Immunodeficiency

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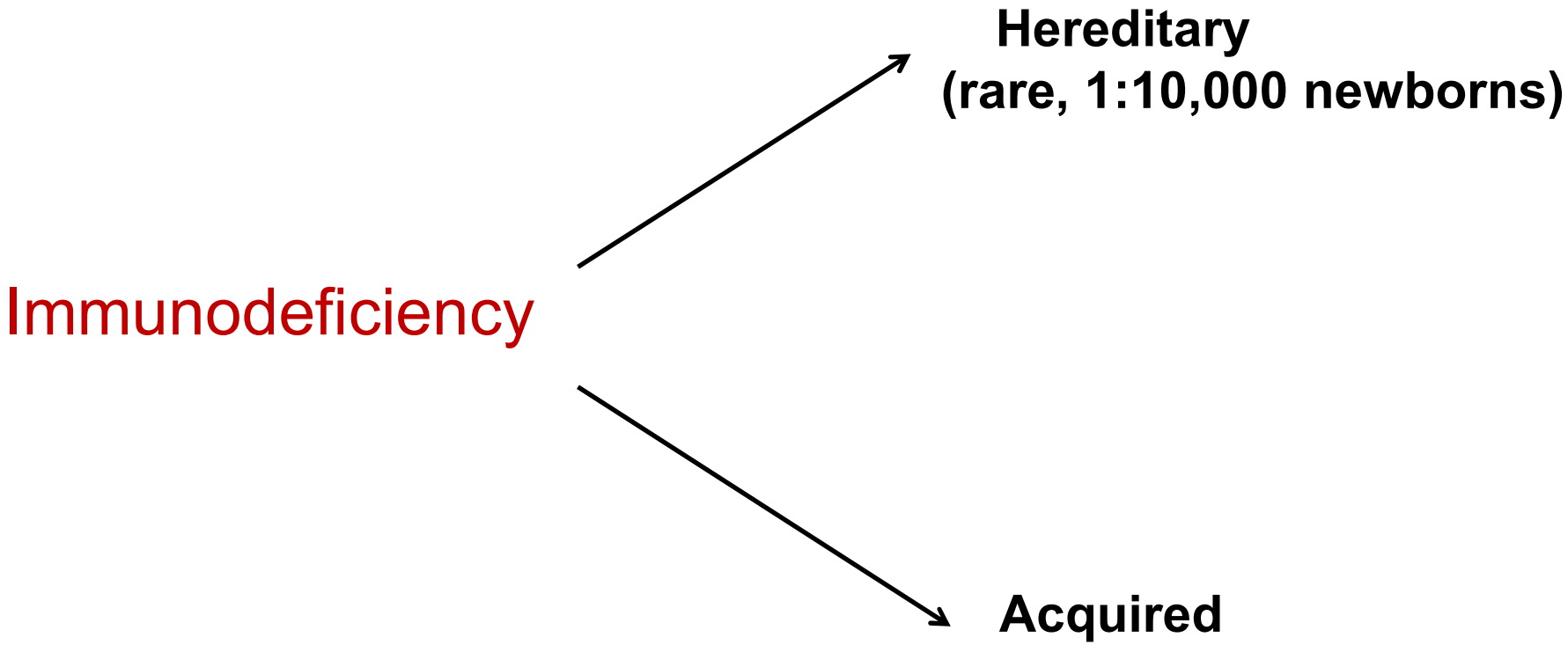

Hereditary
(rare, 1:10,000 newborns)
Immunodeficiency
Acquired

Hereditary Immunodeficiency

Hyper IgM syndrome (Case study): **CD40L deficiency, AID deficiency**

CD40 deficiency

DiGeorge Syndrome, no thymic tissue (22q11.2 deletion)

Severe Combined Immunodeficiency (SCID), many types
(Case studies)

C3 deficiency (very rare), abnormal lymph nodes
(No germinal centres) and abnormal B cell function

Acquired Immunodeficiency

MalNutrition: lack of nutrient availability, vitamins, antioxidants, etc....
(**Highest** cause of immunodeficiency worldwide)

