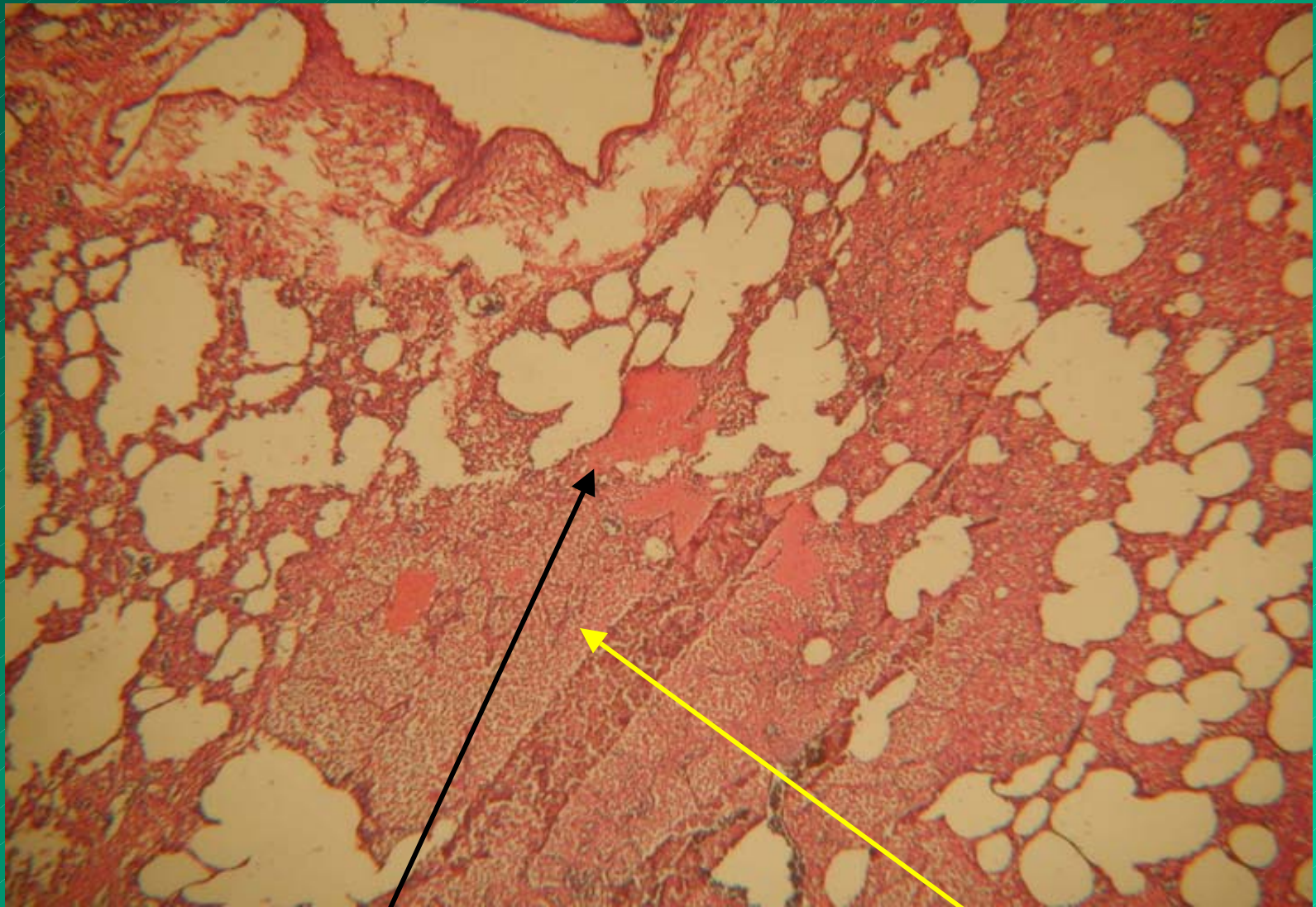


Adaptivt immunrespons og
Pseudomonas aeruginosa
biofilm meget kort
- og vice versa?

