AIDS AND OTHER IMMUNODEFICIENCY

Autoimmunity: immune system attacking self cells.
Immunodeficiency: Loss of immune response due to weakened immune system.

Types of immunodeficiency –

(i) Primary immunodeficiency

→ Most of these diseases attack the humoral system (B cells)

→ Targets: ~~Reti & M~~
- Hematopoietic stem cells → Reticular dysgenesis
- innate immune system → Chronic Granulomatous disease
  → Leukocyte-adhesion deficiency
- Adaptive immune system → severe combined immunodeficiency (SCID)
- B cells → X-linked hyper-IgM syndrome
- T cells → Bare lymphocyte syndrome

→ ~~im~~ diseases will target the impaired production of a particular type of Ab.

→ Genetic origin; present since birth.

Treatment –

→ Replacing missing protein
- through injecting Abs.
- Express gene in vitro

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→ Replacing missing cell type
• Bone marrow transplantation

→ Replacing missing or defective gene
• Gene therapy

(ii) Secondary immunodeficiency
→ Acquired immunodeficiency
→ No genetic basis
→ Eg: Hypogammaglobulinemia, AIDS

AIDS - HIV :-
[Acquired immunodeficiency syndrome – Human immunodeficiency virus]

HIV :
* It has two surface glycoproteins: gp120, gp41
* gp120 → binds to CD4 receptors (mainly T_H cells)
gp41 → binds to chemokine receptors (mainly T_H cells)
* Through gp120 & gp41, HIV attaches & to host T_H cells & infects it.
* HIV is a ~~ds-DNA~~ ds-RNA virus (2 copies)
* Genome is protected by capsid protein (p24) and matrix protein ~~(p51)~~ (p17).
* It also have p10 protease, p32 integrase & p64 Reverse transcriptase
* Integrase (p32) → helps newly synthesized viral genome ~~RNA~~ to integrate into host DNA
Protease (p10) → cleaves newly synthesized viral proteins ~~DNA~~ and make them active
Reverse transcriptase (p64) → converts viral RNA to viral ~~RNA~~ C-DNA.
* Pro-virus: viral DNA integrated into host genome.

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Pro-virus has 3 imp structural genes: gag, pol & env.

* gag → ~~gene~~ codes for protective proteins (matrix & capsid proteins) that surround the genome.

pol → codes for reverse transcriptase, integrase & the protease proteins.

env → codes for surface glycoproteins (gp120, gp41).

* The transcription of the pro-virus requires two transcription factors: NF-kβ, NF-AT

upon activation of these factors, they will transcribe viral-pro-virus DNA leading synthesis of mRNA that results in production of viral proteins.

* Viral proteins are assembled inside the cells and new virions will be released.

* Major drawback in AIDS: For a long period (5-10 years) symptoms will not arise so diagnosis takes place only at end-stage of the disease making it difficult for curing.

Treatment:-

1) Therapeutic Antiviral Drug

eg: AZT (Azidothymidine)

↳ targets Reverse transcriptase

↳ limits: not efficient since it can target only cells where ~~viral DNA~~ cDNA hasn't been integrated into the host DNA yet.

eg: HAART (Highly active Antiretroviral therapy)

↳ cocktail of viral protease inhibitors

NOTE: These drugs can not remove the pro-virus.

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2) Vaccine

Challenges:
- HIV mutates rapidly
- Even neutralizing Abs can't prevent viral spread
- Do not have good animal models to test the vaccines.