V.H. ALTERATIONS IN THE IMMUNE RESPONSE TP VH-pre 1 HWA

H.a. IMMUNODEFICIENCY DISEASE (**IDD**) [deficiency or defect of immune system that inhibits the normal immune response]

i.e., <**IDD**> –> deficient immune response (T 5.7, p 111)

H.a.A. CLASSIFICATION BY ONSET HWA

1) Primary hereditary or congenital
2) Secondary acquired after birth

} –> same spectrum of disease, varies in severity; essentially –> / susceptibility to opportunistic infections

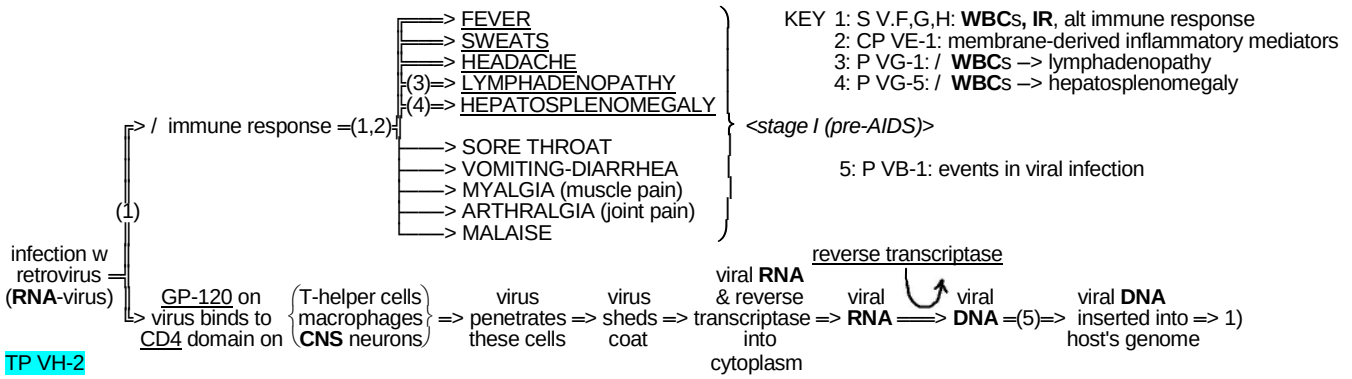
H.a.B. CELLULAR (T-CELL) **IDD**

H.a.B.a. SECONDARY

H.a.B.a.(A.) **AIDS** (Acquired Immunodeficiency Disease Syndrome)

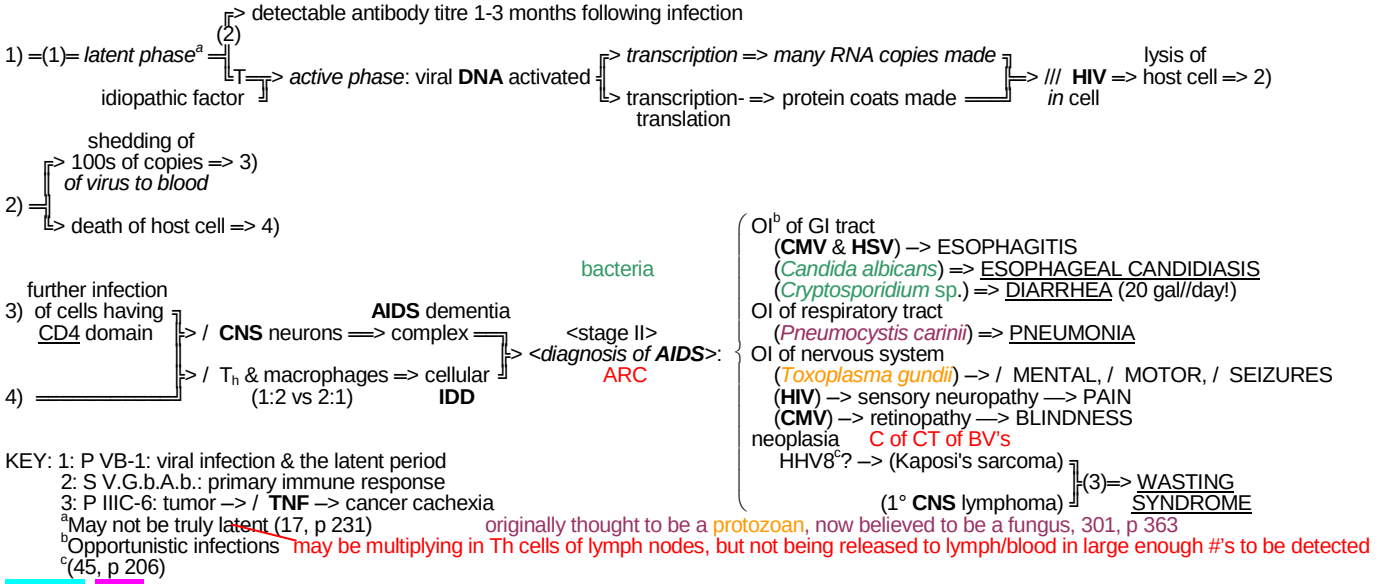
CDC: latest estimate I've seen (Nov 03) is 1//265 Americans is **HIV** positive. Although it is not as prevalent as, say cancer, it is probably 100% fatal, ∴ we need to study & respect it.