Claus Moser, afdelingslæge

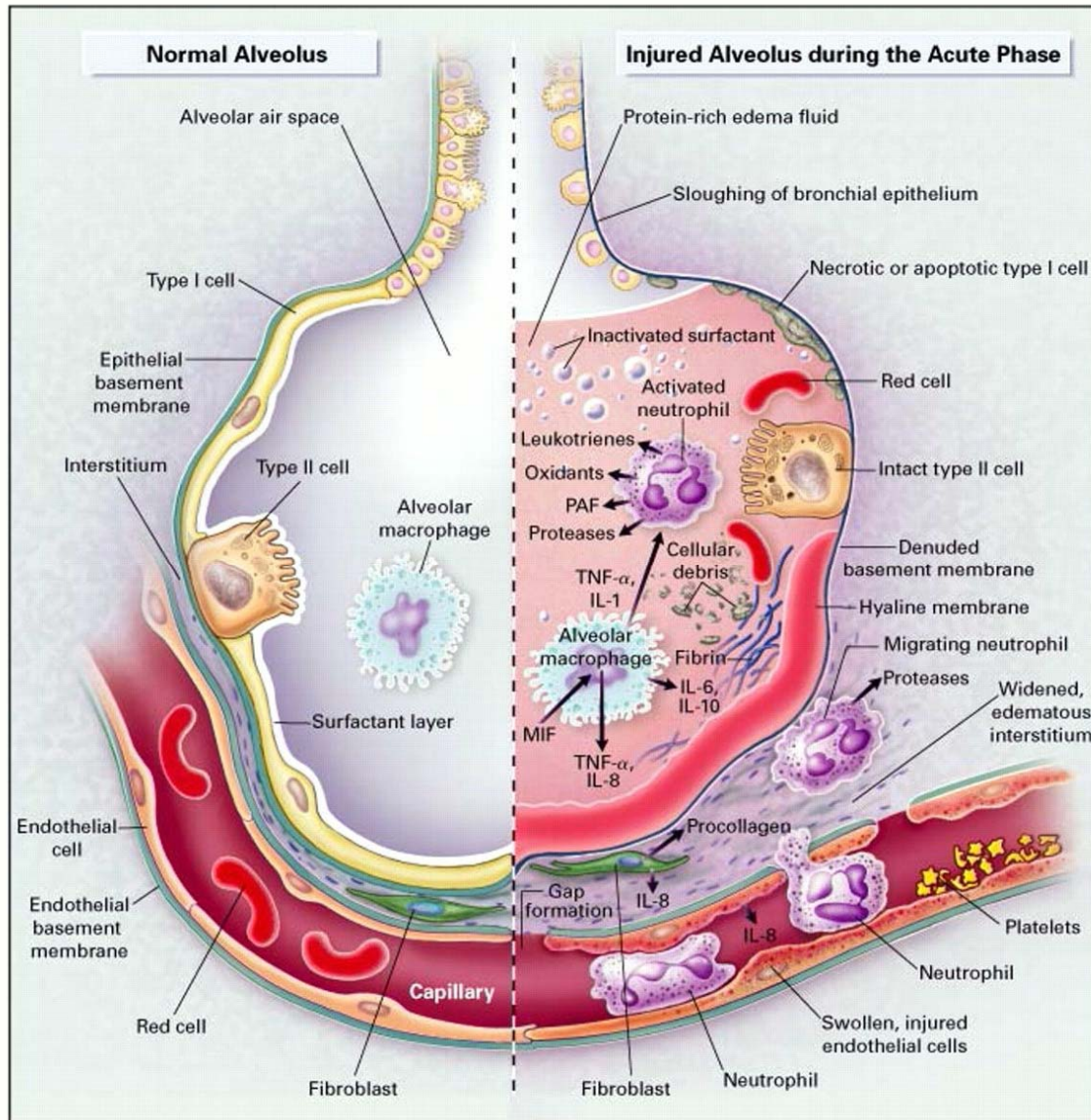
KMA, RH



Mucoid biofilm of *P. aeruginosa* in an alveolar surrounded by severely inflamed tissue (PMNs, pneumonia). Autopsy (BS242/74) of a CF girl (MLM) who died due to chronic *P. aeruginosa* lung infection and 21 precipitating antibodies against *P. aeruginosa*. HE stain x 40

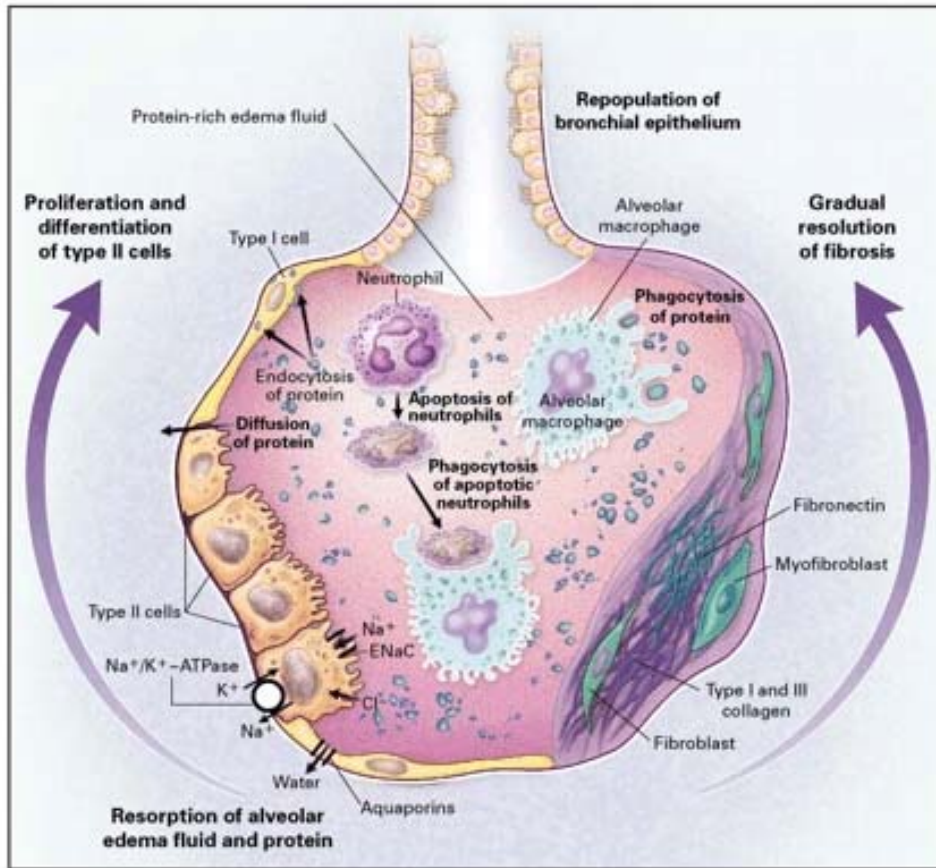
Courtesy of Niels Højby

Lung inflammation



- In addition:
 - Cytokines: IL-6, G-CSF, GM-CSF, IL-3, PGE2, LTB4, IL-10
 - Cells: Dendritic cells, mast cells, NK-cells, endothelial cells, fibroblasts, thrombocytes

