Erasmus MC
University Medical Center Rotterdam

How the immune system functions

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IPOPI, Praque
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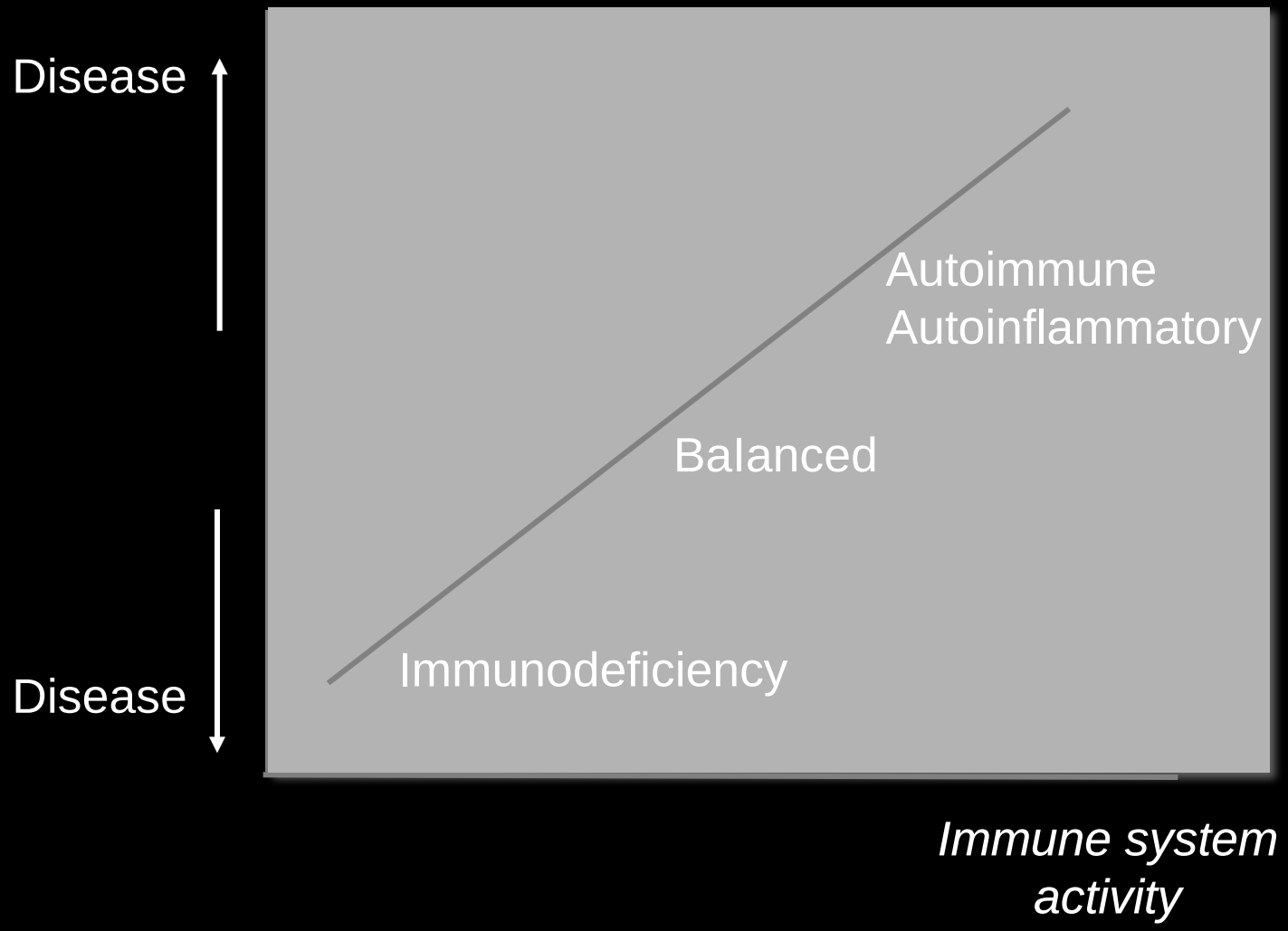
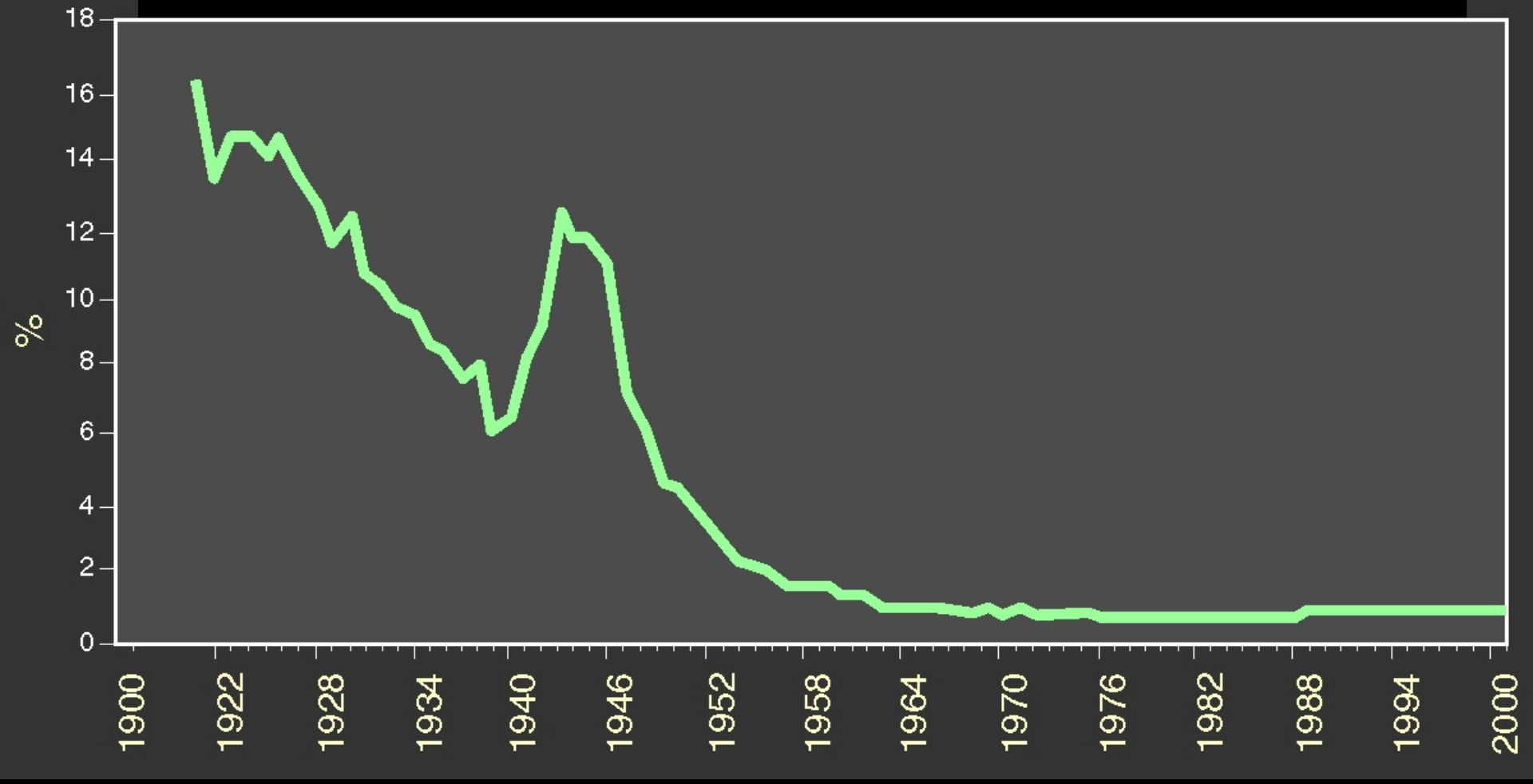
Immunodeficiencies

- Introduction
- Innate immunity
- Adaptation of the immune system
- Cytokines, the hormones of the immune system
- Influence of body systems on the immune system
- Conclusions

Clinical Immunology



Mortality caused by infectious disease from 1906 – 2000
% of the total community mortality



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Department of Immunology, Erasmus MC, Rotterdam