1) **AIDS** Epidemic (Pandemic) & Transmission of **HIV** Infection (read pp 112-115)
2) Pathophysiology (F 5.24, p 115) (PF VG-1a & VG-1b) TP VH-1



TP VH-2

Critical Path VH-1a. Pathophysiology of Stage I (pre-**AIDS**)



KEY: 1: P VB-1: viral infection & the latent period
2: S V.G.b.A.b.: primary immune response
3: P IIIC-6: tumor –> / **TNF** –> cancer cachexia
[a]May not be truly latent (17, p 231) originally thought to be a protozoan, now believed to be a fungus, 301, p 363
[b]Opportunistic infections may be multiplying in Th cells of lymph nodes, but not being released to lymph/blood in large enough #'s to be detected
[c](45, p 206)

TP VH-3 HWA

Critical Path VH-1b. Pathophysiology of the Latent Stage & Stage II of **AIDS**

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3) Diagnosis, Management & Prevention of **HIV** Infection (pp 121-123)

H.a.C. HUMORAL (ANTIBODY~B-CELL) **IDD**

H.a.C.a. PRIMARY [isolated~selective deficiency of IgA] (1//500 individuals)

lack of serum & secretory IgA –> ↑ respiratory infection
–> ↑ asthma
–> ↑ diarrhea

H.a.C.b. SECONDARY

[↓ synthesis of immunoglobulins] (occurs w/ lymphomas) (S V.F.b.B.c.)
[↑ loss of immunoglobulins] (occurs w/ nephrotic syndrome) (S VIII.A)
[production of defective immunoglobulins] (occurs w/ multiple myeloma) (S V.F.b.B.a.)

H.a.D. COMBINED HUMORAL & CELLULAR **IDD**

H.a.D.a. PRIMARY

Severe Combined **IDD** "bubble babies" (sex-linked or autosomal recessive)

H.a.D.b. SECONDARY

aging –> / metabolic functions –> / combined **IDD** –> / infections –> DEATH

H.b. ALLERGY~HYPERSENSITIVITY

[abnormality of immune system that causes it to attack antigens~allergens that are not intrinsically harmful –> inappropriate **IR**]

H.b.A. TYPE I, ALLERGIC RESPONSES~IMMEDIATE HYPERSENSITIVITY~ANAPHYLAXIS (F 5.14, p 99) TP VH-4

1) quick summary:

1° exposure: allergen--◊–IgE on B cells =(1)=> / plasma cells => // shed IgE => IgE binds to mast cells/basophils
T=> / dormant/memory B cells

some T later:
once again: allergen--◊–IgE on dormant B cells =(2)=> /// IgE => IgE binds to mast cells/basophils => 2)

2) => allergen cross-linked to IgE on mast cells =(3)=> // anaphylactic chemicals (esp histamine) => Path VH-3

KEY: 1: S V G.b.C.f.(A.) clonal selection & proliferation
2: S V.G.b.A.b: secondary immune response
3: S VE.b.B.a: degranulation & cell-derived inflammatory mediators