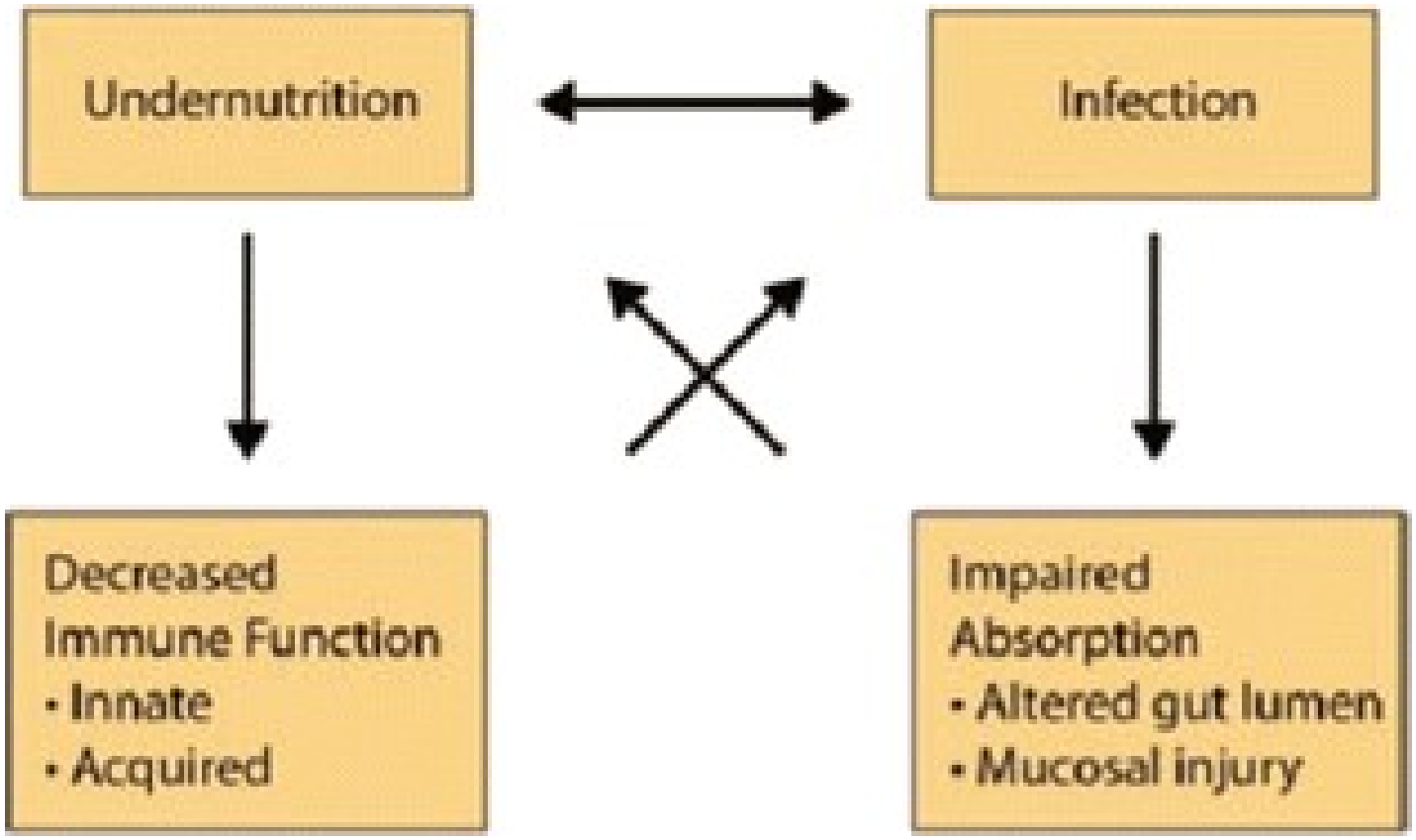
Medications/Treatments: Cyclosporins (Transplants)

Chemotherapeutic agents
(Effect on BM and mature immune cells)

Ionizing Radiation

Infections (ex: HIV, measles infection)

Nutrition and Infection



Katona *et.al*, Clin. Infect. Dis., 2008

Human Immunodeficiency Virus (HIV)

37 Million people infected worldwise (WHO, 2016)

1 Million died in 2016 (WHO).

Physicians alerted to immune nature of disease by cases of *pneumocystis carinii* pneumonia, and rare cancers such as Kaposi sarcoma, usually both seen in immunodeficient patients.

HIV-1 was discovered and over a billion dollars is spent every year to research it.

