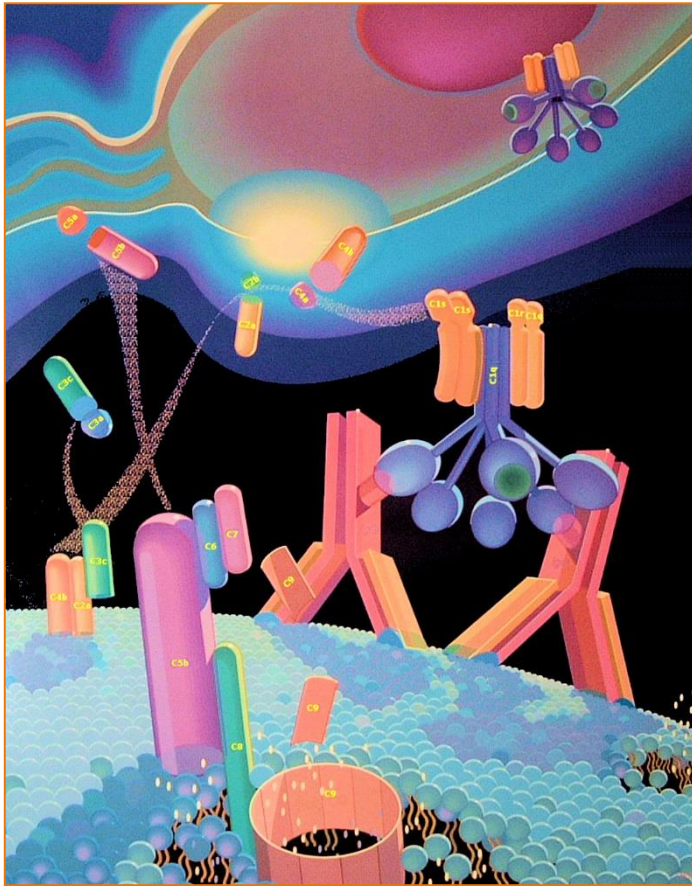




Rondzending complement

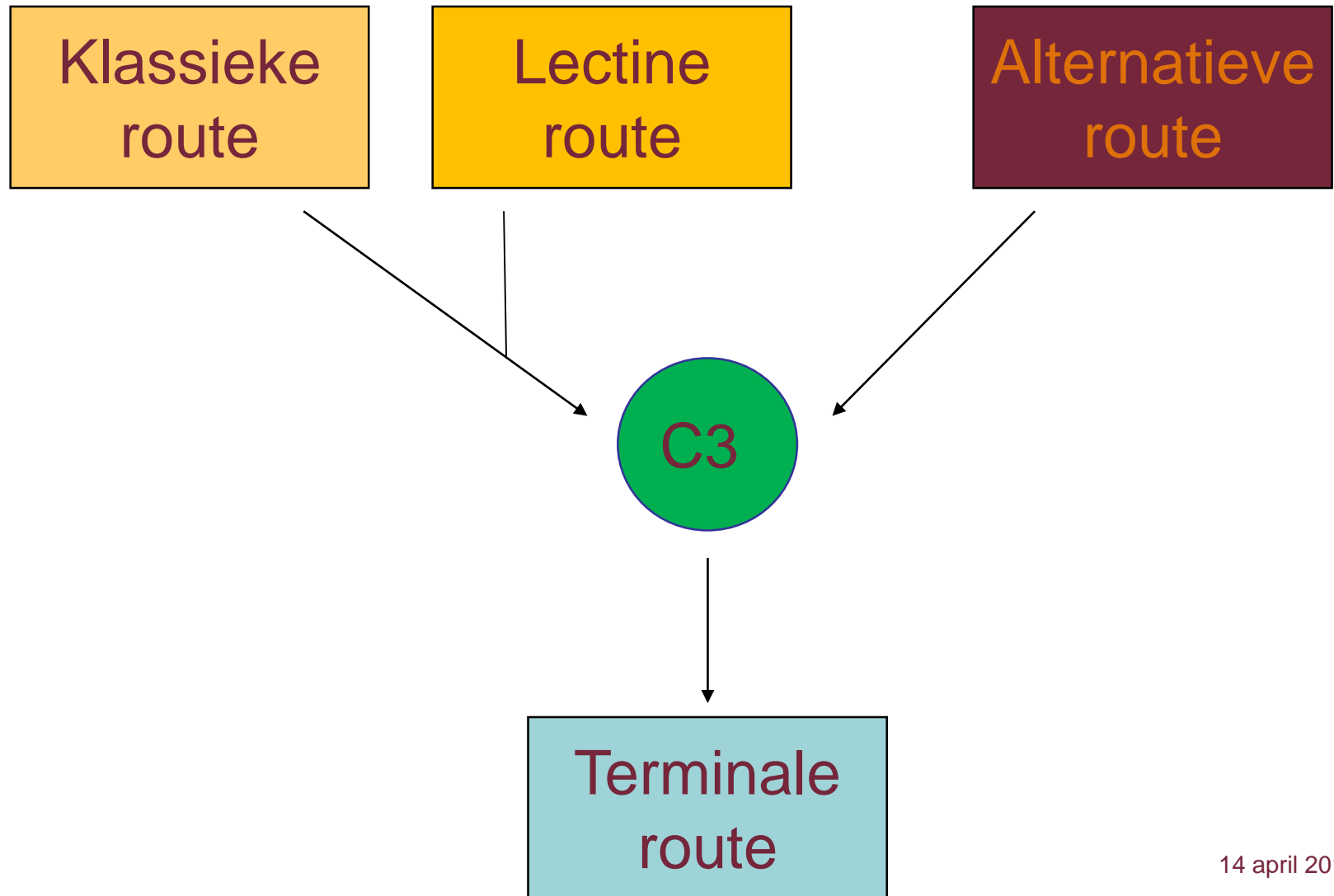
Kyra A. Gelderman, medisch immunoloog
Immunochemie, Sanquin Diagnostiek

