Viruses, Viroids & Prions

nonliving **"infectious agents"** capable of causing diseases

too small to see with regular microscope

even though they are not alive; we still use the terminology of biology to describe them and how they work

Viruses

viruses are not alive (remember characteristics of life)

→ they do not consist of cells
→ they do not contain both DNA and RNA
many completely lack DNA
→ they do not grow
→ they do not take in nutrients or release waste products
→ they don't have the machinery to reproduce themselves

viruses are strict parasites

→infect virtually every form of life, every kingdom

viruses are by far the most abundant and diverse of all "genetic entities"

viruses are millions of times more common than previously thought

they are also the smallest

→ millions could fit on the head of a pin

yet if you stacked all the world's viruses end to end they would reach a distance of over 200 million light years (almost to the Andromeda galaxy)

History of Study of Viruses:

remained part of the invisible world until late 1800's

1880's: Pasteur knew that rabies was caused by something smaller than bacteria

1890's: viruses were first isolated

1930's: viruses crystallized;

life doesn't crystallize, cannot be living organisms

1940's: viruses first seen in with newly invented electron microscope

most of our knowledge of viruses has come in the last 50 years

Viral Structure

size: millions could fit on head of pin

20 – 14000 nm (0.2 – 14 μm)

bacteria are 1000's - 10's of 1000's of times larger (1-10μm)

there may be about 100 Million different kinds of viruses

all viruses are made of at least 2 parts;

1. an inner core of **nucleic acid**
2. enclosed in **protein capsid**
3. some also contain **lipoprotein envelope**

1. Nucleic Acid

viruses contain a single kind of nucleic acid

can be circular, linear or in several separate segments

can be DNA or RNA, never both

only a few genes:

viruses don't need lots of genes like living cells

they use the genes, synthesis machinery and enzymes of host cells to reproduce

no one gene is found in all viruses but a small group of genes are found in most viruses

most viruses have 6-10 genes

smallest have 4, largest have 100's of genes

eg. smallpox has 200-300 genes

(but bacteria, eg. *E. coli* 16 time more)

includes few 1000 to 250,000 pairs of nucleotides
(E. coli → 4M pairs of nucleotides)

2. capsid or **protein shell** surrounds the nucleic acid

makes up most of the mass of the virus particles

many different shapes of capsids

3. some covered with viral **envelope**

derived from membrane of host cell

Origin of Viruses

80% of the genes found in individual virus particles are completely unknown and not found anywhere else, not even in other kinds of viruses

we used to think that viruses were degenerate fragments of their hosts DNA

most virologists now think that they arose as independent genetic entities

probably prior to the first living cells

we cannot construct an "evolutionary tree" of viruses

each virus seems to be a random grab-bag of genetic material assembled from a worldwide pool of nucleic acids

this and their rapid rate of mutation make viruses the most fertile sources of novel nucleic acid sequences

10-20% of the DNA in all life forms seems to be derived from viral DNA

these viral genes apparently play important roles in the function and evolution of many life forms

some now believe that life arose, probably many different times, from a 'primoridal stew' of virus particles trading genes and continuously generating new and more efficient metabolic pathways

Typical Virus "Life Cycle":

1. attachment

onto specific host cell
→ its what makes them host specific

2. penetration

either by

1. injection of nucleic acid
   →injection can by hypodermic like

2. enzymes may dissolve a hole in cell membrane of host

3. entire virus particle gets taken in by phagocytosis triggered by virus

3. Synthesis of new virus particles

once inside, host protein synthesis is stopped

then virus has host make proteins to:
seal cell puncture wound
copy viral genome
make capsid proteins
produce enzmes for lysis of host

enzymes needed for protein synthesis, ribosomes, energy production are supplied by host cell

4. Lysis

release of virus and death of host cell

a single virus can give rise to up to 1000 new virus
particles from one host cell

(average = 50-200)

duration of viral life cycle in host cell averages 20-40 minutes

polio: 6-8hrs
herpes: 12-30min

some viruses remain dormant for a time in host cell and become part of the hosts genome temporarily