Path VH-2. General Pathophysiology of the Type I Allergic Response

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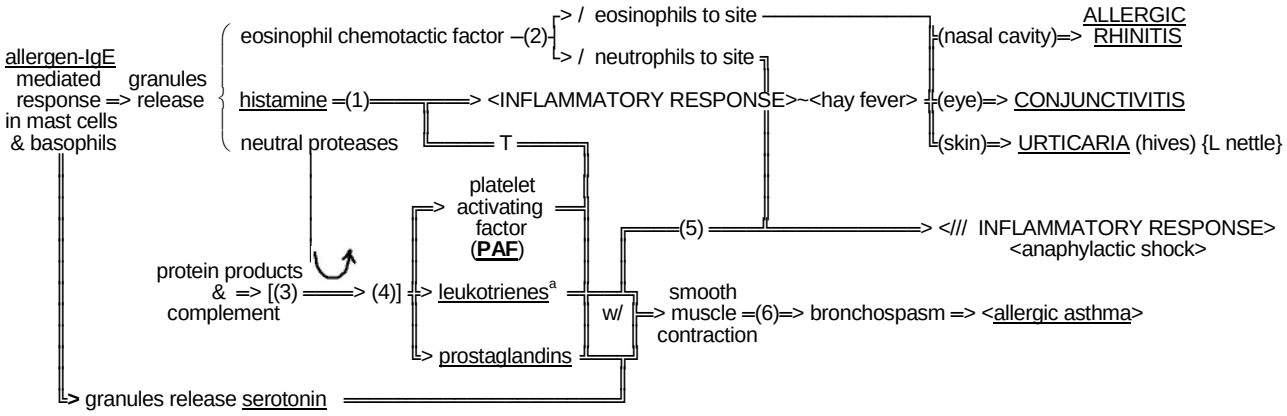
2) details (P VH-3) (Also see Text Figures 5.15, p 100 & 5.16, p 101)



KEY: 1: CP VE-1: inflammatory mediators
2: CP VE-3: margination, + chemotaxis, lysis, diapedesis
3: CP VG-3: complement pathway –> cell lysis
4: CP VE-1: phospholipids & arachidonic acid
5: CP VE-1: all inflammatory mediators, but especially leukotrienes –> [a]Slow-Reacting Substances of Ana\phylaxis
{G up, throughout\G guard, present} (SRS-A; 1000's of times more potent than histamine, but takes longer to form.
6: S VI.G: respiratory pathophysiology

TP VH-5

Path VH-3. Pathophysiology of the Secondary Type I Allergic Response

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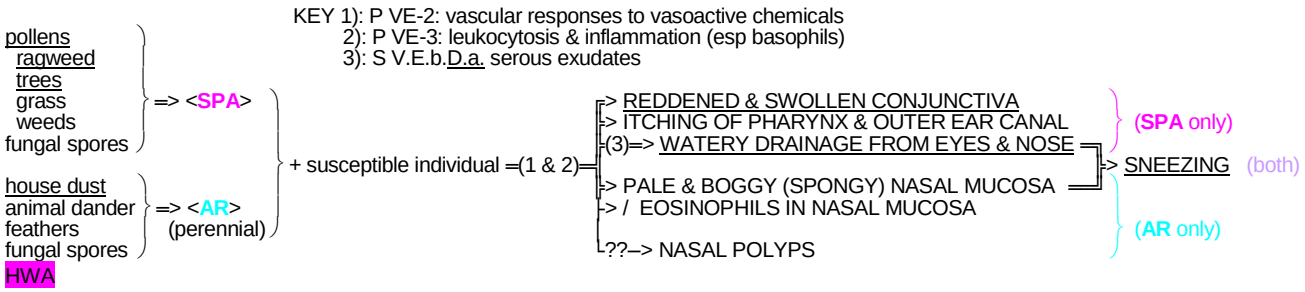
H.b.A.a. SEASONAL POLLEN ALLERGY (**SPA**) (hay fever) & ALLERGIC RHINITIS (**AR**)



Path VH-4. The Pathophysiology of Seasonal Pollen Allergies & Allergic Rhinitis

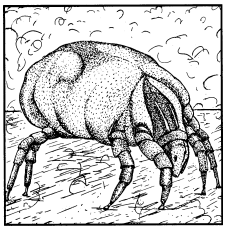
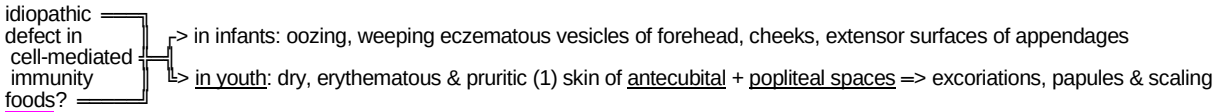