Lung resolution

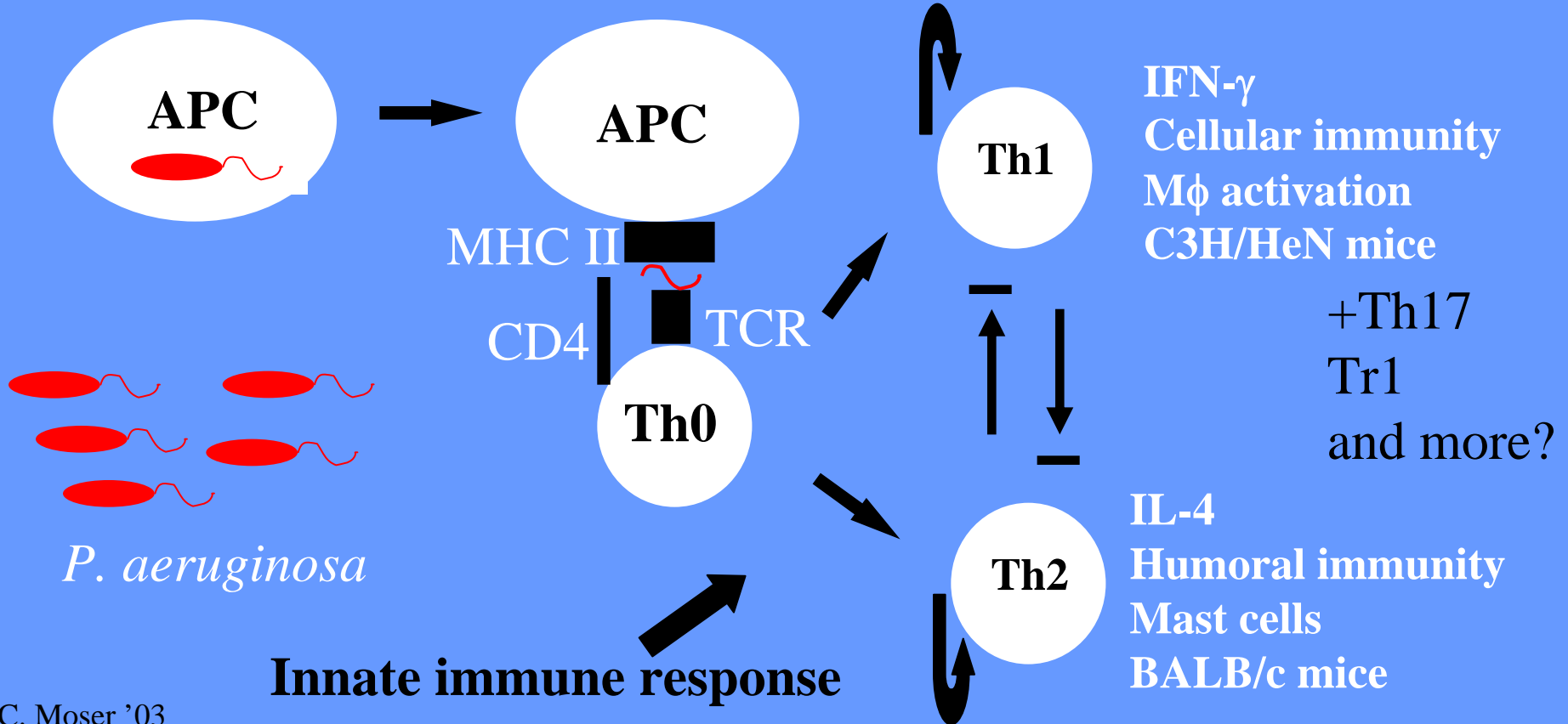


- **Inflammation is accelerated upon activation of adaptive immune response!**
 - **Skewing of Th1/Th2 balance**
 - **Immune complex disease**

Th1/Th2 "brush up"

Antigen uptake. Processing/presentation.

Activation.



