

Cystic Fibrosis

a) Diagnostic Dilemmas

b) The New Problems

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So what exactly is CF?

- A genetic diagnosis
- An electrolyte diagnosis
- An electrical diagnosis
- A symptomatic diagnosis

- It depends
- Management is *not* dependent on diagnosis

Consensus Statement - Diagnosis

- **Clinical phenotype, or CF in a sibling, or positive newborn screening test**

Plus

- **Abnormal CFTR: elevated sweat [Cl⁻], nasal PD abnormal, or positive genotype**

J Pediatr 1998; 132: 589-595

CF Diagnosis - Lessons From USA

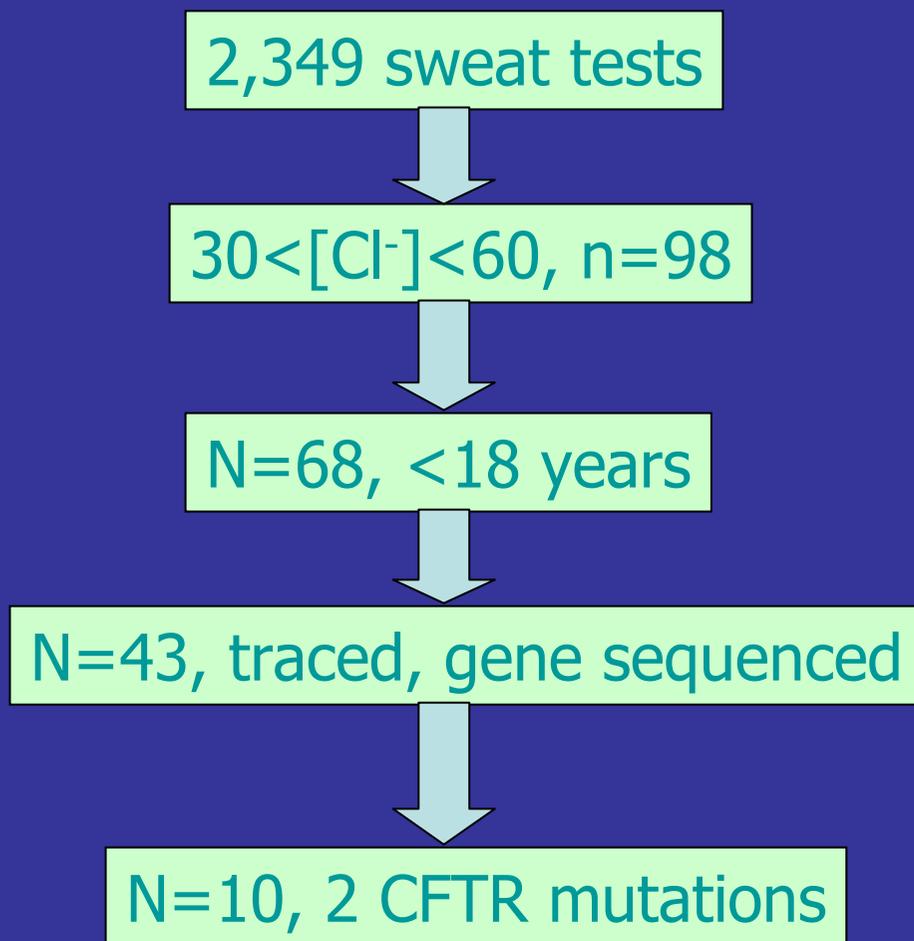
- Virtually all can be diagnosed by a sweat test - (98% of 19,992)
- False positive diagnoses are not unknown - 45 reversed in 1996
- Late diagnoses are too common - 10% not diagnosed until adult life

*Source: CFF patient registry, 1996 annual data report,
Bethesda, Maryland, 1997*

Diagnosis of Grey Case CF

- You do not need 2 genes for a diagnosis
- You do not need a positive sweat test for a diagnosis.
- **AND.....**
- The child who is very well
 - ❖ But, has positive tests for CF!