Barriers

Epithelia
Lysozyme
Anti-microbial peptides

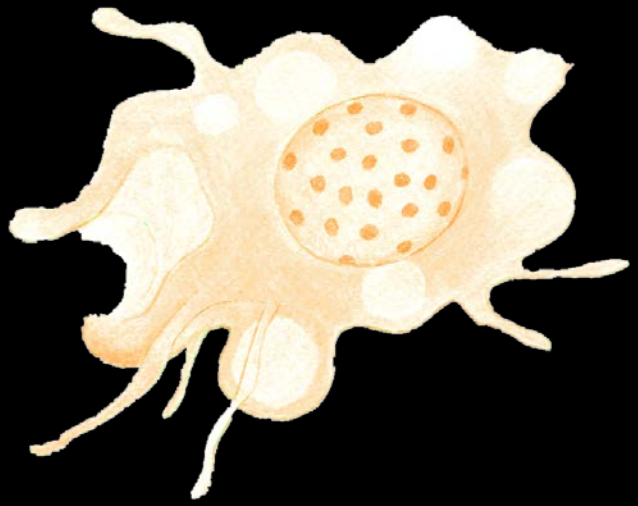
Body level

Inflammation
Circulation
Hormones
Neural system

Specialized systems

T- B cells
APCs, Mast cells
Immune organs

Cellular level



Anti microbial peptides
TRIMs
TLRs
NF-κB/P53

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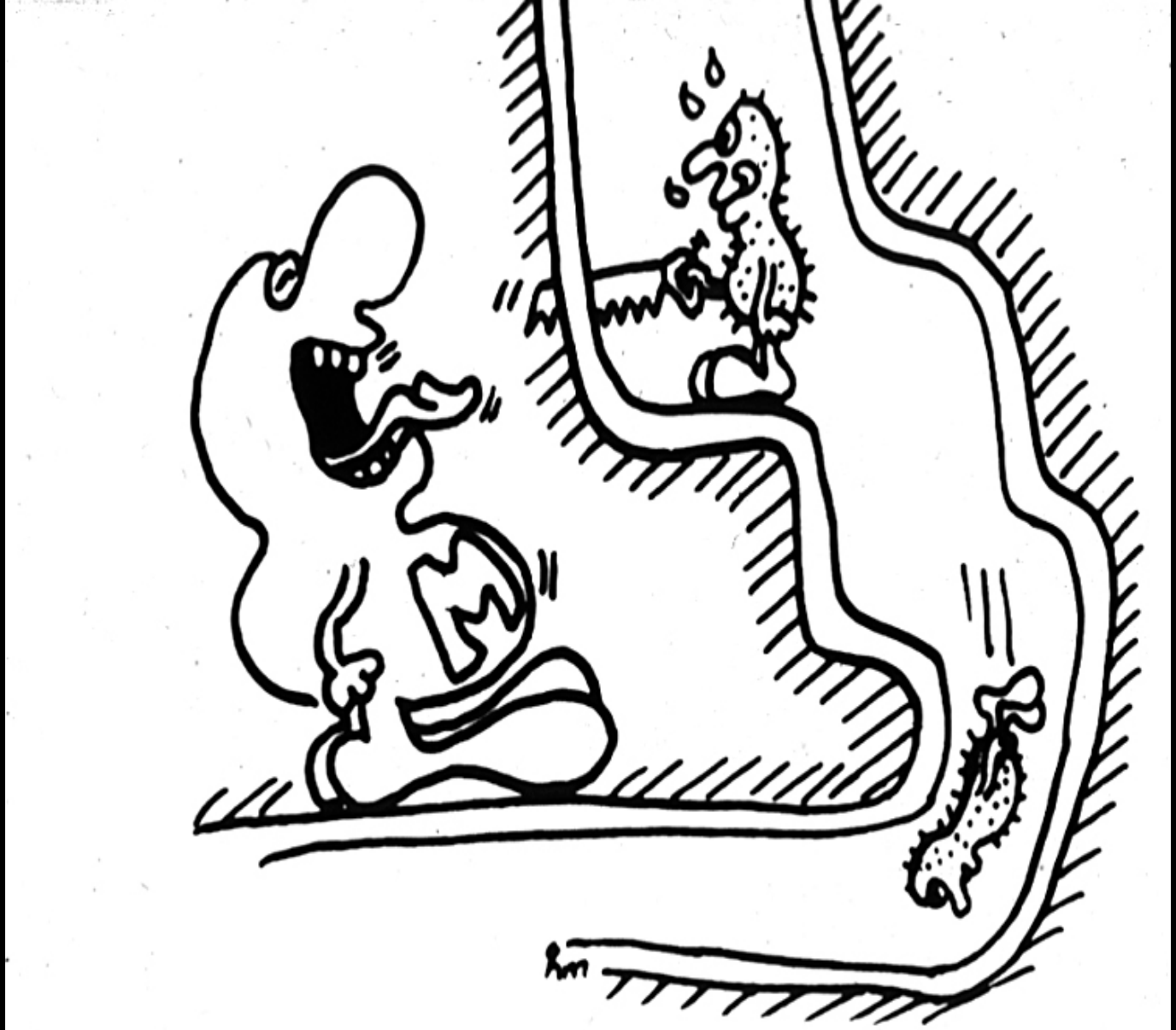