Role of Viruses in Biosphere

viruses outnumber bacteria 10 to 1 in most ecosystems

est 10 quintillion (1 followed by 31 0's)

viruses infect every form of life

Beneficial Effects:

eg. bacterial viruses play an important role in protecting our bodies

our membranes are filled with bacteriophages (viruses that kill bacteria) by destroying invading bacteria

eg. we are learning that viruses play a major role in transferring genes from one organism to another

often a major part of adaptation and evolution of life

when viruses are replicated by host cell the new virus particles are often released containing genes from their host

when they infect a new host cell those genes can be introduced into it

in many cases the virus lies dormant for extended periods allowing the host to incorporate the new genes into its genome

in this way viruses have been a main force in the evolution of life on earth

eg. a sea slug is able to use the chloroplasts from algae that it eats only because it has incorporated a couple of essential genes given to it by a virus

eg. viruses also play a huge role in controlling nutrient and energy cycles in the biosphere

viruses are the most numerous entities in the ocean

→ a thimble of seawater contains millions

→ placed end to end, all the virus particles in the ocean would stretch into space further than the nearest 60 galaxies

eg. viruses infect and kill ~20% of algae and cyanobacteria in the ocean every day

such large scale death of these microorganisms profoundly affects:

→ the makeup of the oceans microbial communities

→ the cycling of nutrients in biogeochemical cycles

→ sedimentation and accumulation of biogenic deposits

eg. white cliffs of dover

→ affect global climate by removing 3 gigatonnes of carbon from the sea each year

a completely new kind of virus has been recently discovered = **pandora viruses**

they are the largest viruses known, they have almost as many genes as some bacteria (1000-2500) , and 90% of their genes are new to science

Pathogenicity of Viruses

pathogenicity = how easily disease is spread

most viruses are easily spread

most common means of transfer is by contact with secretions from infected person

eg. Colds & Flu

when you cough you can deposit up to 1M viruses in your hand

one person can leave 1000's of viral particles behind by touching things

takes as few as 10 particles to infect average person

cold viruses can survive up to 72 hrs on glass, steel and formica surfaces

susceptibility to any microbial disease depends in part

on its **infectious dose (ID)**

= the number of particles required to be likely to cause an infection

if only a few they may be overcome by a persons defense system

humans tend to be susceptible to a lower ID for viruses than for most other kinds of pathogens

eg. infectious hepatitis (hep A) ~10-100

eg. rabies ~10 virus particles

eg. polio ~2

eg. measles ~1

Virulence

virulence = how bad the disease actually is; how much damage it causes

symptoms of viral diseases range from very mild (asymptomatic) to lethal

acute to **chronic** infections

many are **childhood diseases**,

some **self limiting**

others remain a lifetime

Examples of Viruses

1. **viral diseases**
   eg rabies, cold, flu, HIV
2. viruses have also been implicated in some "chronic diseases" but connections are still unclear:

   diabetes
   obesity
   breast cancer
   prostate cancer

Examples of viral Diseases:

eg. Rabies

animal disease = **zoonosis**

worldwide most commonly passed to humans by dog bites; in US mainly by wild animals

in nature rabies is a viral disease of carnivores
skunks, foxes, raccoons, bats, coyotes

also infects other domesticated animals:
cats, cattle, sheep

transmission to humans is rare and almost always fatal if not treated

100's/yr in US infected

usually transmitted by bite or lick from infected animal
→ virus particles are in saliva

~80% from bites of wild animals
~20% from bites of domestic animals

might also be transmitted by aerosols and enter the lungs

eg. in bat caves

long incubation time (1-1.5 months) before symptoms appear

→can be vaccinated after exposure if in the first week or so

vaccines are typically given BEFORE exposure

initially the virus multiplies in skeletal muscle and connective tissues

→ remains localized for days or months

then it enters peripheral nerves and travels along nerves to CNS (can take up to 3 months)

once it enters the CNS it is no longer accessible to the immune system

there causes encephalitis and painful death

if the original bite is in an area rich in nerve fibers (eg. hands or face) the incubation period is shorter

Symptoms:

Initial: mild then muscle spasms →esp in face and neck

Once it gets in CNS:

agitation vs calm periods

spasms of mouth and throat muscles esp when swallowing

→ painful throat spasms & convulsive choking

causes fear of swallowing=**hydrophobia**

End Stage: extensive brain & spinal cord damage, delerium, renal failure, coma

death usually occurs within 6 days of onset of final symptoms

eg. Herpes simplex

large group of viruses

relative of chicken pox and Epstein Barr viruses

herpes simplex:	fever blisters & genital infections
herpes zoster:	chickenpox & shingles
cytomegalovirus;	infects internal organs
Epstein-Barr virus:	lymphatic tissue

tendency to produce creeping rash

some have tendency for oncogenesis

humans are only host

requires direct contact to spread

very high infection rate

→90% infected in US

initial infection often goes unnoticed
→ ~15% develop lesions

once infected 20-50% of cases virus enters nerves
latent virus persists in nerves