Wanneer complement diagnostiek?

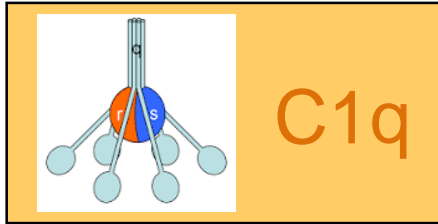


- 1) Aangeboren en verkregen complement deficiënties
- 2) Afwijkingen met complement activatie

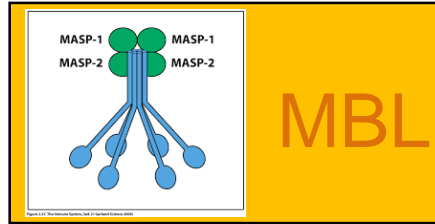
3 routes van activatie



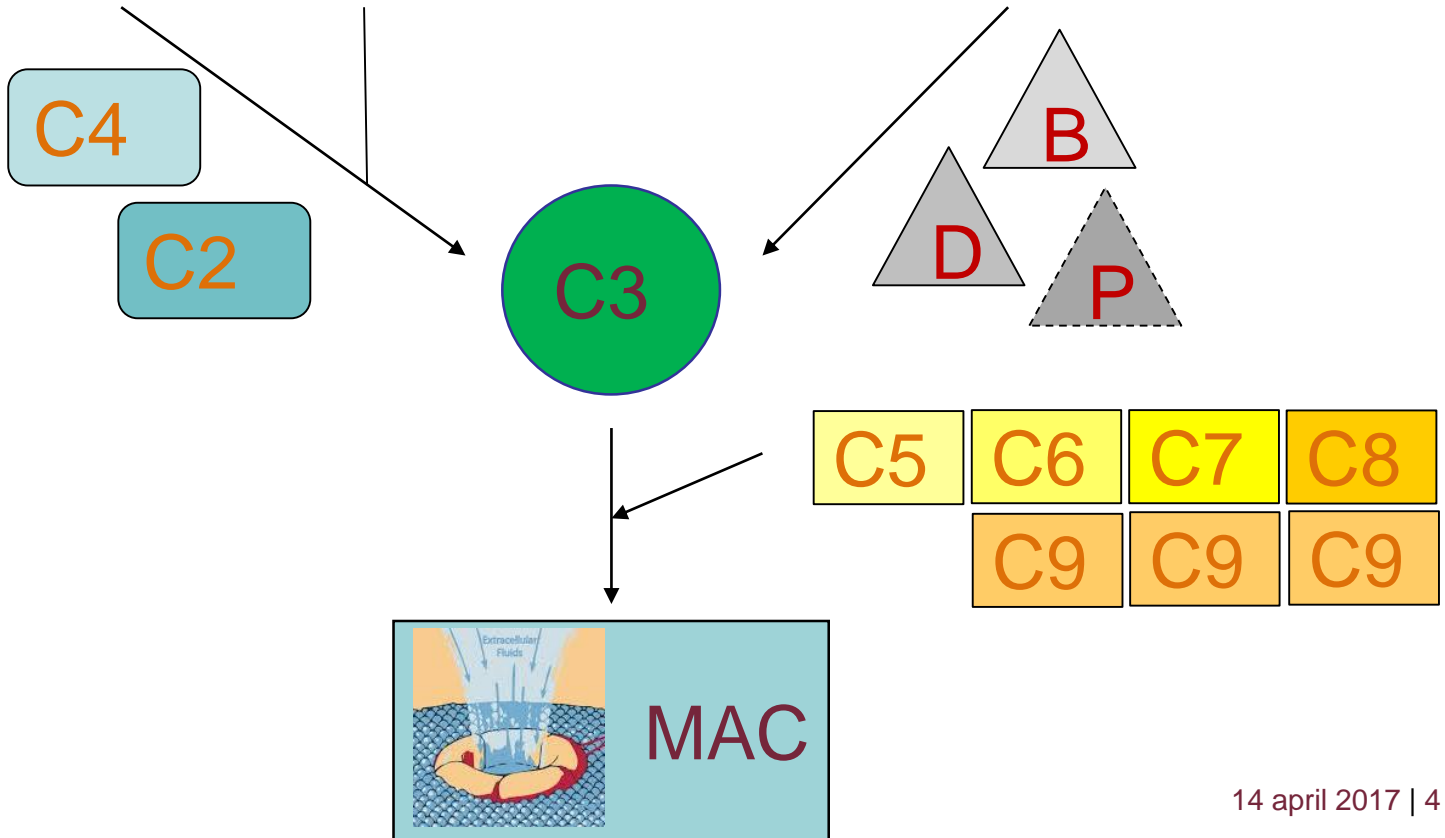
IgG $\lambda\lambda$