Dichotomized response in CF

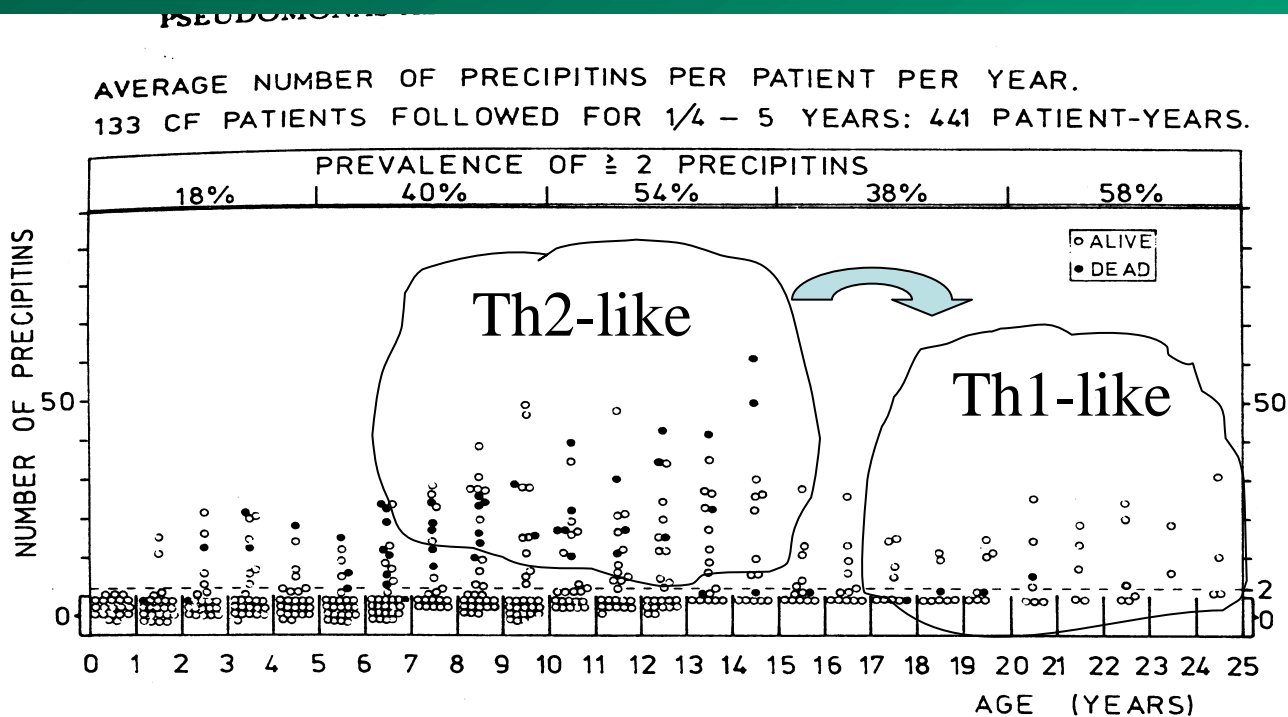
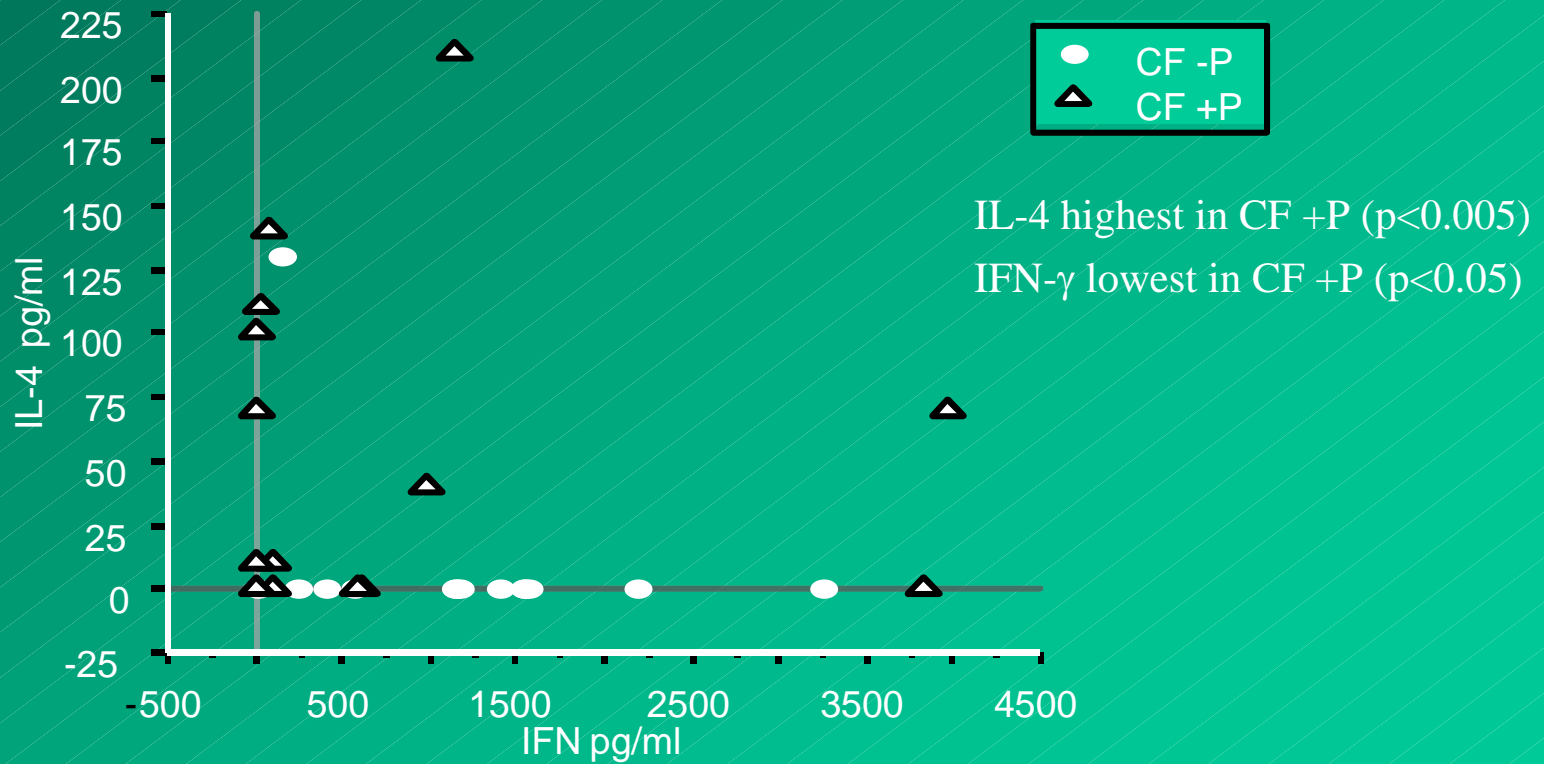