innate immunity

Direct (innate) immunity

- macrophages,
  granulocytes,
  dendritic cells

- starts almost directly

- no memory

Adaptive immunity

- lymphocytes and antibodies

- starts in a few days

- immunity for years

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Memory
specific
immunity

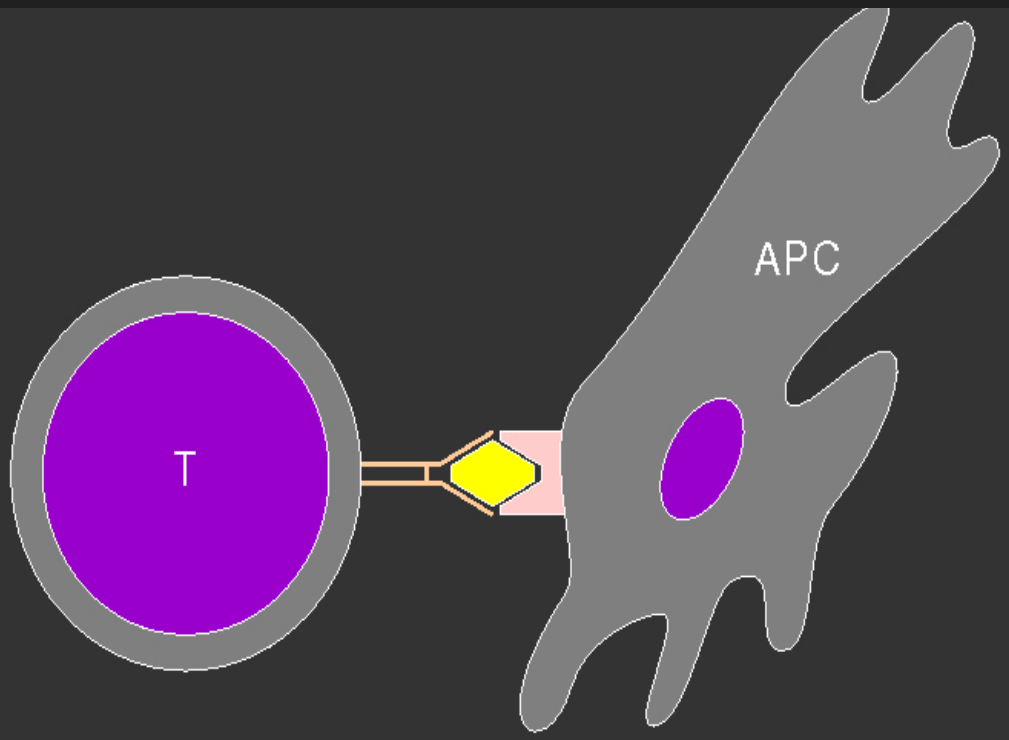
The adaptive immune system

10^{12} B-lymphocytes

