mutation rate — wide antigenic repertoire
  - antigenic display is limited because of lipid layer

- the vaccine should help immune system clear all of the incoming virus, because even if one virus integrates with immune system, it can skyrocket about ID (infective dose). The efficacy dose rate would have to be ridiculously high.

Cure is also hard because virus develops resistance against drugs.

2/11/22

Lecture

Revision of HIV. AIDS module and the novel.