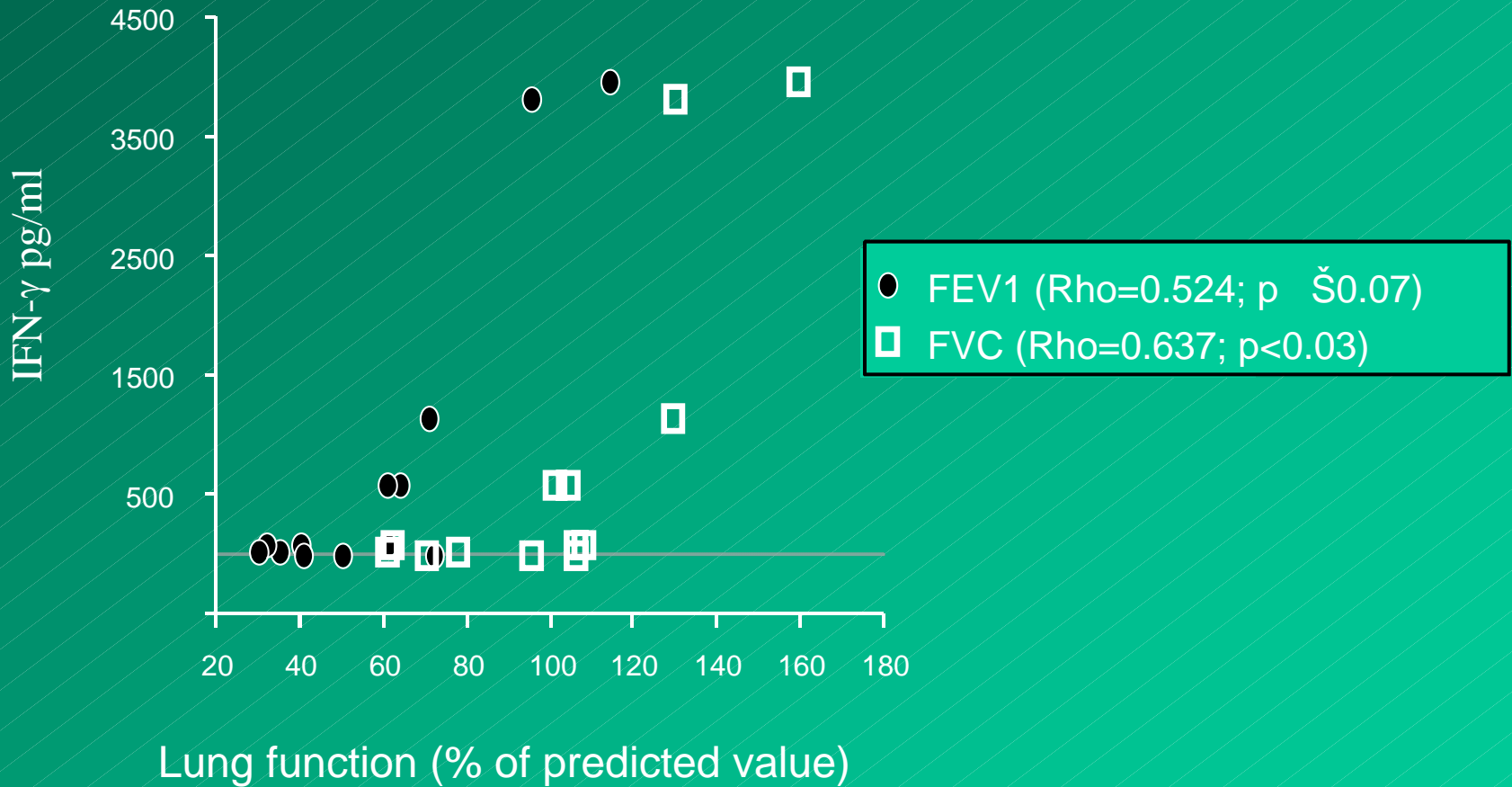
Figure 3. Prevalence and number of precipitins against *P. aeruginosa* in sera from patients with cystic fibrosis classified into different age groups. Each circle represents the average results per year of the crossed immunoelectrophoreses which have been carried out with sera from a given patient. Filled circles represent 18 patients who have later succumbed. The broken line (2 precipitins) is the borderline between normal (0-1 precipitin) and abnormal number of precipitins.

Højby N, *et al* (Scand J Resp Dis 1977).

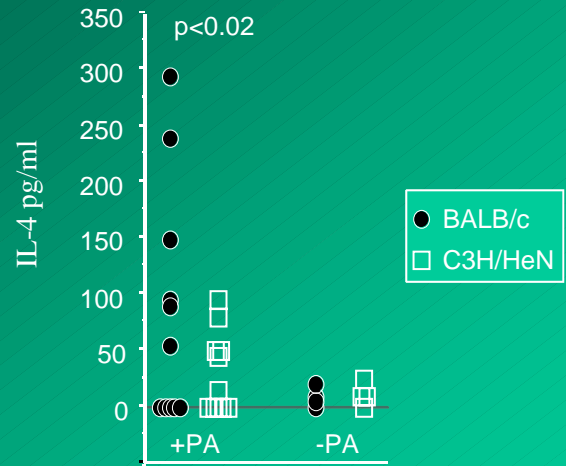
Dichotomy in CF



Cytokines and lung function



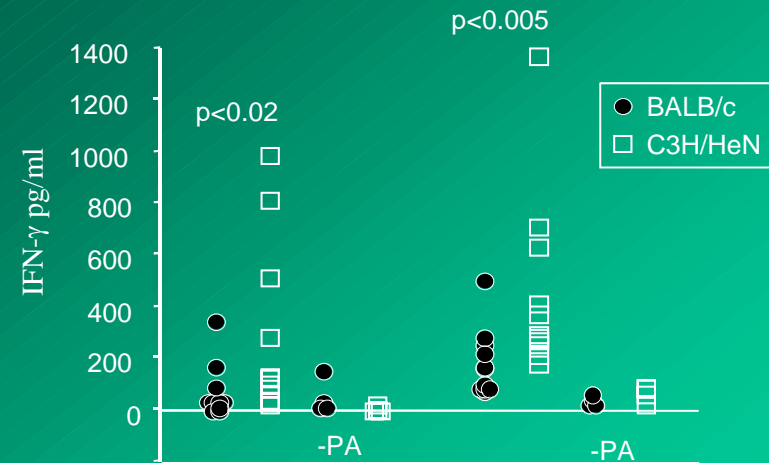
Th1/Th2 reacting mice cont.