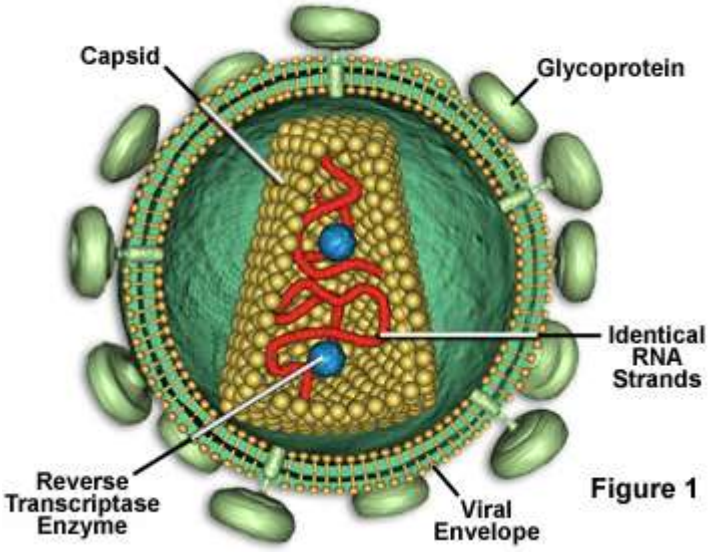


Figure 1

HIV-2 vs. HIV-1

Mostly restricted to West Africa

Longer Asymptomatic stage

Lower plasma RNA levels

Lower mortality

However, progression to AIDS does occur

Modified treatment plans

Optimal treatment strategy not well defined

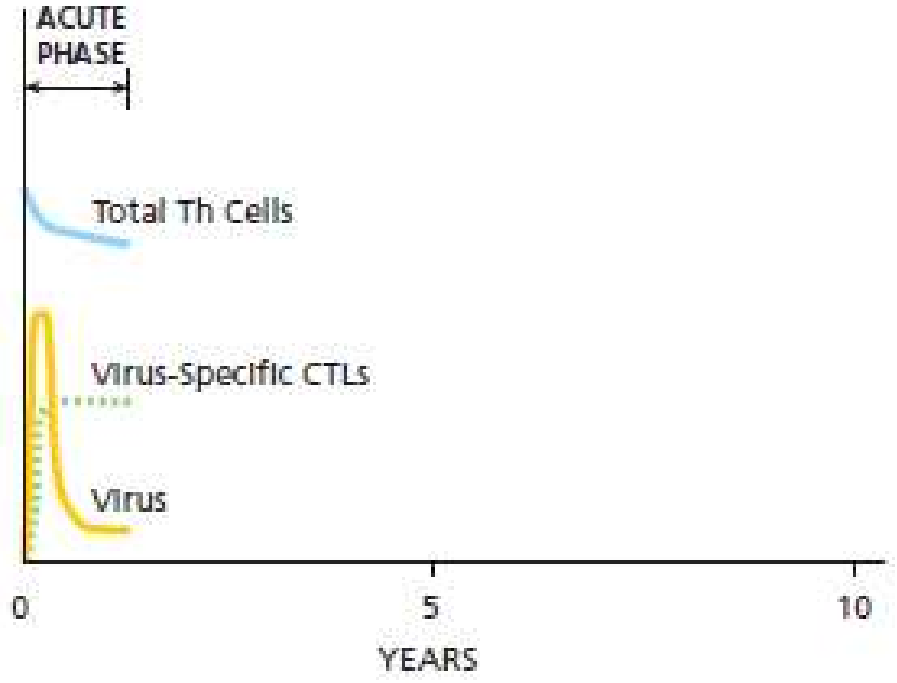
HIV Infection

Infection starts when the virus penetrates rectal or vaginal mucosa
(or enter directly via blood) and infects Th cells which lie below those protective surfaces.