Figure VH-1. The Dust Mite (*Dermatophagoides* sp.), the Organism Responsible for Dust Allergies (19, p 66)

H.b.A.b. FOOD ALLERGIES

food allergen--◊–IgE in intestinal mucosa –> intestinal responses similar to those in P VE-3 & P VH-2

H.b.A.c. ECZEMA~ATOPIC DERMATITIS {G atopia\strangeness} "Atopy" means it has a familial (genetic) disposition



Path VH-5. General Pathophysiology of Atopic Dermatitis

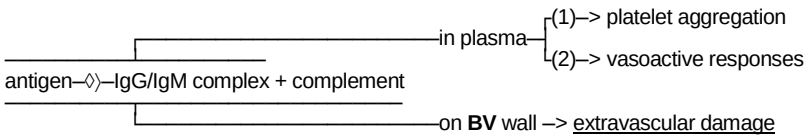
H.b.B. TYPE II, CYTOTOXIC REACTIONS (F 5.14, p 99) TP VH-4 again

RBC surface antigen--◊–IgG/IgM complex –> complement system activated against cell (**ABO** & Rh blood groups, more in S VI.A.)

occurs in transfusion reactions, hemolytic disease, autoimmune hemolytic anemia

H.b.C. TYPE III, IMMUNE COMPLEX REACTIONS (F 5.14, p 99) (Also see F 5.17, p 103) TP VH-4 again TP VH-6

The cause of glomerulonephritis & adverse drug reactions



e.g. adverse drug reaction (e.g. to penicillin)

KEY: 1: S V.I.A.: mechanism of platelet plug formation
2: CP VE-1: vasoactive chemicals & inflammation

Path VH-6. Antigen-antibody Complex as an Activator Substance

H.b.D. TYPE IV, CELL-MEDIATED HYPERSENSITIVITY (delayed hypersensitivity) (F 5.14, p 99) (Also see F 5.18, p 104) TP VH-4 again

antigen --◊–T-lymphocytes –> cytokines (contact dermatitis, poison ivy, tuberculin test)

H.b.E. SUMMARY

Table VH-1. Summary of Hypersensitivity Reactions
TP VH-7

TYPE	MEDIATOR	Ig	CELL TYPE	CHEMICAL INVOLVED	EXAMPLE
I	Allergen	E	Mast	Histamine	"Allergies"
II	Self-Antigen	M/G	T_c	Complement	**ABO** bld grp
III	Antigen	M/G	**PMNL**	Complement	Adverse drug reaction
IV	Allergen~ Antigen		$T_{h&}$ Macrophage	Cytokines (Lymphokines)	Poison ivy

H.c. TRANSPLANT REJECTION (F 5.20, p 106)
H.c.A. HOST VS GRAFT (matching of Class II **MHC** haplotypes more important than Class I) (F 5.21, p 108) TP VH-8

1) Hyperacute Rejection (usually occurs immediately upon establishment of blood flow to organ)

2) Acute Rejection (first months following transplant) humoral & cellular **IR** –> <acute rejection> –> renal failure (S VIII.B.)

3) Chronic Rejection (over a period of months following transplant) type IV cell-mediated immune response –> gradual ↑ in serum creatinine (S VIII.A.) (creatinine & renal function)
TP VH-9

H.c.B. GRAFT VS HOST

in bone marrow transplants (hematologic malignancies), donor's immune cells recognize recipient's as foreign –> DEATH

H.d. AUTOIMMUNE DISEASE (T 5.10, p 124)
H.d.A. NORMAL DELETION OF ANTI-SELF CAPABILITIES <self antigens (peptides)>

1) Anti-self T-cells are deleted early in development in the thymus (13, pp 74-81)
2) Anti-self B-cells ?

H.d.B. FAILURE (thesis at this point)

1) Self haptens must be in or transported to thymus early in development to be identified as self -- haptens inside body cells that are destroyed later in life may be regarded as non-self

2) Interactions w/ other agents that modify self antigens to appear as non-self or interactions w/ other agents that modify **MHC** to recognize self as non-self

3) **IR** against a non-self antigen that has a shape similar to a self antigen = CROSS REACTION

4) All 3 may have a genetic component