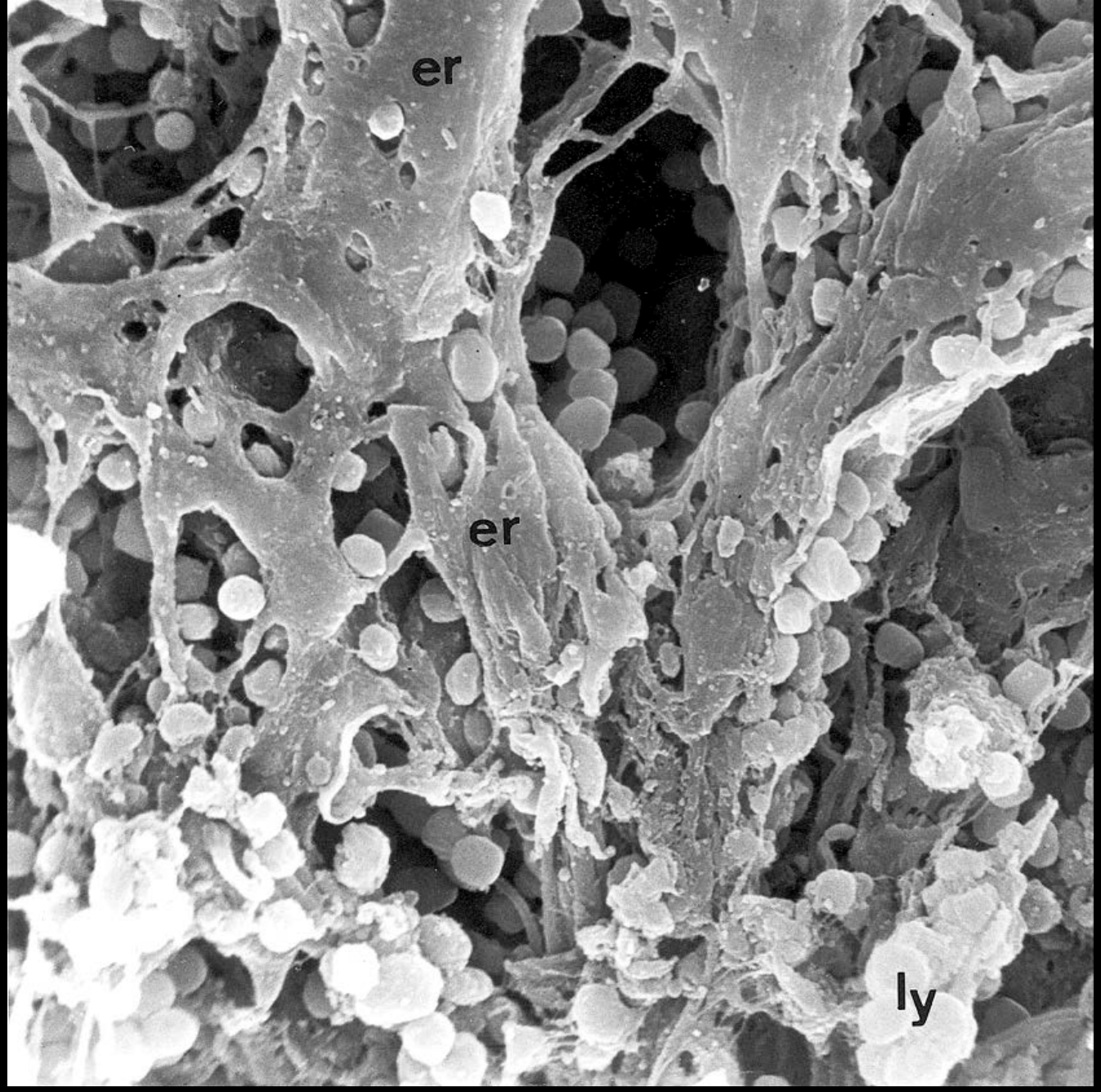
10^{12} T-lymphocytes

Antigen presenting cells (APCs)

10^{20} antibodies



T cells and tolerance



scanning
EM
thymic
cortex

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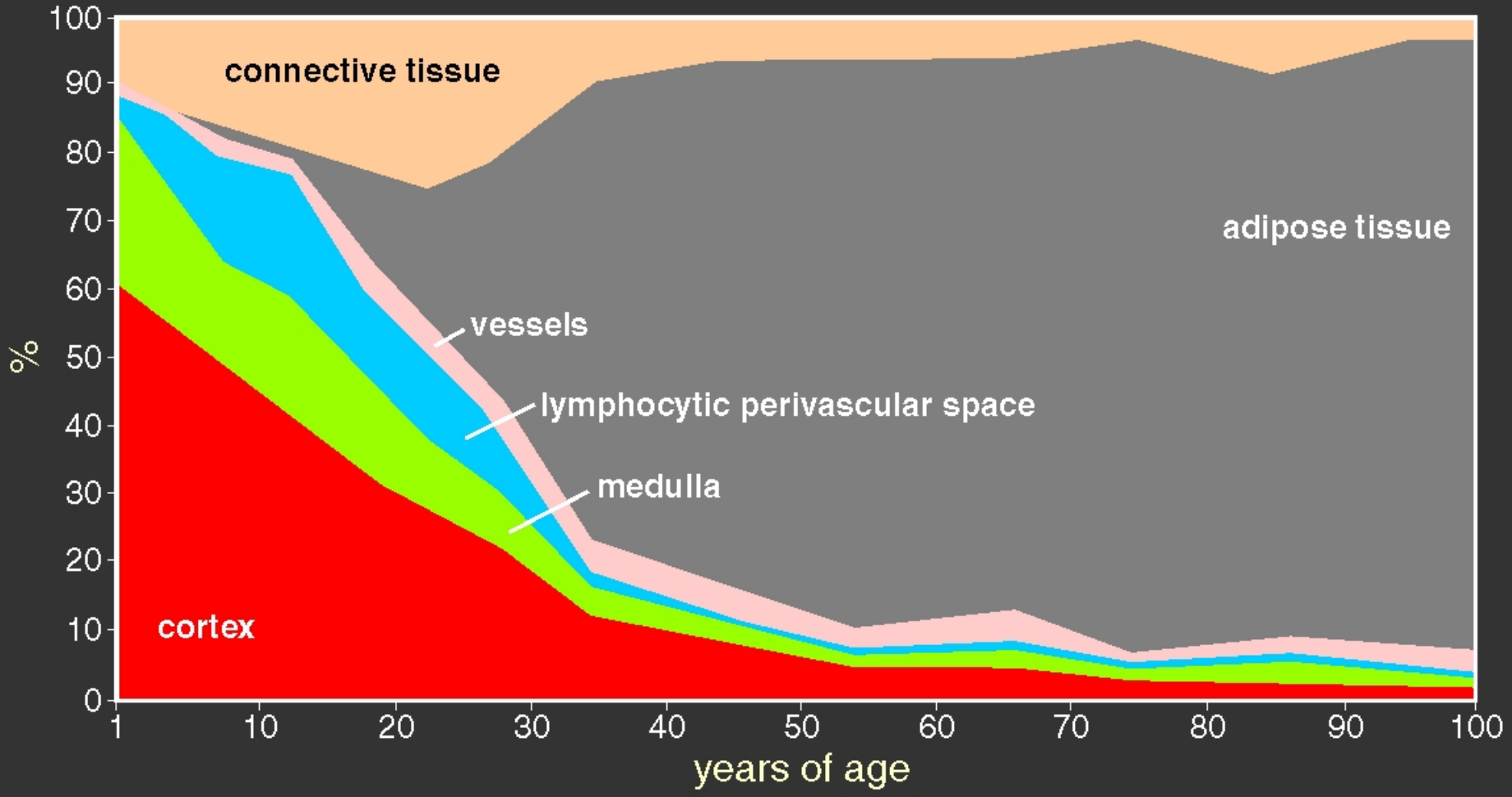
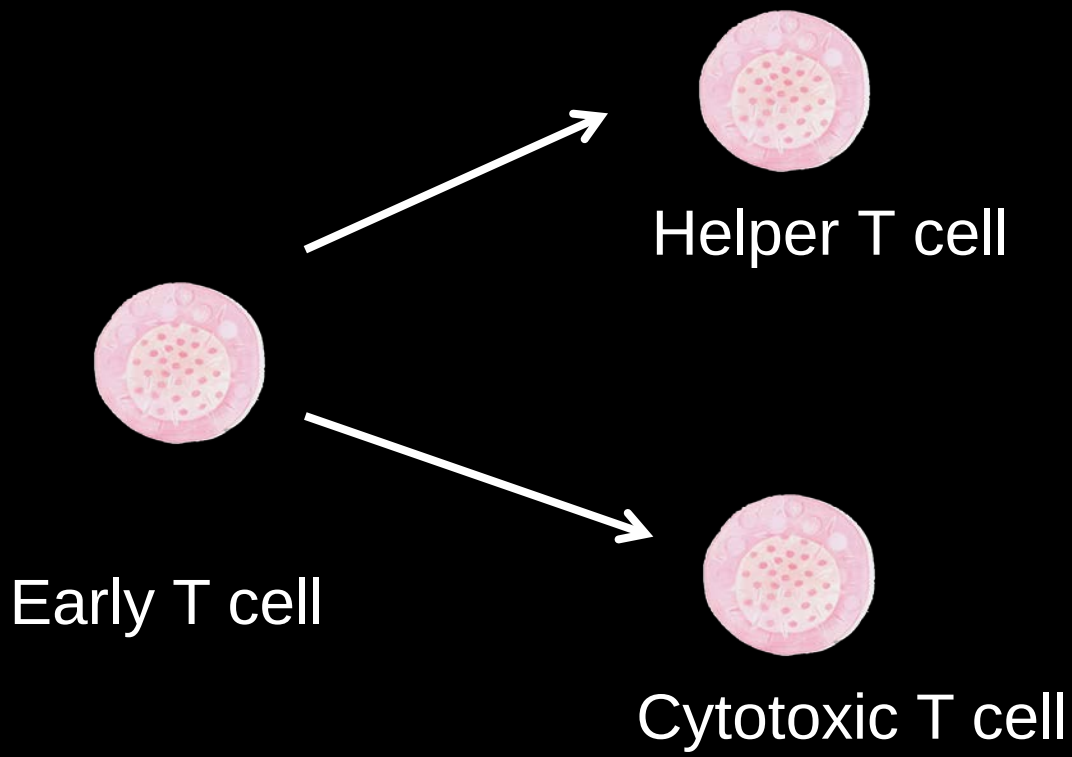
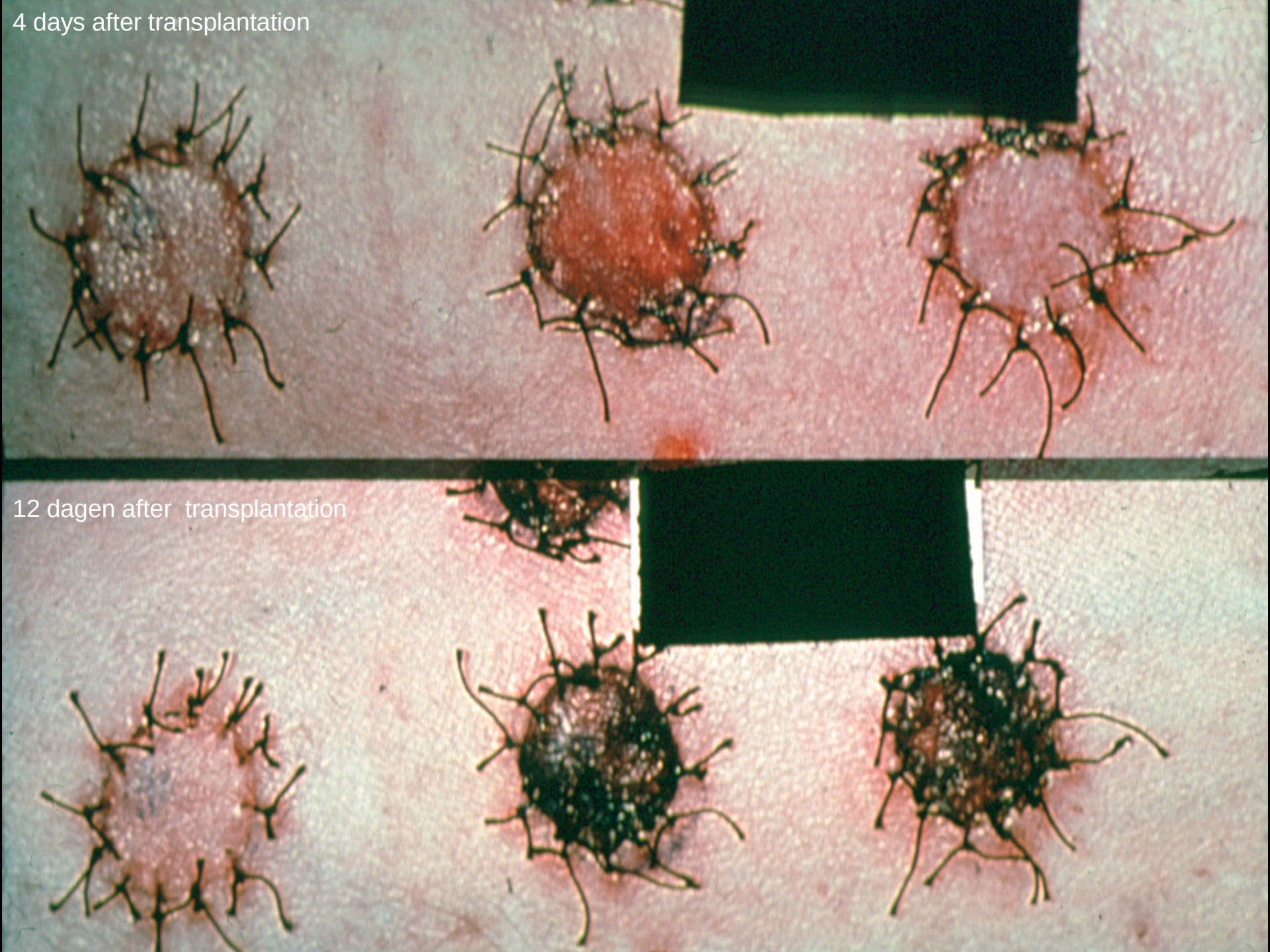
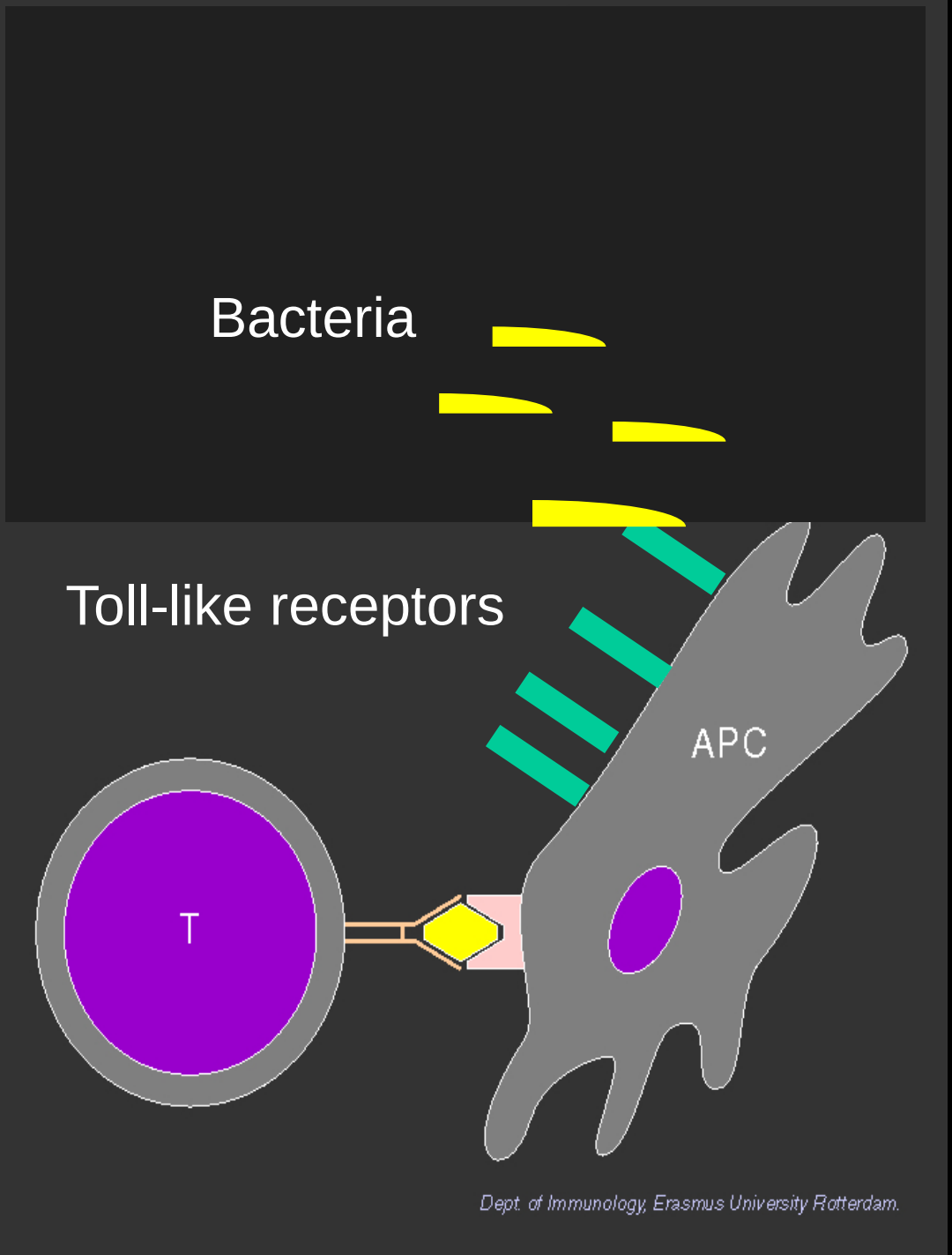