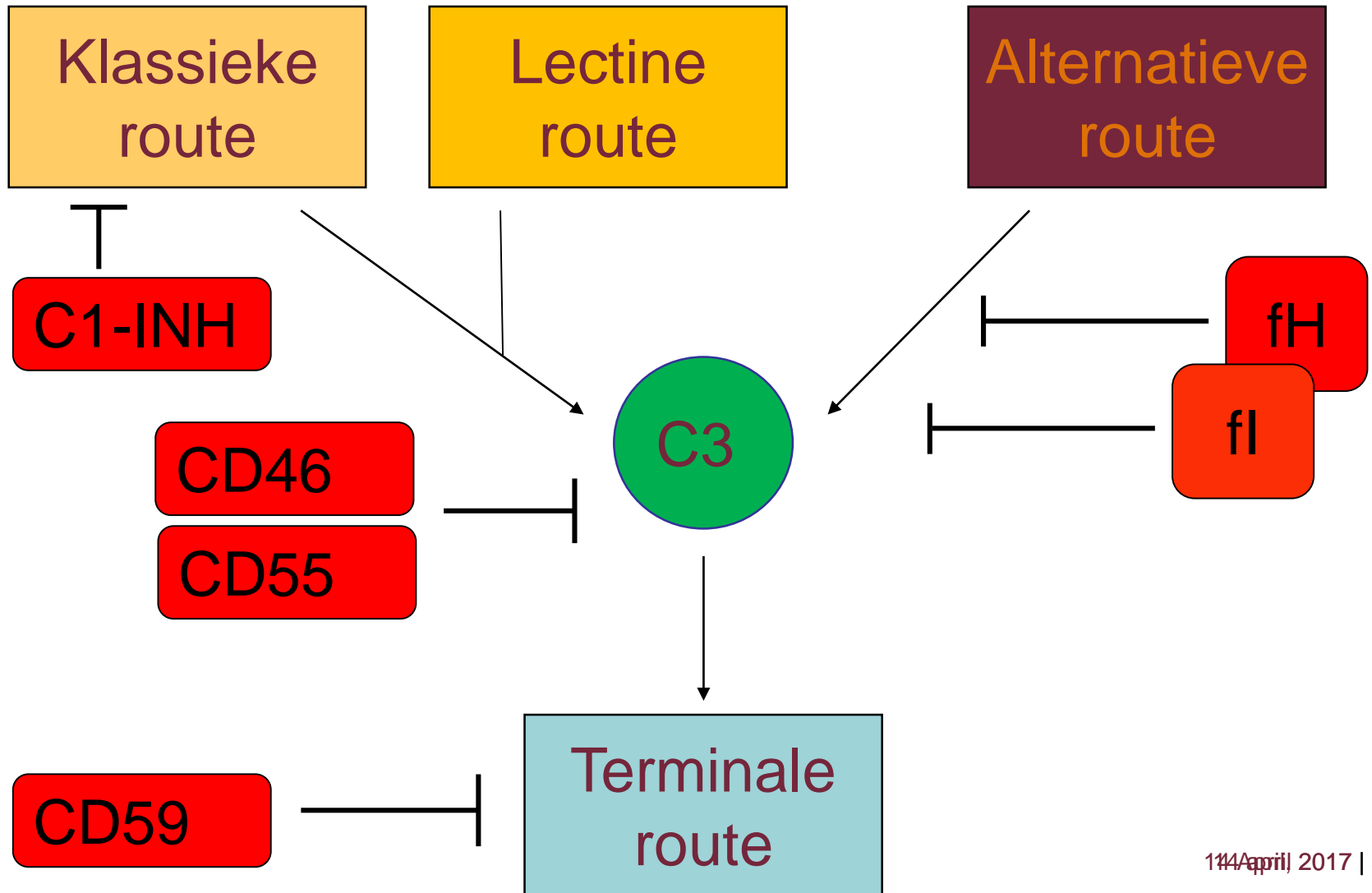
Suikers, IgA



Niet beschermd oppervlak

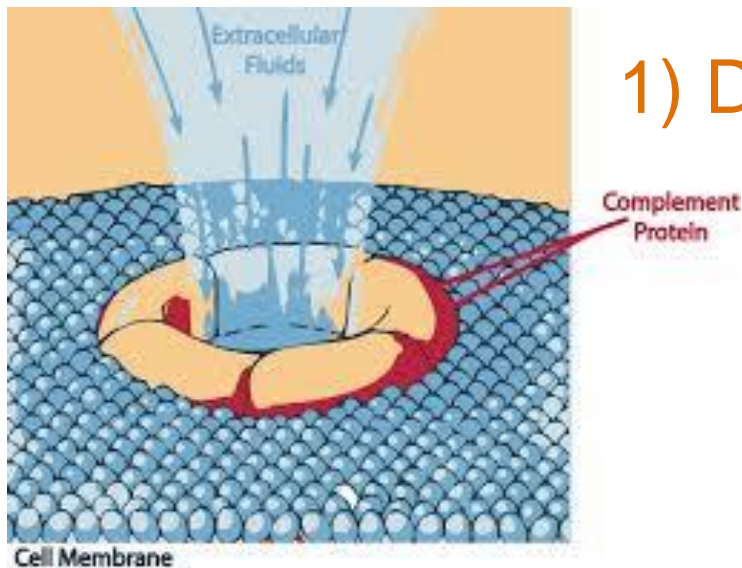


Complement inhibities



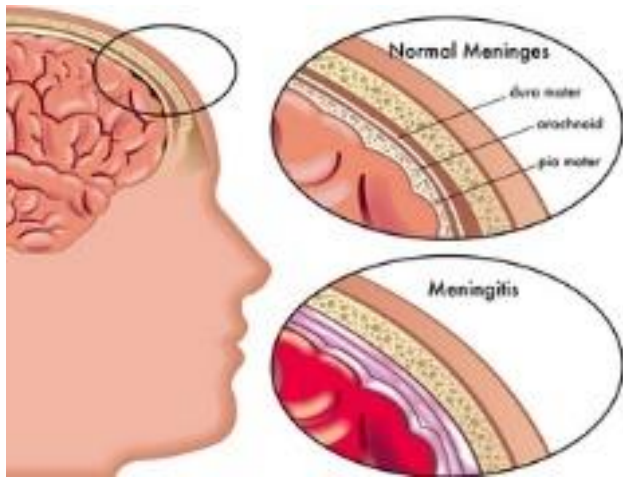
Waar is complement voor?

1. Doden indringers (bacterien)
2. Amplificeren cellulaire respons
3. Opruimen IgG gecoate partikels