→lifetime infection = **chronic**

recurrence triggered by stress:

fever, menstruation, injury, colds, etc

recurrent infection usually less severe than initial

outbreaks become less frequent with age

two major forms **cold sores** (type I) and **genital herpes** (type II)

both can occur in either area

HSV-1 (type I) - cold sores

usually in skin, eyes, mucous membranes, nervous system

alternate with latency when virus "hides" in nerves

symptoms often exhibit during stress,

less frequent with age

Herpes gladiatorum
esp head and neck
3% incidence in HS wrestlers

HSV-2 (type I) - genital herpes

sexually transmitted; esp 14-29 yr olds

more severe form of virus: can cause painful urination

one of top 5 STD's →5 M cases total → 300,000/yr

condoms not particularly effective

especially dangerous for pregnant women

→fetus can be infected before birth
→ virus can cross placenta

often lethal

→newborns can be infected during birth esp if active lesions are present

→ caesarian may be required

severe or fatal in patients with immunologic deficiencies

no good treatment; no vaccine yet

eg. HIV/AIDS

second most lethal infectious disease in the world:

~10's of millions are infected,3 Million die each year worldwide (2008)

first recognized in US in 1981

→ today (2005) 1 M in US have the disease

many are people who do not know they are infected

originated in central Africa

similar virus infects green monkeys in central Africa

→ harmless infection for monkeys

→ probably mutated from common primate virus

Infection requires direct contact with body fluids;

sexually transmitted, needles, mothers milk, organ transplants

only slight risk today from blood transfusions; was once a major source of infections

most dangerous sexual contact is anal intercourse

vaginal intercourse → woman more at risk than male

rare → oral genital contact

30% of children born to HIV+ mothers are infected

one possible case of spread by saliva

Can't get it from kissing, touching, sharing utensils, etc

HIV particles in body fluids of infected person:
Blood 10-1000 inf particles/ml
Semen 10-50 IP/ml
Saliva <1 IP/ml

highest risk group in US:

male homosexuals and bisexuals
those with multisexual partners
IV drug users

today incidence is declining in these groups but increasing in heterosexual contact

in SubSaharan Africa and parts of Asia males are as likely to contract the disease as females

a crucial factor in heterosexual spread in eg. Africa
poor obstetric care
multiple births
high incidence of VD
malnutrition

a few individuals of high risk groups seem to be completely resistant to HIV

once inside body it hides in body's own immune cells to avoid detection and immune response

can spread directly from cell to cell without entering the blood where it would be more easily detected

Symptoms

begins with sudden flu-like symptoms

few weeks may produce fever, fatigue, swollen glands, some get rash

but most show no symptoms at all

for several years the only indication of its presence may be swollen glands

→ virus hides in lymph nodes

progression of the disease depends on:
how much virus a person is exposed to
condition of patient

Incubation period lasts years before AIDS symptoms appear

typical incubation period is ~10 yrs

eventually HIV infections are so widespread that they begin to produce recognizable symptoms: AIDS

night sweats
malaise
nausea
headaches

symptoms may persist for years

Its virulence is due to the fact that it infects the T-cells of the immune system

→these are the cells that control the entire system

if they are knocked out the immune system fails

eventually, immune system is inactivated
→ opportunistic infections and cancers ravage the body

HIV reproduces and mutates so fast that body cannot produce antibodies to fight it

few actually die of HIV
→ they die of pneumonia, cancer, TB, hepatitis, etc

in past couple of years incidence and death rate has decreased dramatically in US with intensive treatment regimes

but still a very deadly disease in the rest of the world

2. Some viruses cause cancer

~100's different kinds of cancer
numerous causes: genetic, chemicals, viruses
viral causes – not contageous
eg. Epstein Barr virus: mononucleosus → lymphatic cancer
90% of US carry latent stage of this virus in WBC's with no signs of disease
eg. Hepatitis B virus → implicated in liver cancers
eg. HTLV 1&2 → leukemia

Viral Applications

1. Genetic Engineering

viruses are sometimes used as **vectors** in genetic engineering research to transmit a specific gene to engineered cells

eg. cystic fibrosis

eg. plants – tobacco mosaic virus

2. Bacteriophages (bacteria viruses)

are being looked at as a way to treat some bacterial infections without the use of antibiotics, to which many bacterial are becoming resistant.