Change in volume of the thymus during life

Carrier of T cells




4 days after transplantation
12 dagen after transplantation


Bacteria
Toll-like receptors
APC
T
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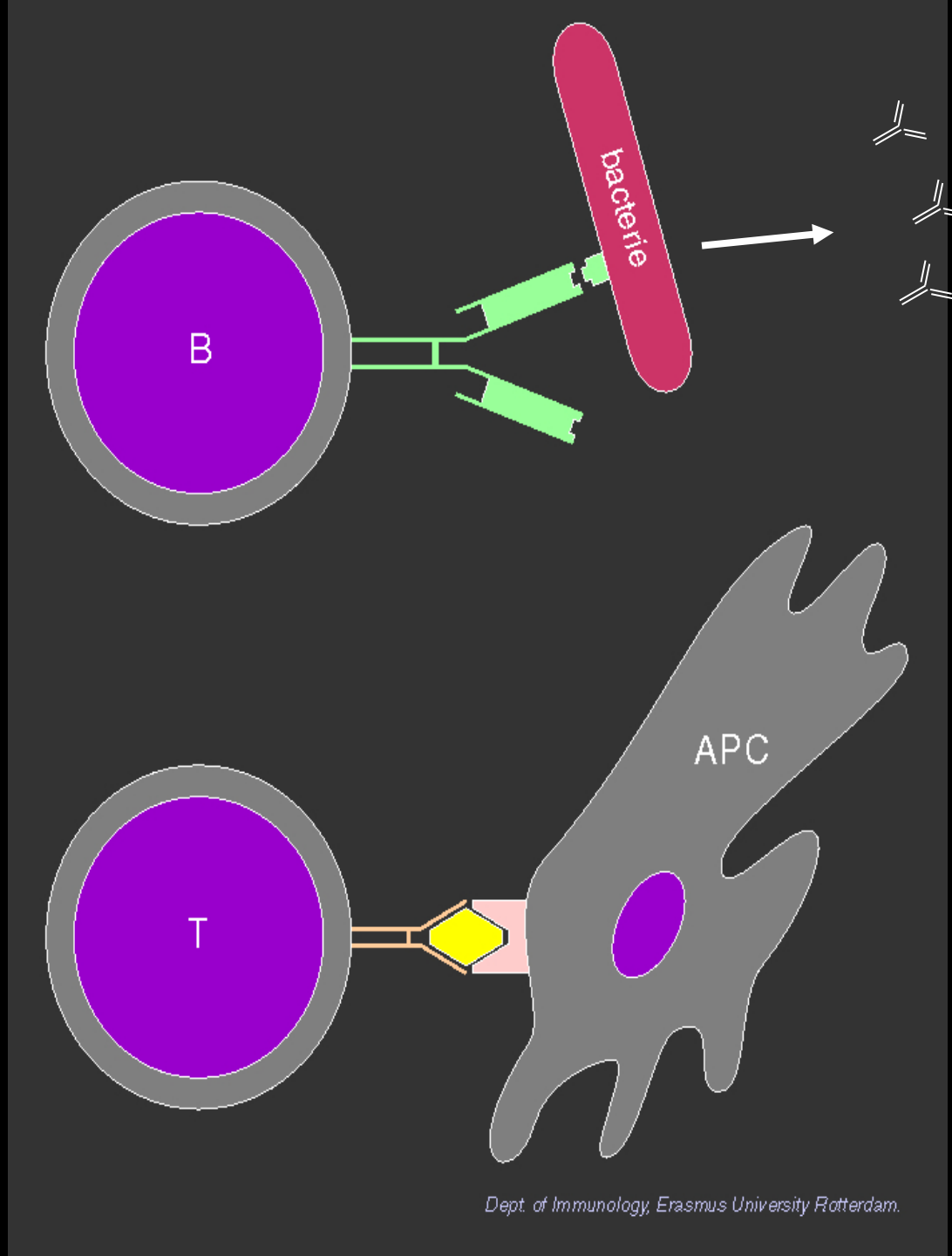
What happens when the dendritic cell – T cell interaction is damaged?