4. Verbeteren B cel (antilichaam) respons
5. Opruimen dode cellen en immuuncomplexen

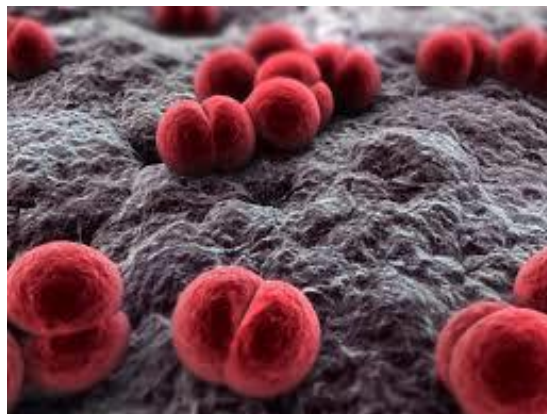
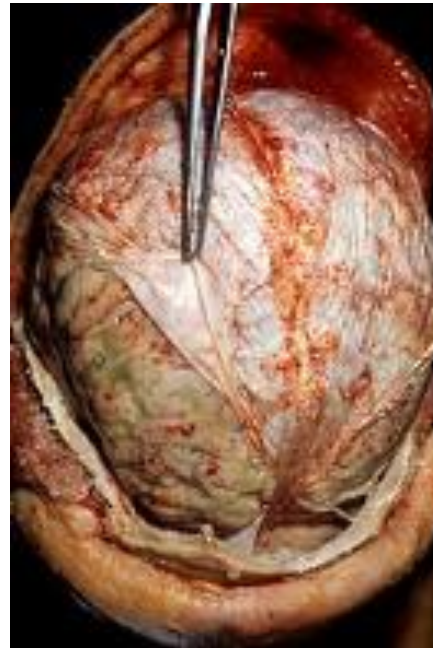


1) Directe lysis target cel (C5b-9)

1) Doden indringers: geen directe lysis (terminale route deficiëntie)



Infecties met
gekapselde bacteriën
(*N. meningitidis*)