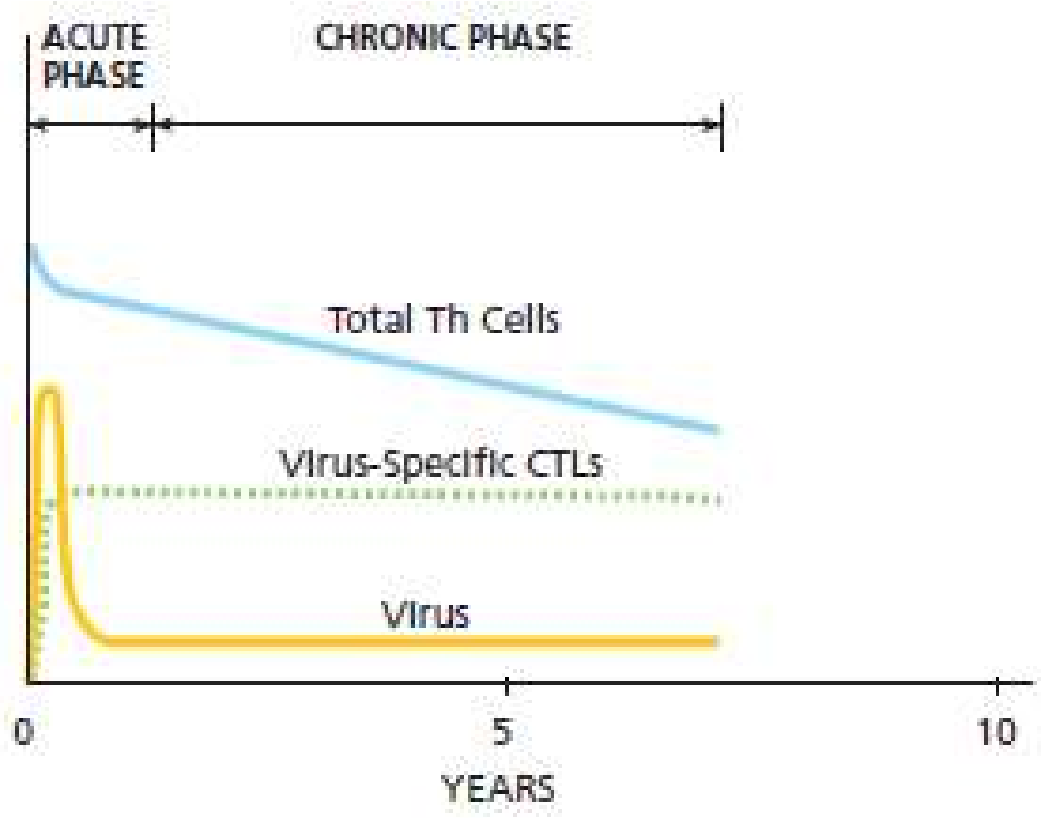
Th cell machinery is used to produce more of the virus which goes on to infect other cells.

Viral load increases in acute phase

Adaptive system causes viral load drop = Chronic phase (> 10 years)