- No T cells in SCID
- Low numbers in HIV infection
- Interaction problem;
  - No HLA
  - T cell receptor problems

T cell; infections like fungal infection and mycobacteria


bacterie
B
APC
T
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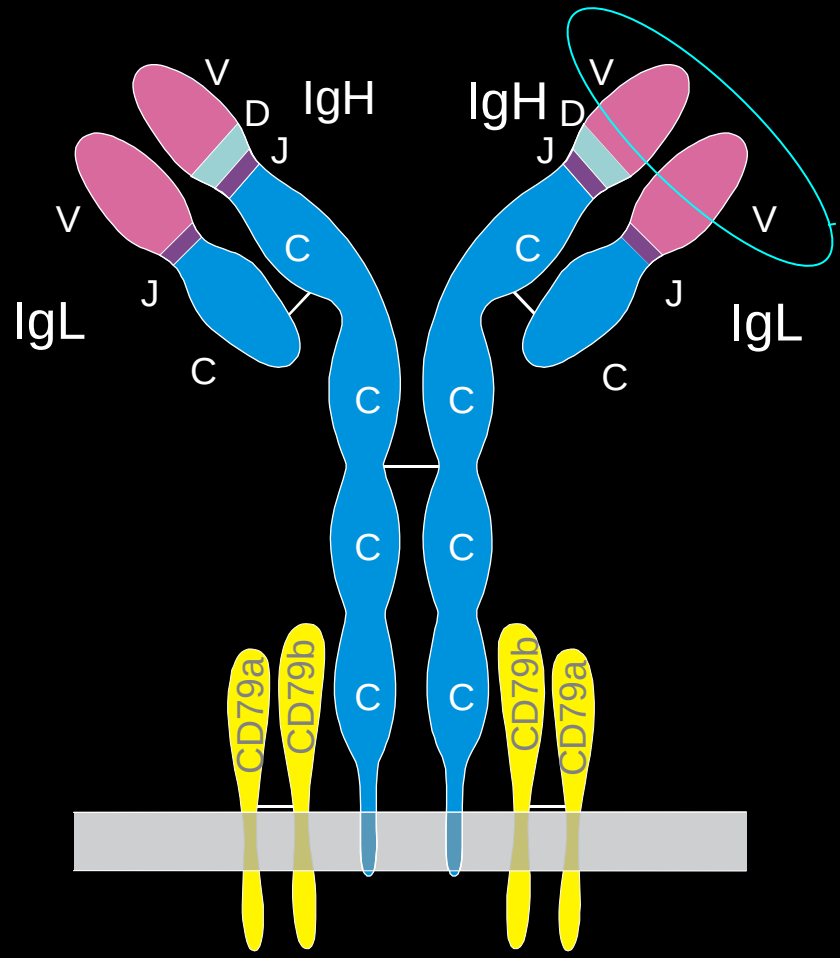
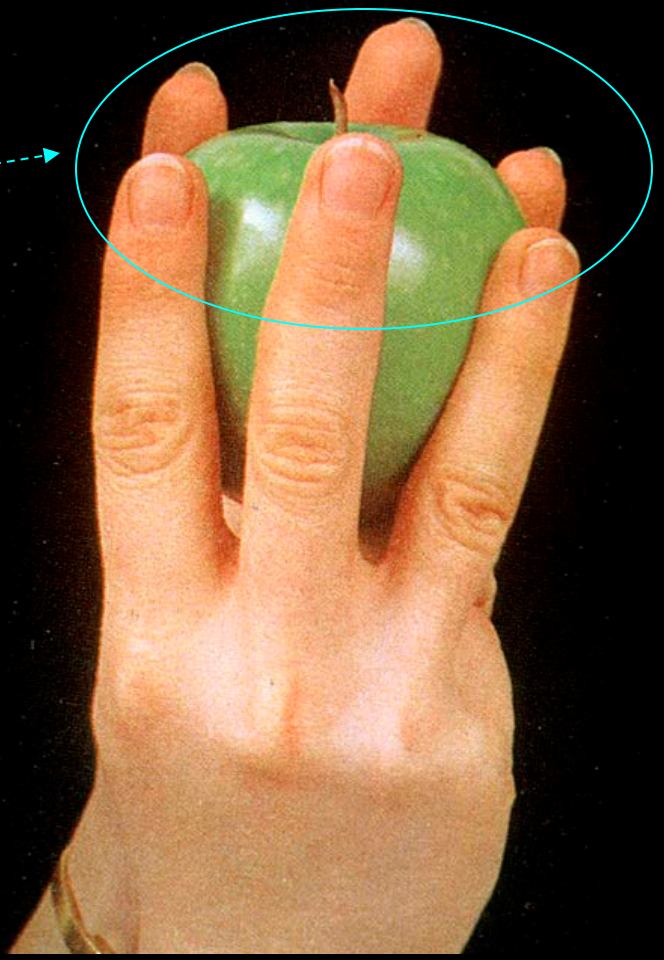
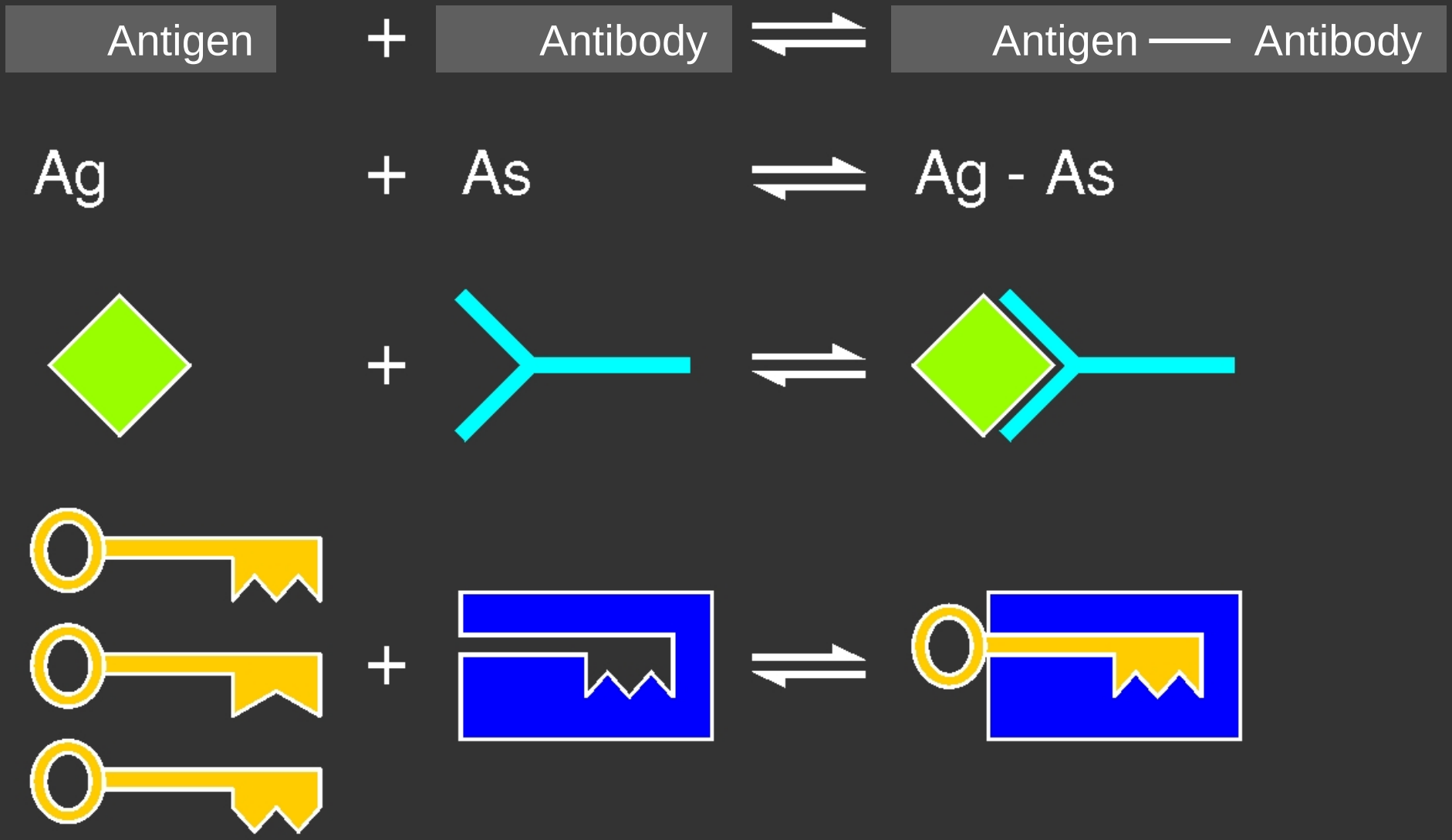
Immuunglobuline classes