Moser C *et al.* APM

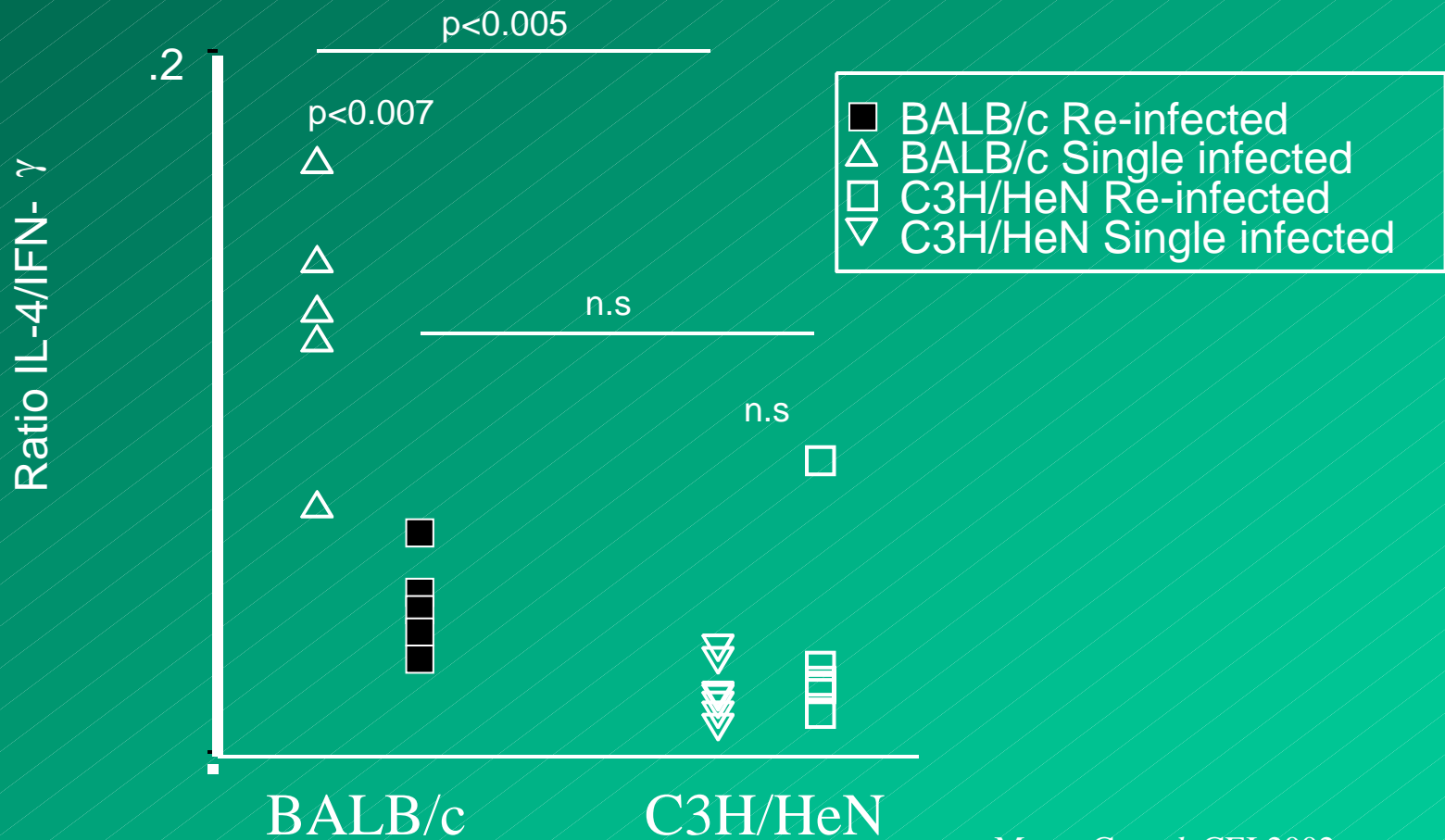
Moser C *et al.* APMIS 1999

Th1/Th2 reacting mice cont.

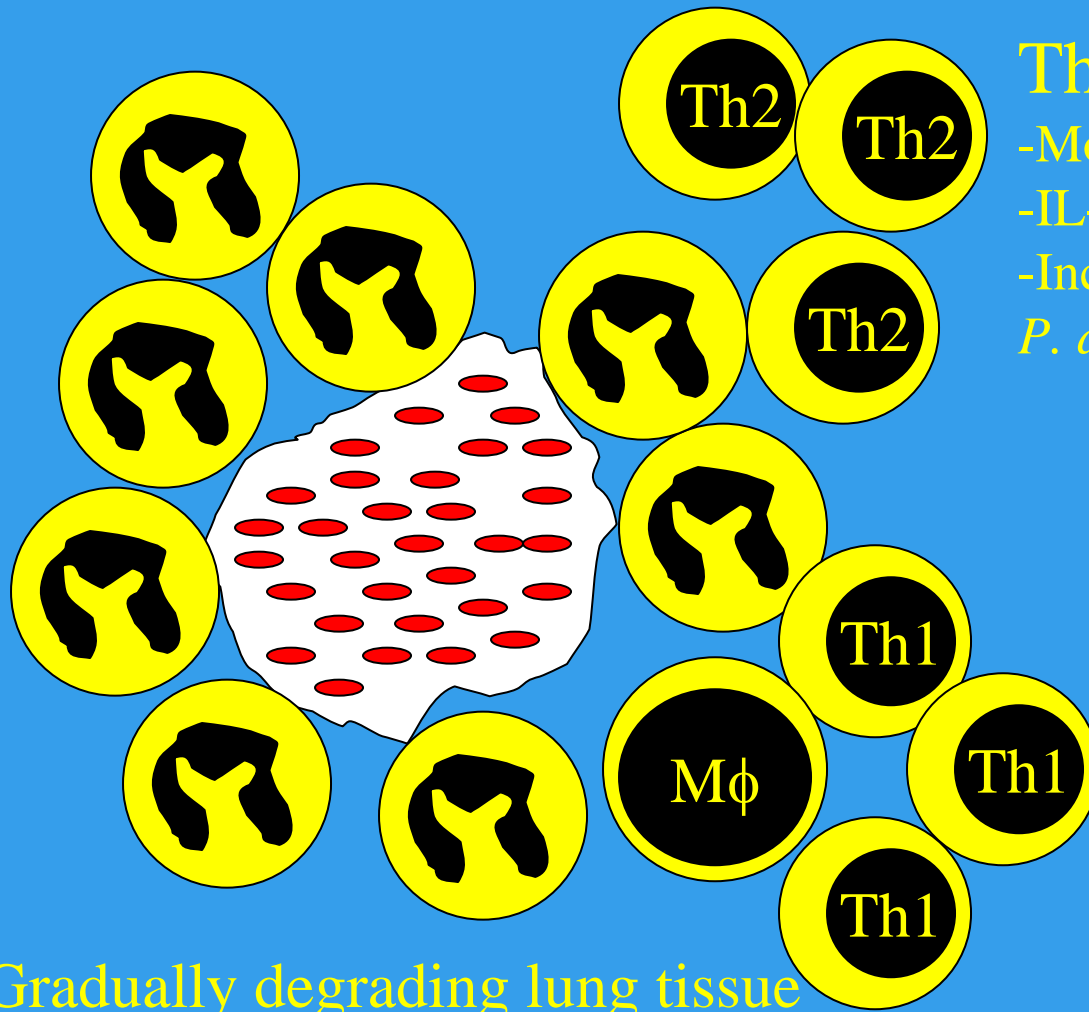


Moser C *et al.* APMIS 1999

Re-infection cont.