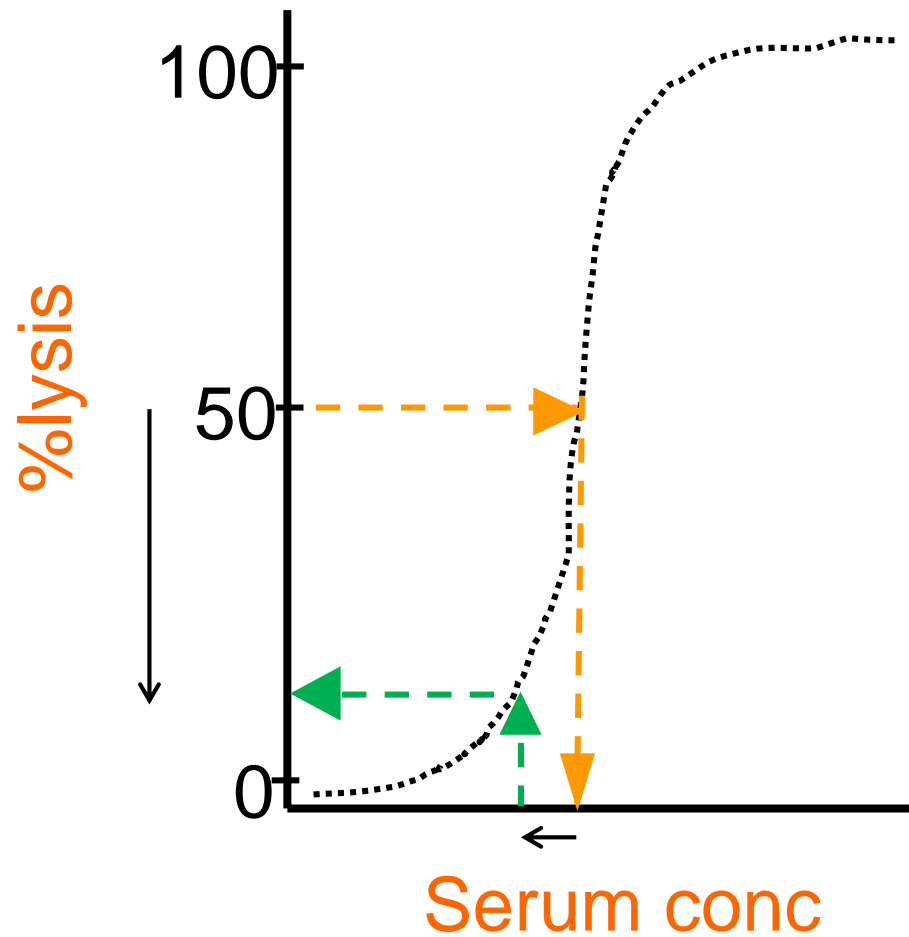


Functie:
CH50/AP50

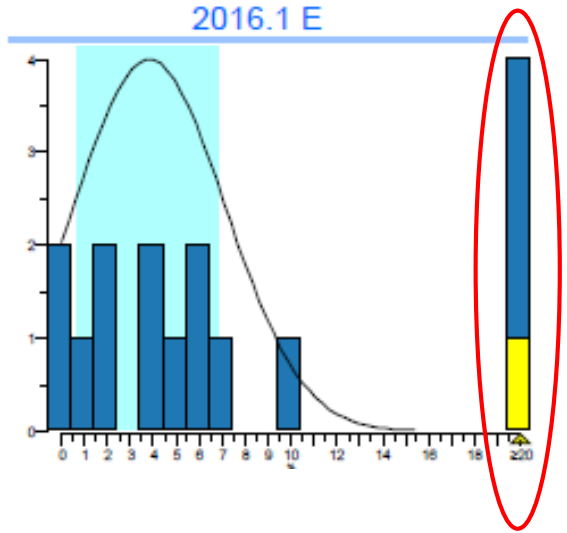
Concentratie:
C5
C6
C7
C8
C9

AP heeft een steile curve

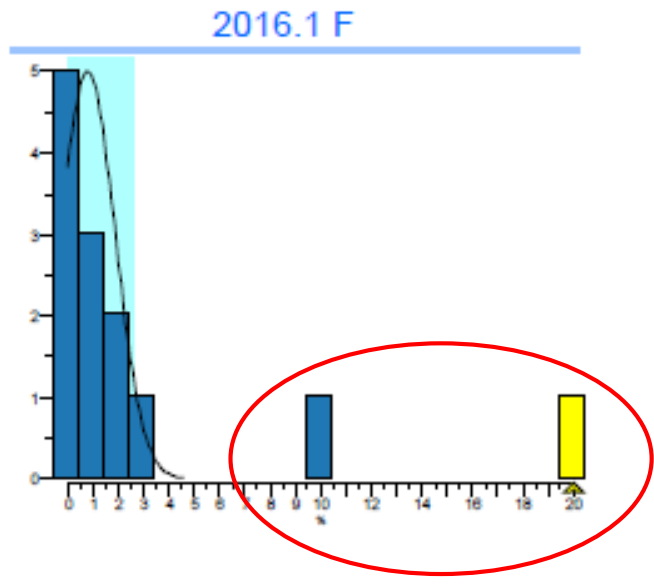
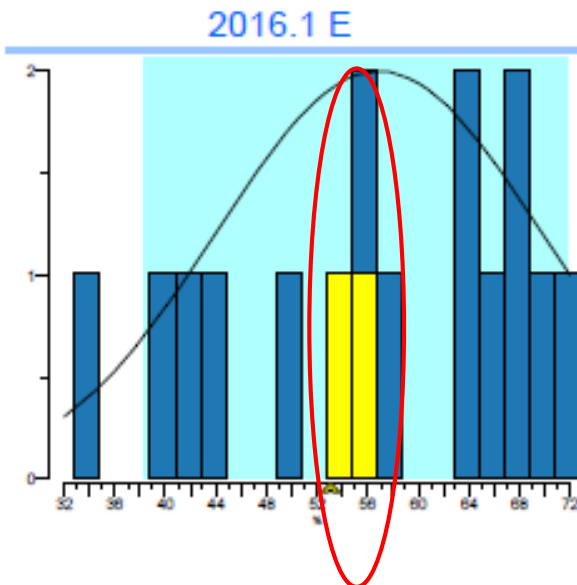
Een klein verschil in serum conc,
geeft een groot verschil in lysis/C5b-9 depositie



Elisa 1 punt vs titratie/AP50



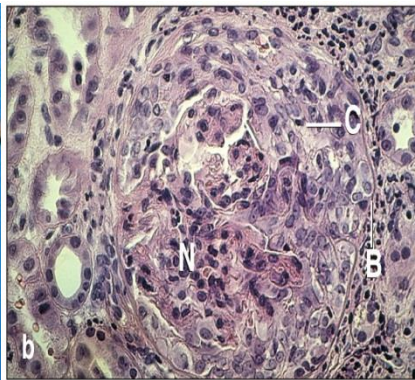
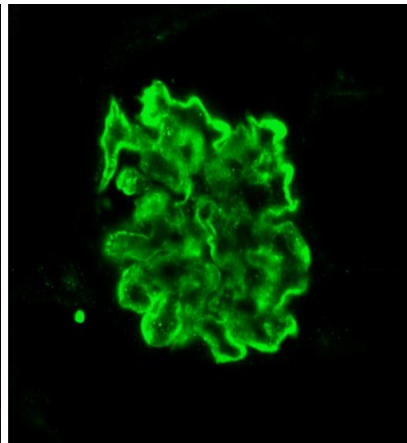
AP



CP

5) Opruimen Immuuncomplexen en dode cellen

Immuun complex ziekte (SLE) Systemische lupus erythematosus



Concentratie

C1q

C2