	IgG (IgG1-IgG4)	IgA (IgA1-IgA2)	IgM	IgD	IgE
Mol weight	150.000	160.000	900.000	185.000	200.000
Serum level	7-16 g/l	0.7-4 g/l	0.4-2.3 g/l	0-0.4 g/l	<0.0001 g/l
% total Ig	80	13	6	0-1	0.002
T1/2	23	6	5	3	2
Complement binding	++	-/±	+++	-	-
FcR binding	+	±	-	-	+ (mastcel)

Immunoglobulines: structure



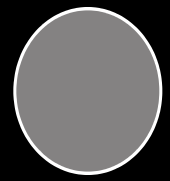




Model interactie antigeen - antistof

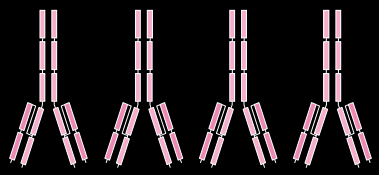
However, what is your repertoire?

Person 1

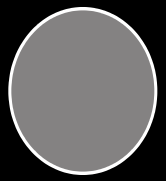


memory B cell

time

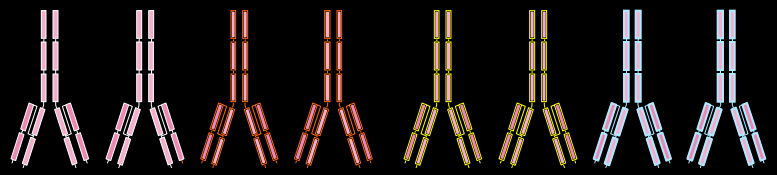


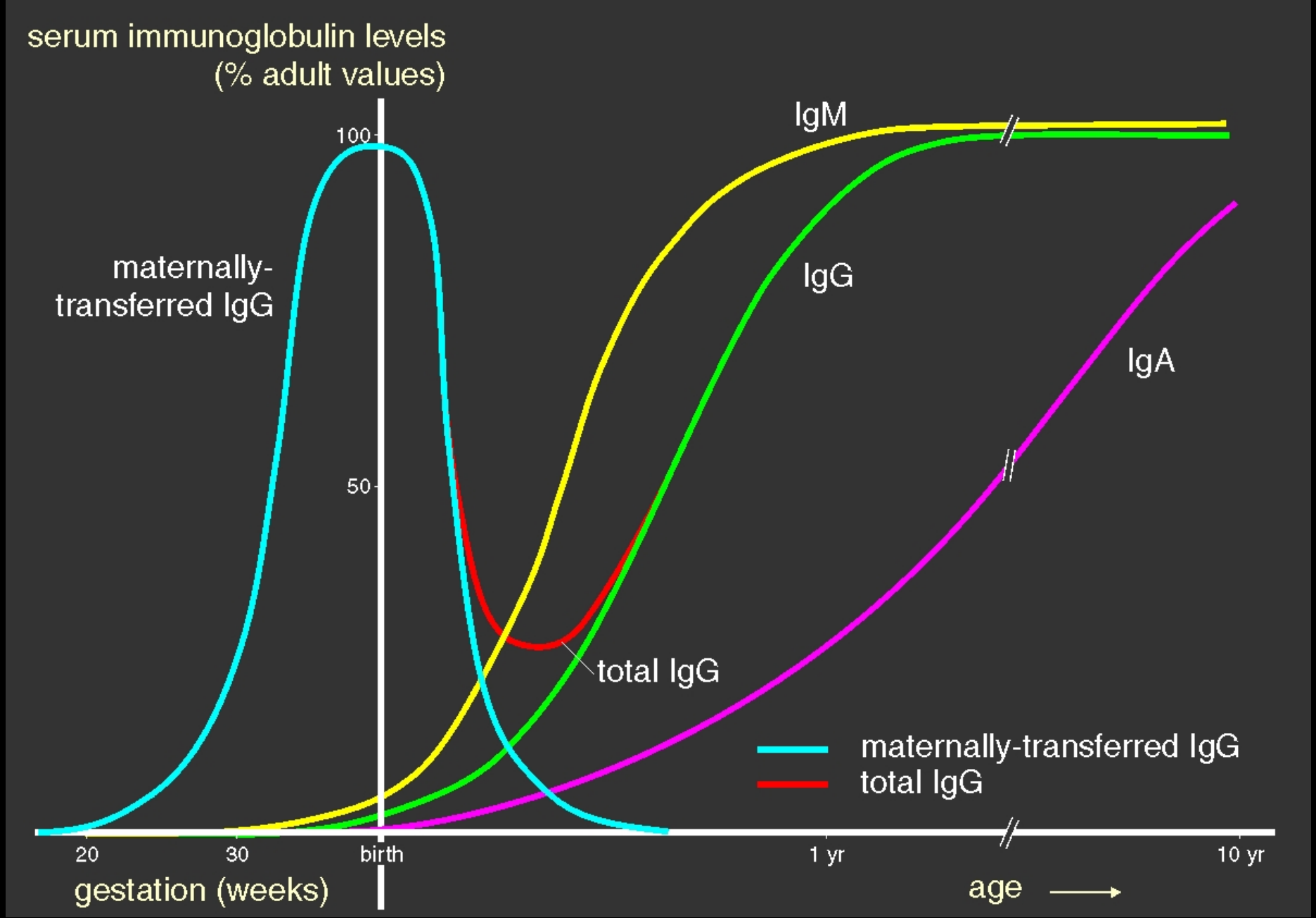
Person 2



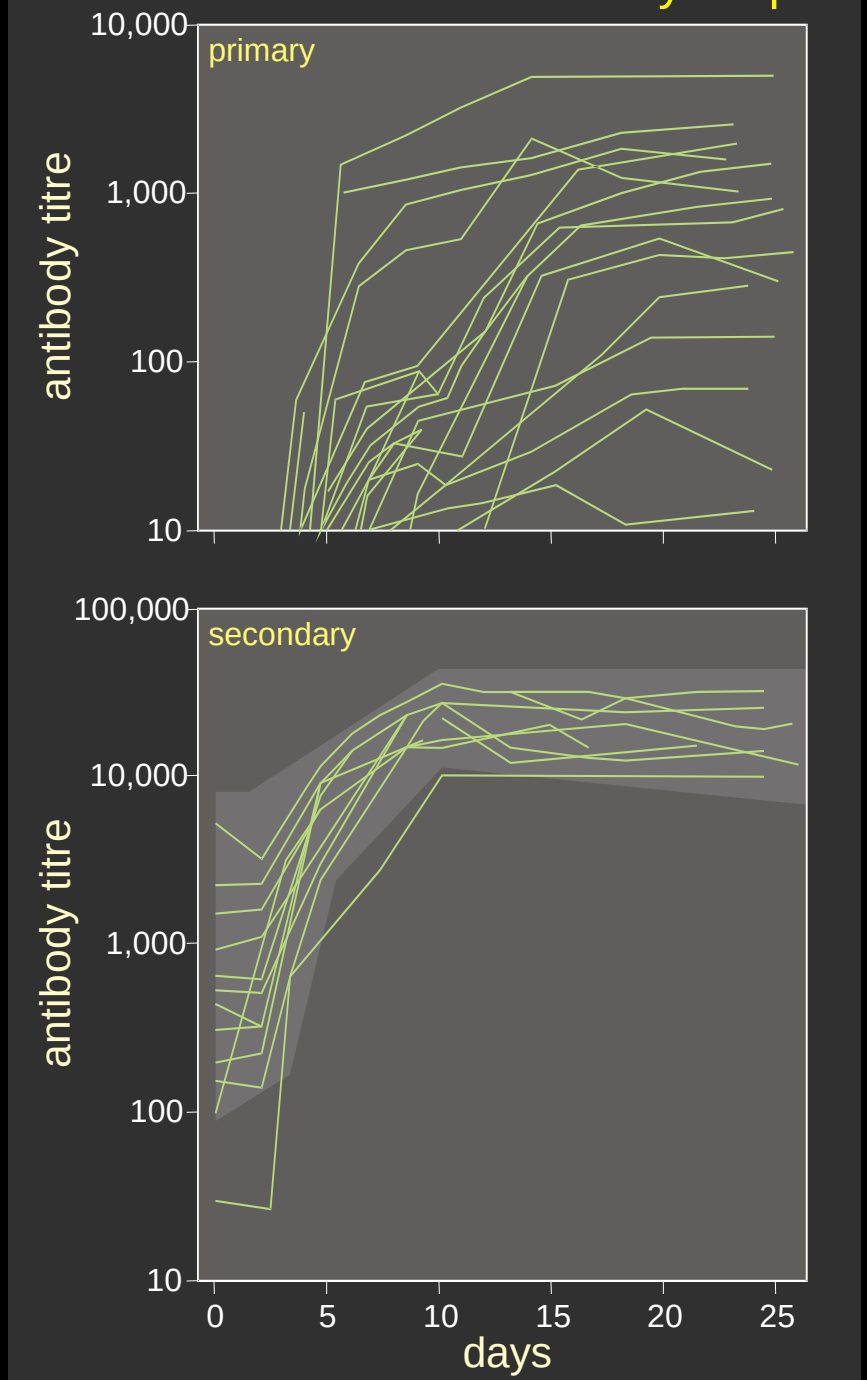
memory B cell

time

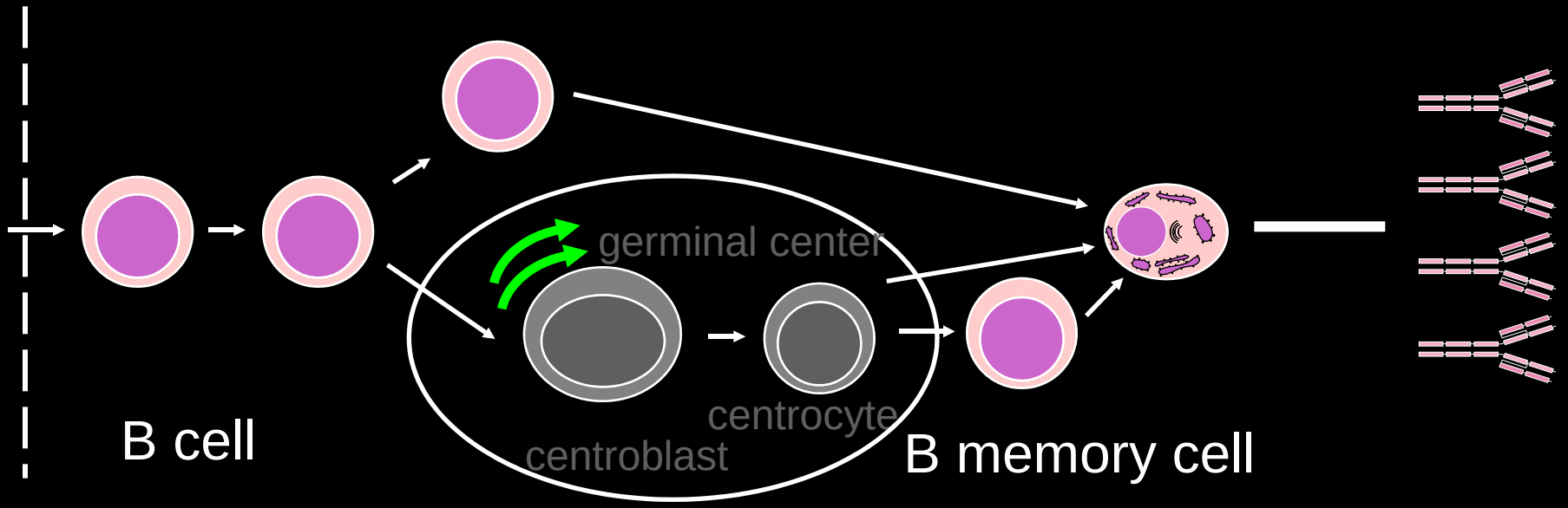



serum immunoglobulin levels
(% adult values)
100
50
IgM
IgG
IgA
maternally-
transferred IgG
total IgG
maternally-transferred IgG
total IgG
20
30
birth
1 yr
10 yr
gestation (weeks)
age

1° and 2° antibody responses

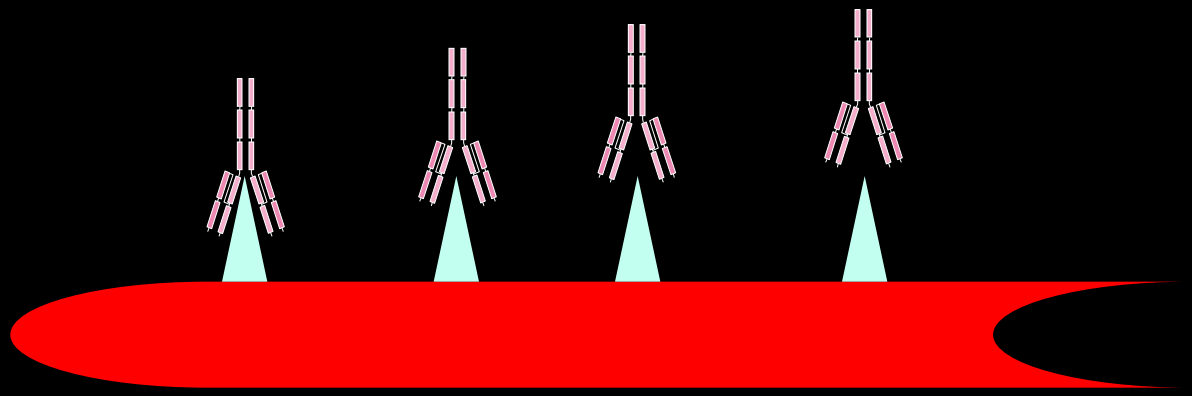


and, how your machinery is working?



How good can you attack?

Affinity



Immunoglobulins

Description of a young boy who suffered 19 episodes of clinical sepsis over 4.5 years. Pneumococcus was isolated on 10 occasions.

Bruton OC. Agammaglobuliemia. Pediatrics 1952(9):722;195

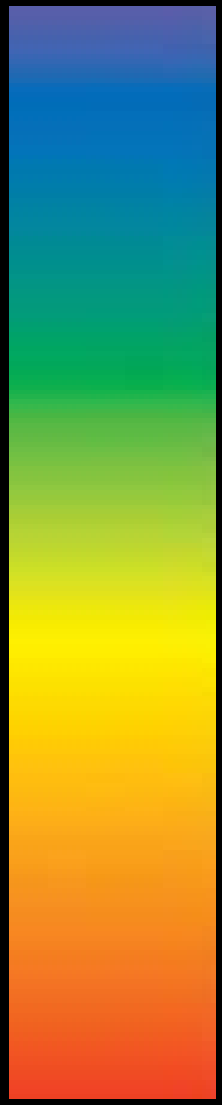
The spectrum of antibody deficiencies

- Selective IgA deficiency
- Selective IgM deficiency
- IgG subclass (1-3) deficiency
- Specific polysaccharide antibody deficiency (SPAD)

- Transient Hypogammaglobulinemia of Infancy

- Common Variable Immunodeficiency (CVID)
- Hypogammaglobulinemia with thymoma (Good's syndroom)

- Hypogammaglobulinemia with known genetic defects (CD19,CD81,ICOS,BAFF-R)
- Class Switch Recombinatie defects (Hyper IgM syndromen)
- Agammaglobulinemia's (XLA, AR)