Th1/Th2 and CF in theory



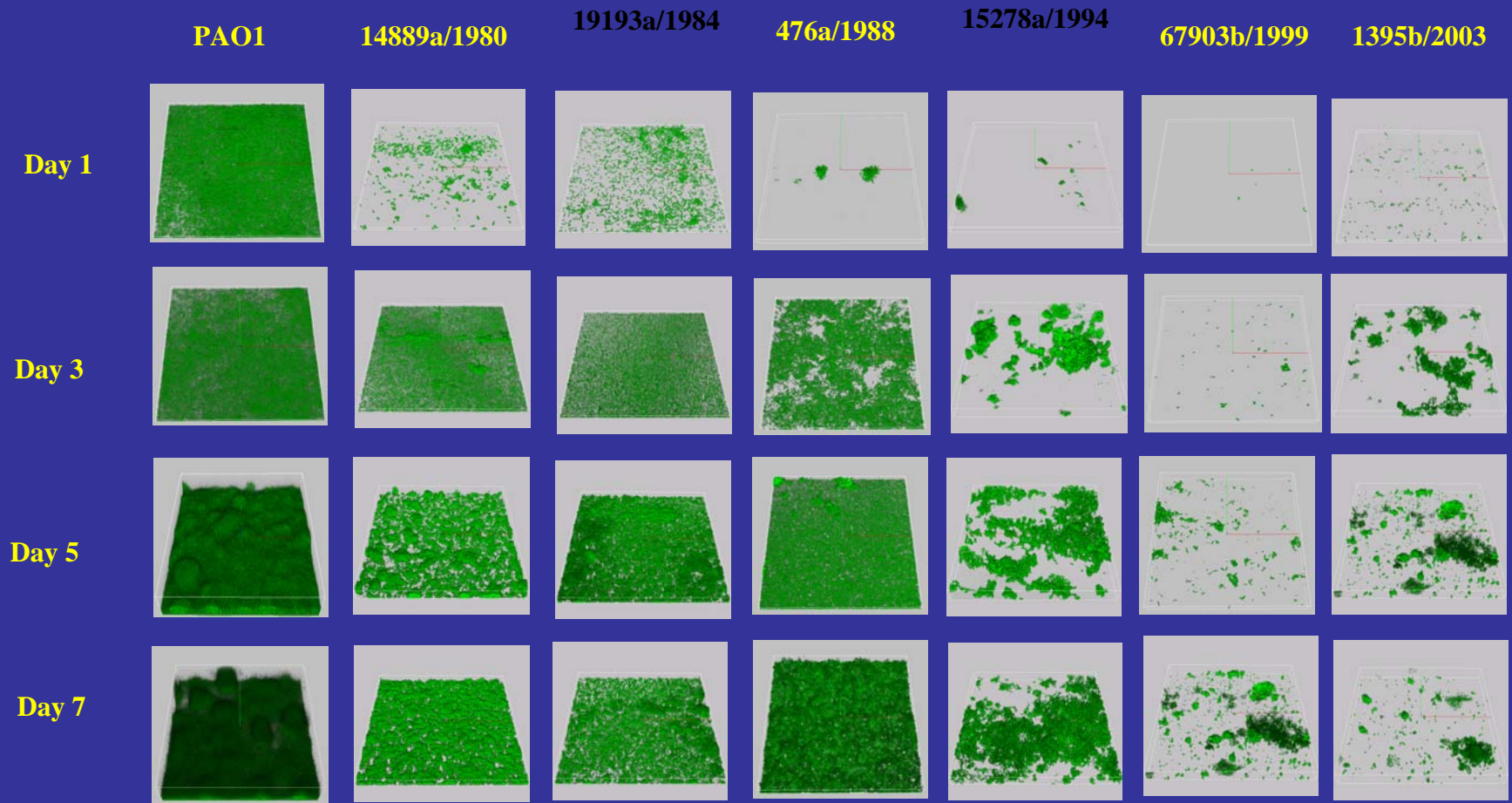
Th2 dominated:

- More immune complexes
- IL-4 inducing burst
- Increased oxidative stress of *P. aeruginosa*

Th1 dominated:

- IFN- γ induced macrophage clearing of debris
- Reduced PMN mediated burst
- Reduced oxidative stress of *P. aeruginosa*
- Reduced amount of immune complexes

CLSM images of biofilm formed by longitudinal *P. aeruginosa* isolates

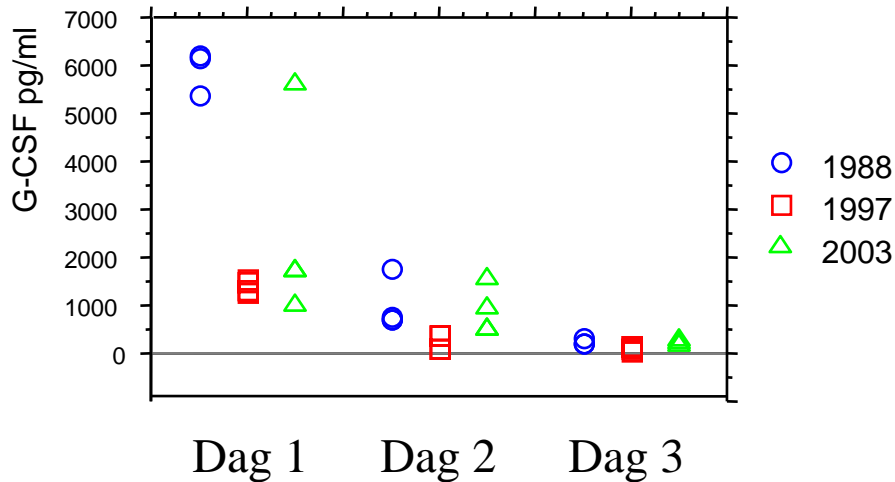


Biofilm development of wild type PAO1 and sequential isolates from patient no 1. Flow chambers were inoculated with *gfp*-tagged wild type and *P. aeruginosa* isolates grown on Casamino Acids minimal media. CLSM images were acquired at 1, 3, 5 and 7 days after inoculation.