C3

C4

Antistoffen

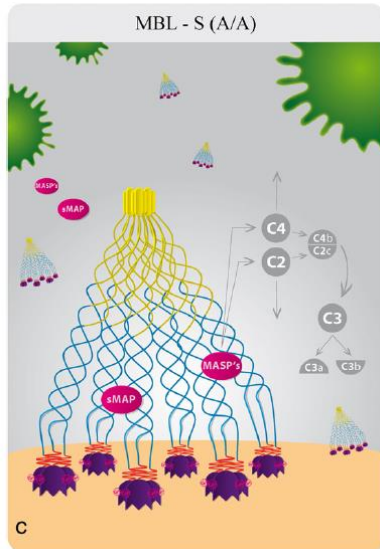
Anti-C1q (monster B)

Figure 11-3 The Immune System, 2/e (© Garland Science 2005)

6 samples A t/m F
2 tot 19 deelnemers per bepaling
goed vergelijkbare resultaten

bepaling		Methodes
C1q	Conc.	Nefelometrie (9)
C3	Conc.	Nefelometrie (11) Turbidimetrie (4)
C4	Conc.	Nefelometrie (14) Turbidimetrie (5)
MBL	Conc.	ELISA (2)
CP	Activiteit	ELISA (14) Hemol assay (2)
AP	Activiteit	ELISA (15) Hemol assay (1)
MBL-P	Activiteit	ELISA (9) ELISA in-house (1)

MBL deficiencies



5–10% van de Kaukasiërs (meest voorkomende imm.def.)