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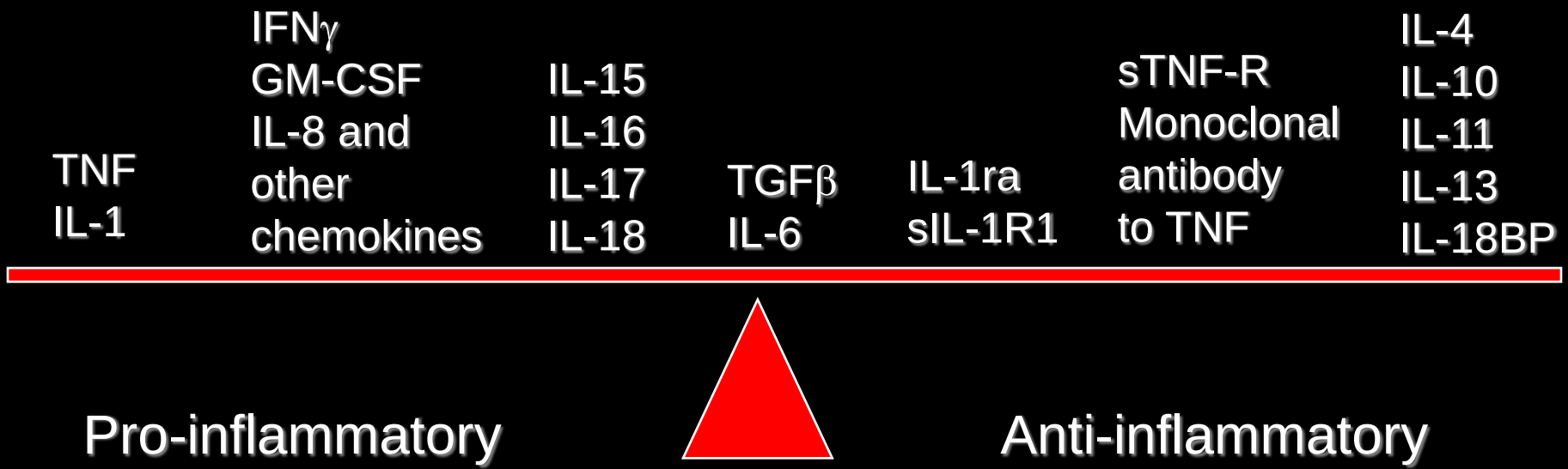
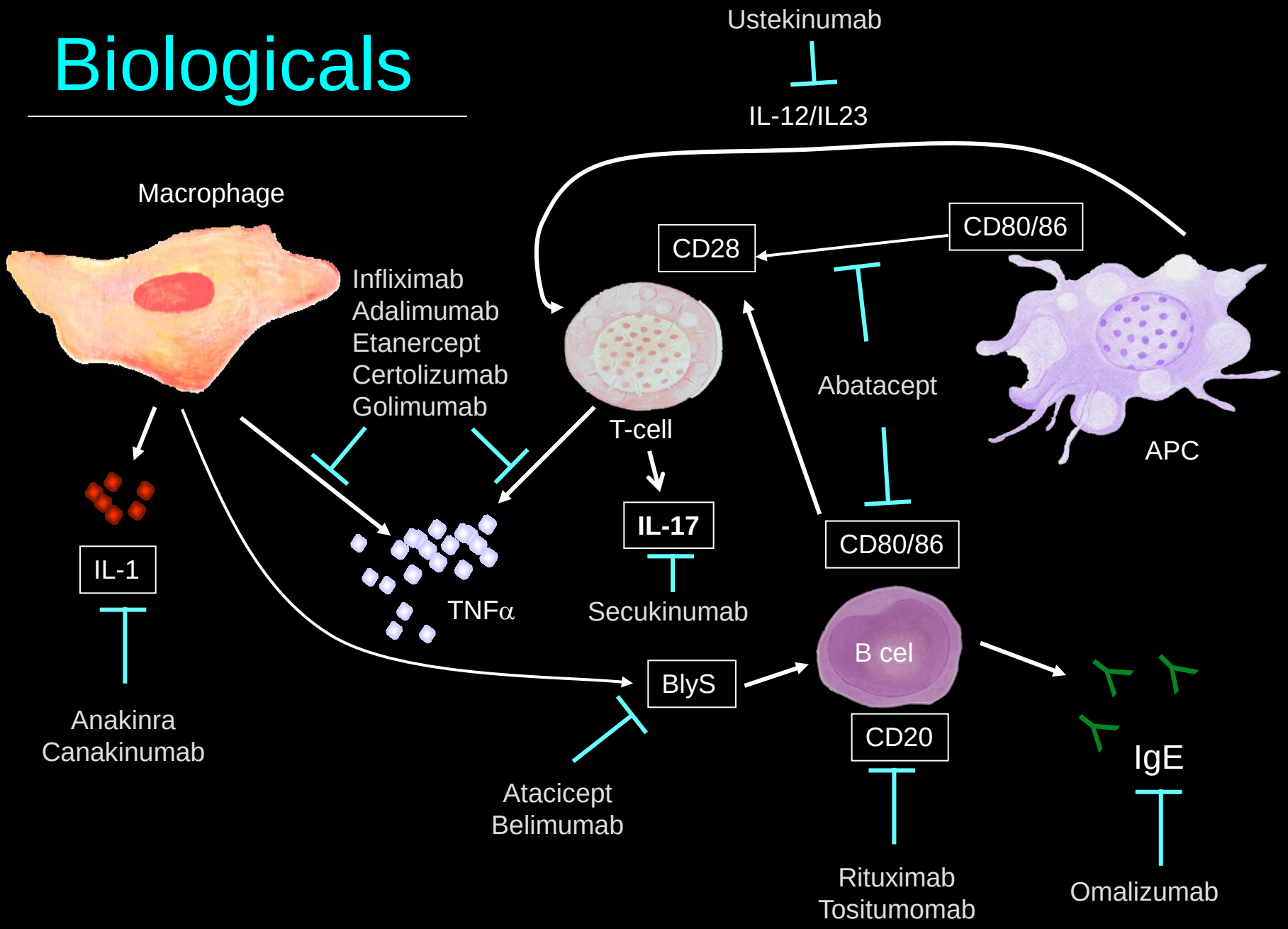
Cytokines

Cytokines and inflammation: the equilibrium



Arend. *Arthritis Rheum* 2001

Biologicals



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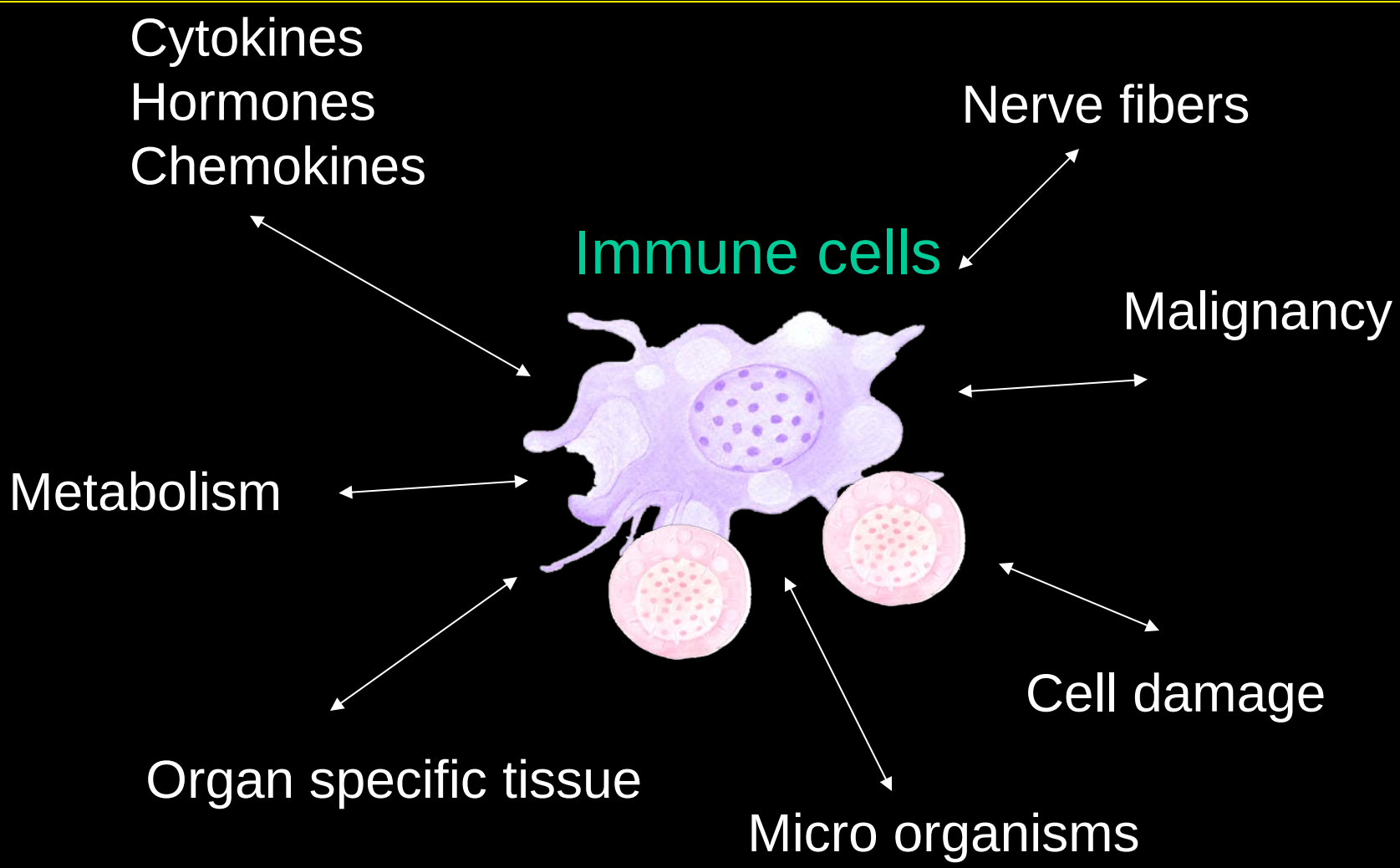
Interactions of the Immune System



Ageing in PID

- Holes in the immune system
- And who is taking care of your co-morbidities?
  - Diabetes
  - Liver disease
  - Cardial disease
  - Inflammatory disease
  - Lung disease
  - Adipositas
  - etc

White adipose tissue - Composition

- Adipocytes
- SVF (stromal vascular fraction)
  - Pre-adipocytes
  - Endothelial cells
  - Leukocytes
- Blood vessels
- Lymph nodes
- Nerves

BMI in relation to disease activity

- Vasculitis
- Rheumatoid arthritis
- Asthma
- Psoriasis

More disease activity

In conclusion

- The immune system is a highly complicated system.
- Disturbance of the balance results in disease, immunodeficiency or inflammatory diseases
- On systemic level the immune system interact with other systems such endocrine system, this may result is disease or may inhibit diseases.

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Immunodeficiency Centre Rotterdam

Immunology department
Laboratory

Patients

Family

Pediatrics
Infection/Immunology

Internal Medicine/Immunology
Clinical Immunology