Inflammatorisk respons

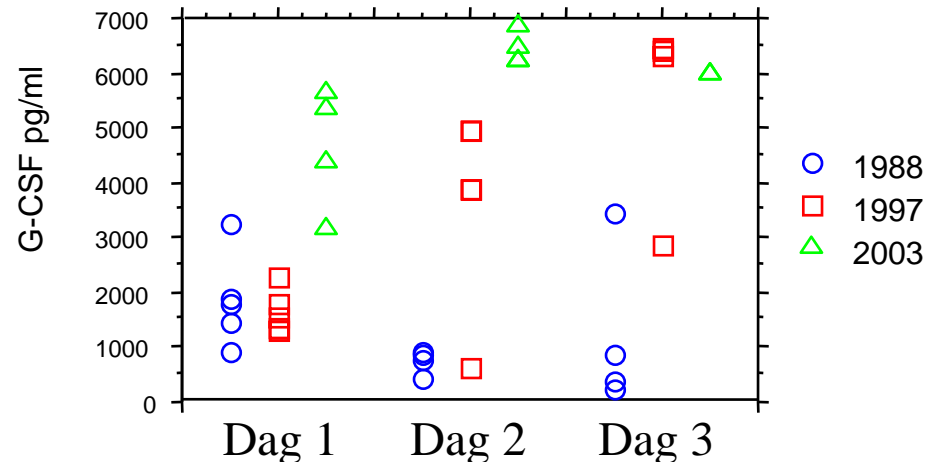
Non-mucoid versus mucoid.

Non-mucoid



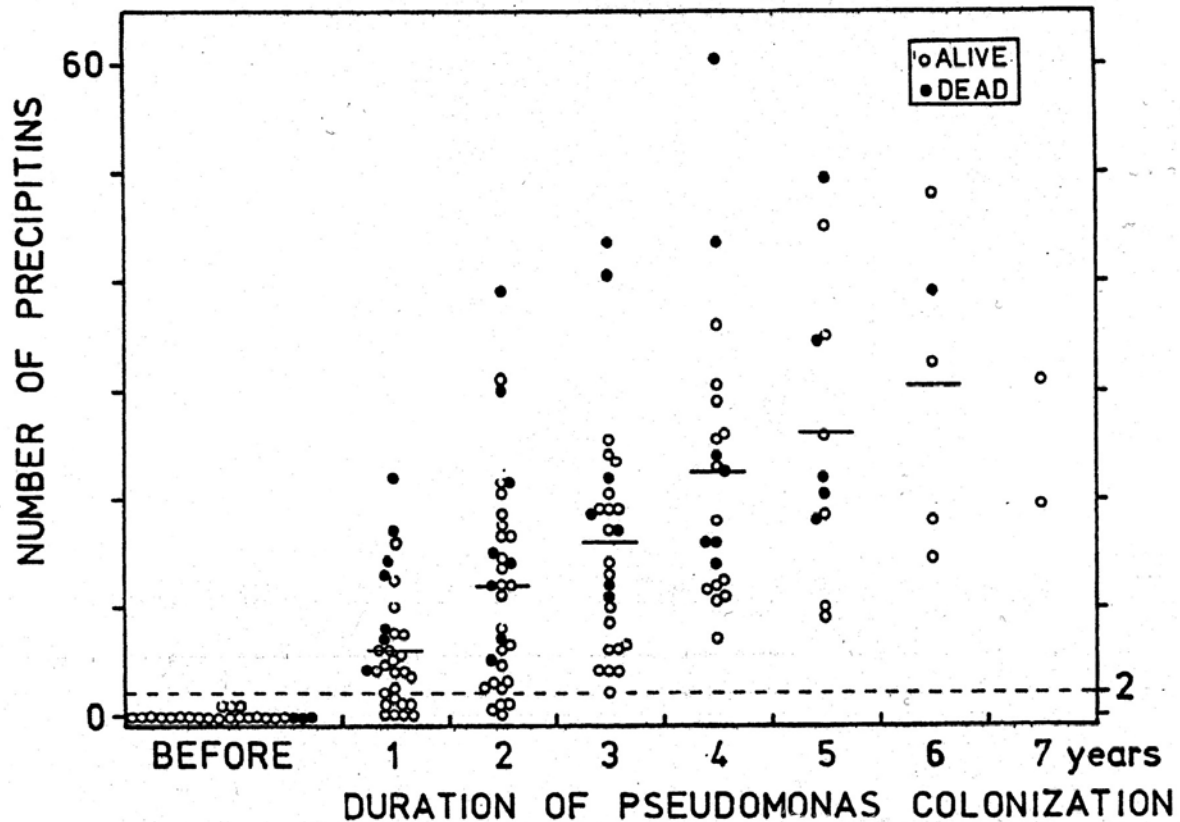
G-CSF: PMN mobilisator fra knoglemarven

Mucoid



AVERAGE NUMBER OF PRECIPITINS PER PATIENT PER YEAR

CF WITH CHRONIC PSEUDOMONAS COLONIZATION



Høiby et al. Scand. J. Resp. Dis. 58:65;1977