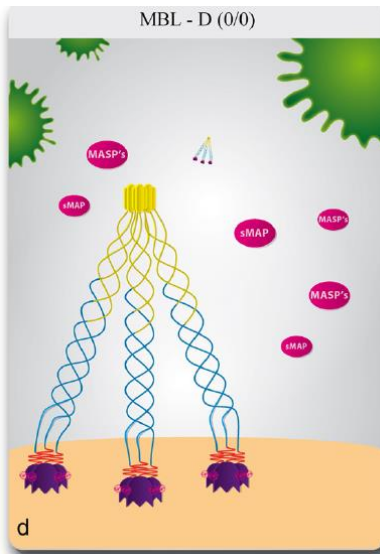
3 bekende puntmutaties

MBL →

- instabiel
- bind slecht aan ligand
- slechte LP activatie

MBL functie
(LP activatie)

MBL concentratie

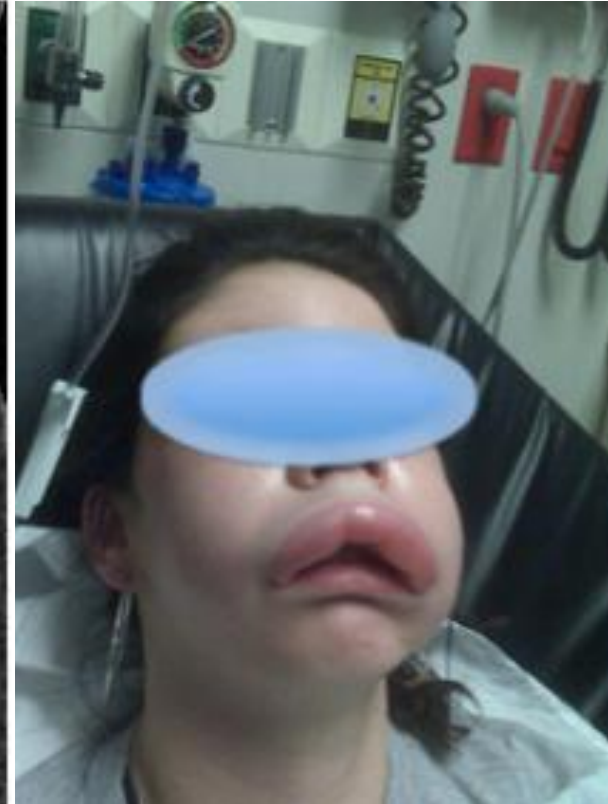


~ AIZ / infectie (in combi met andere defecten?)

Promoter polymorfismes: lagere levels van functioneel MBL

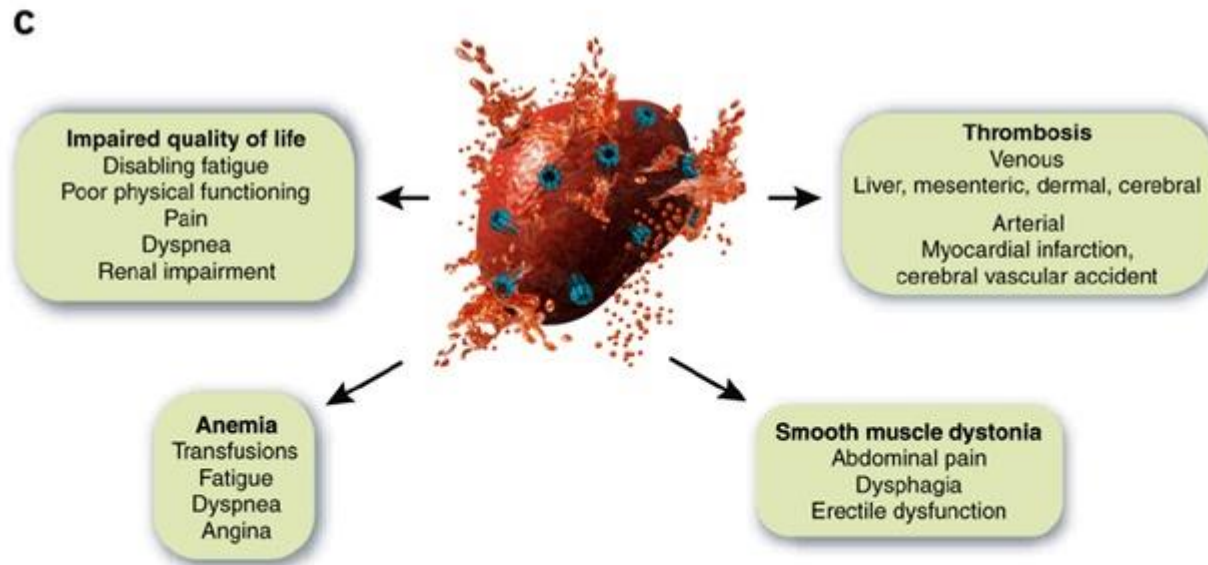
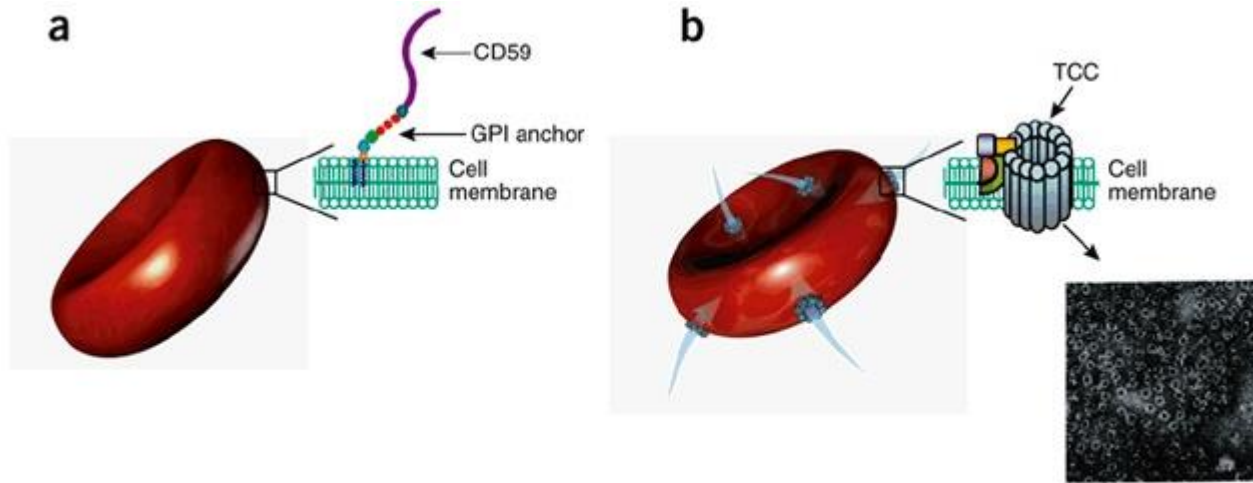
Angioedema