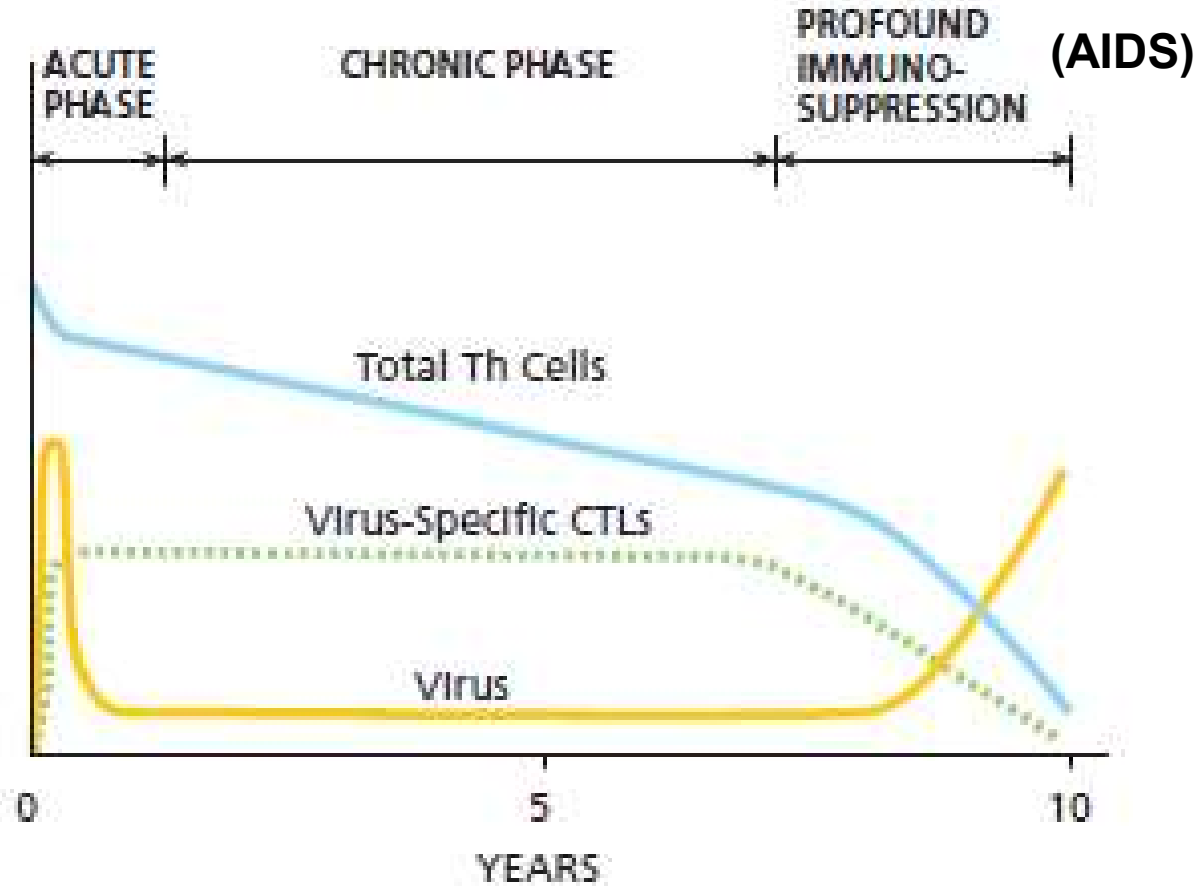


HIV Infection, Cont'd



Fight between virus and immune system is ongoing during chronic phase, Gradual drop in Th cells.

HIV Infection, Cont'd



HIV-1 vs. The Immune System

Why does the immune system eventually fail to kill the virus???

Nature of the virus: RT converts RNA into DNA, which is then inserted into our DNA using a viral enzyme (5-10 days). Latent state goes undetected by CTLs.

RT is error-prone: Lots of copying mutations = Constant changes in Viral peptides

One step ahead of CTLs and Abs generated against it.

Virus mainly targets CD4+ Th cells, the very cells needed to activate CTLs!

Virus uses normal trafficking of immune system cells through lymph nodes (Attaching to surface of DCs, being opsonised by complement or Igs and retained by FDCs for months.

Living with AIDS

If untreated, death usually occurs within 10 years.

Highly Active Anti-Retroviral Therapy (HAART) is now available. Targets many aspects of virus cycle and extends life by many years.

Side effects of therapy: Cognitive disorders, increased risk of cancer, kidney, liver, bone, and heart disease.

Elite controllers (<1%, remain without symptoms for a very long time)!!!
How?

Immune system firing up more strongly upon infection (Type I Interferon production??)

MHC molecules very efficient at presenting viral peptide early?

CTLs from elite controllers are more aggressive than normal patients.
(Mobilize granzyme B and deliver it into target cells more efficiently)

They are still infected! But control it without medication for a much longer time!

AIDS in mother and child

HIV can pass from mother to child during:

-**Pregnancy**: (HIV can cross placenta)

-**Childbirth**: (Cervical secretions or blood) **C-sections?**

-**Breastfeeding**: (HIV in mother's milk) HIV positive moms should **NOT** breastfeed!

Untreated mothers have a **25%** chance of transmitting the virus to baby.

Babies born to HIV positive mothers usually receive HIV medications for 4-6 weeks after birth to reduce risk of infection

HIV lab testing

HIV-1&2 Antibody test: Less used, diagnostic window 3 months

HIV-1&2 Antigen Antibody combo test: Diagnostic window 1 month- up to 3 months

Confirmation by MoH by Western blotting or ELISA-based technique looking for specific Viral proteins.

HIV-1&2 by PCR: Diagnostic window 10-14 days- up to 3 weeks

For **established** cases:

Follow-up by **Flow Cytometry and PCR (viral load RNA copies/ml)**:

CD4 and CD8 counts, CD4:CD8 ratio

HIV Hotline

HIV hotline number: 06/5697933

Questions

Advice/counseling

Reporting cases

Free treatment

Questions?????