3. using viruses to protect food products

(2006) FDA approved a 6 virus coctail to be sprayed onto ready to eat meats

protects against *Listeria* which causes 2500 cases of severe food poisoning and 500 deaths annually in US

4. using viruses to treat cancer

when healthy cells are infected by a virus they commit suicide

ideal tool to kill cancer cells

mutated herpes virus that can only multiply in tumor cells

still only experimental

5. as biological controls of insect pests

over 300 viruses have been discovered with biological control potential against insect pests

6. New generation of **antiviral drugs**

viruses are completely dependent on genetics of their hosts

trying to find some host protein that is essential for viral replication but not necessary for survival of its host

then attack that protein with vaccine

single vaccine would work for many similar viruses since most viruses conscript the same host genes

Viroids

even viruses are not the smallest infectious particles around.

viroids → naked RNA molecules
no capsid
no coatings

prions → pieces of proteins
no nucleic acids involved

} = disease causing molecules

<u>Viroids</u>

viroids have 0.1th the genetic material of the smallest virus (350 bases)

if bases were 1mm wide:
human sperm → 1800 miles
T2 virus → 2 football fields
viroids → 1 foot long

too small to encode for even a single enzyme

don't know how they cause disease

about a dozen known viroids

so far only infect plants:

tomatoes, potatoes, cucumbers, citrus trees, chrysanthemums

eg. killed 12 million coconut trees in Phillipines

eg. in 50's killed most of the chrysanthemums in US

no one has been able to isolate an animal viroid

but they may be involved in animal diseases like:
arthritis
encephalopathies
cancerous lymphomas

Prions

an infectious agent that can replicate without genetic material

also called "slow viruses"

not really virus → protein fragments

seem to be mutated proteins from "hosts" own brain cells that are able to be passed from host to host

the "normal" proteins play vital roles in brain function and memory

→ stimulates glial cells to make myelin insulation around neurons

at least one genetic disease seems to be due to a similar kind of mutation

eg. a genetic disease in a few families

→ when they reach middle age they can no longer sleep

→ die in a few weeks from exhaustion

prions are similar kinds of mutated proteins that can be **transmitted** from one host to another

prions cause 8 known animal diseases

long term infections; but typically fatal

all 8 are neurological diseases:

→cause mental derangement

→loss of muscle control

→progressive and fatal

eg. kuru
New Guinea – eat brain to spread disease

eg. Creutzfeldt-Jakob disease (= Mad Cow Disease)

first identified in England and found to be spreading to humans from eating contaminated beef (eg hamburger)

spread cow to cow in animal feed that contains ground brains from infected animals

strong measures were taken to identify and destroy infected cows and prevent the contamination of cow feed

by 2011 170 people had died and 4 people are known to have the disease

eg. scrapie

in sheep

a newly discovered prion disease attacks the PNS rather than the brain causing chronic diarrhea

some evidence prions may be involved in:

Parkinsons disease

progressive loss of motor function
begins in 50's or 60's
can be hereditary
due to degeneration of dopamine releasing neurons in substantia nigra (inhibitory neurons)
leads to hyperactivity of basal nuclei and involuntary muscle contractions
results in shaking hands, facial muscles become rigid, range of motion decreases
develops smaller steps, slow shuffling gait with forward bent
posture and a tendency to fall forward
speech becomes slurred, handwriting illegible

Alzheimers Disease

affect 11% in us over 65; 47% by 85
~half of all nursing home admissions
leading cause of death among elderly
AD may begin before 50 with very mild, undiagnosed symptoms
one of 1st symptoms is memory loss, esp of recent events
progresses with reduced attention span, disorientation, moody, confused, paranoid, combative or hallucinatory
may lose ability to read, write, talk, walk, and eat
death usually from pneumonia or other complications of confinement and immobility

possibly also:

Huntington's Disease

a neurodegenerative genetic disorder that affects muscle coordination and leads to cognitive decline and psychiatric problems. It typically becomes noticeable in mid-adult life. HD is the most common genetic cause of abnormal involuntary writhing movements called chorea, which is why the disease used to be called Huntington's chorea.

Amyotrophic lateral sclerosis

(Lou Gehrig's disease) is a debilitating disease with varied etiology characterized by rapidly progressive weakness, muscle atrophy, muscle spasticity, difficulty speaking (dysarthria), difficulty swallowing (dysphagia), and difficulty breathing (dyspnea).