(C1 esteraseremmer deficiëntie)

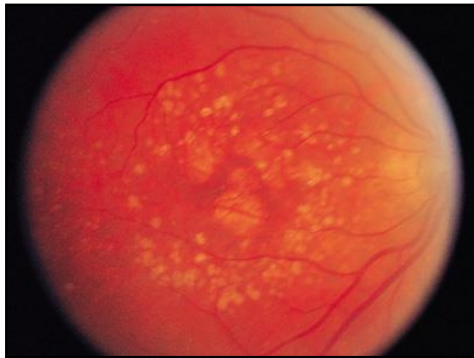
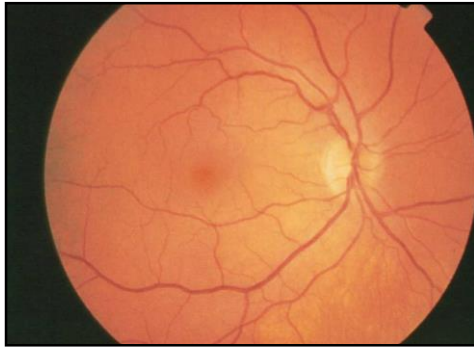


Peroxysmal nocturnal hemoglobinuria

(GPI anchor defect: geen CD55 en CD59)



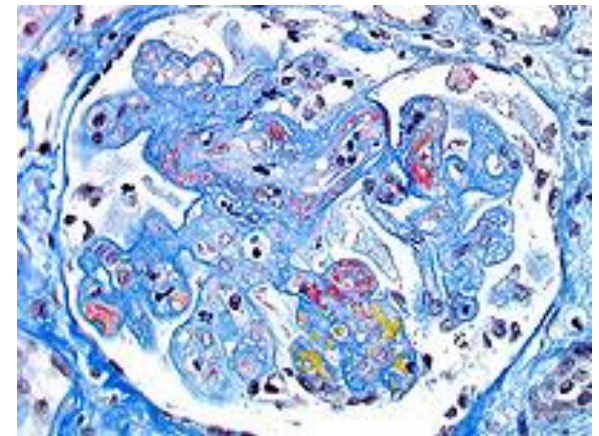
Factor H mutaties en ziekte



Maculaire
degeneratie



mutations in Factor H
especially in SCR-19+20



Bepaling	Gem. resultaat 2012.1 A	Gem. resultaat 2013.1 F	Gem resultaat 2014.A	Gem resultaat 2015.A	Gem resultaat 2016.A
CP (%)	50	48	52	63	56
AP (%)	3.7 (Eurod), 32 (anders)	3.8 (Eurod), 51 (anders)	1.3 (Eurod) 48 (anders)	6.5 (Eurod) 58 (anders)	4.5 (Eurod) 39 (anders)
MBL-P	25	22	21	29	21
C1q (mg/ml)	197	196	180	154	178
C3 (g/l)	1,36	1,30	1,35	1,19	1,32
C4 (g/l)	0,261	0,261	0,264	0,243	0,243
MBL (mg/ml)	1.2	1.95	1.13	1.1	1.1

Conclusie

- Complement is belangrijk
- Het bepalen van complement doen we goed
- Aandachtspunt: interpretatie activiteits assays
- C3 komende rondzending in g/L (2 decimalen)
- C4 komende rondzending in g/L (3 decimalen)