The Child With Equivocal Sweat Electrolytes



The Child With Equivocal Sweat Electrolytes: Conclusions

- **23% children with intermediate sweat electrolytes had two CF genes**
- **4/9 had a normal nasal potential (amiloride, isoprenaline/low chloride)**
- **Beware the 'not abnormal' sweat test**

BlueJ 2002; 165: 757-761

False Positive Sweat Test

- **Eczema**
- **Untreated adrenal insufficiency**
- **Type 1 glycogen storage disease**
- **Nephrogenic DI**
- **Malnutrition**
- **Panhypopituitarism**
- **Artifact - sweat test incorrectly performed**
- **Aids**
- **Fucosidosis**
- **Hypothyroidism**
- **Ectodermal dysplasia**
- **Mucopolysacharidosis**

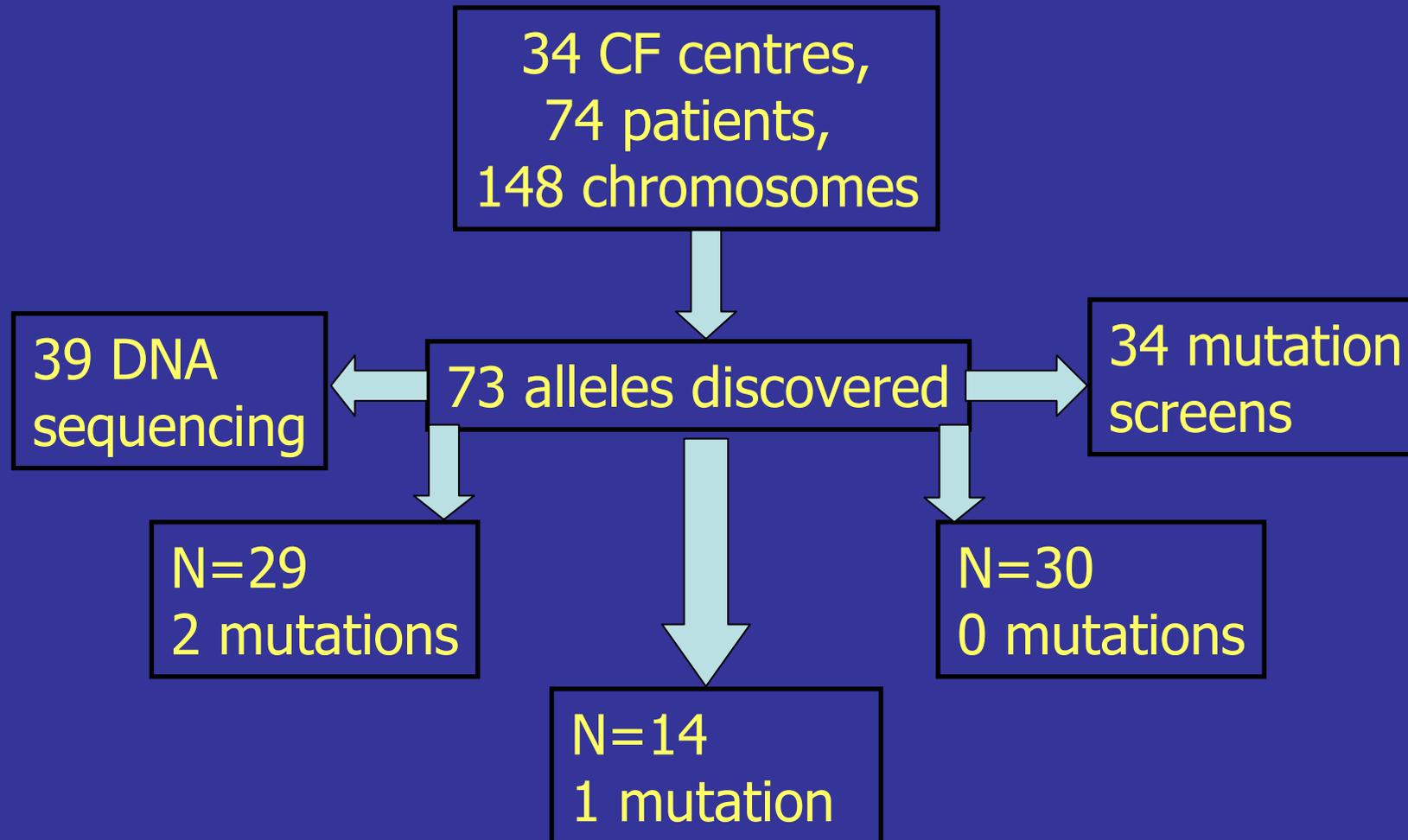
The Concept of 'Pre-CF'

Child completely well

Plus

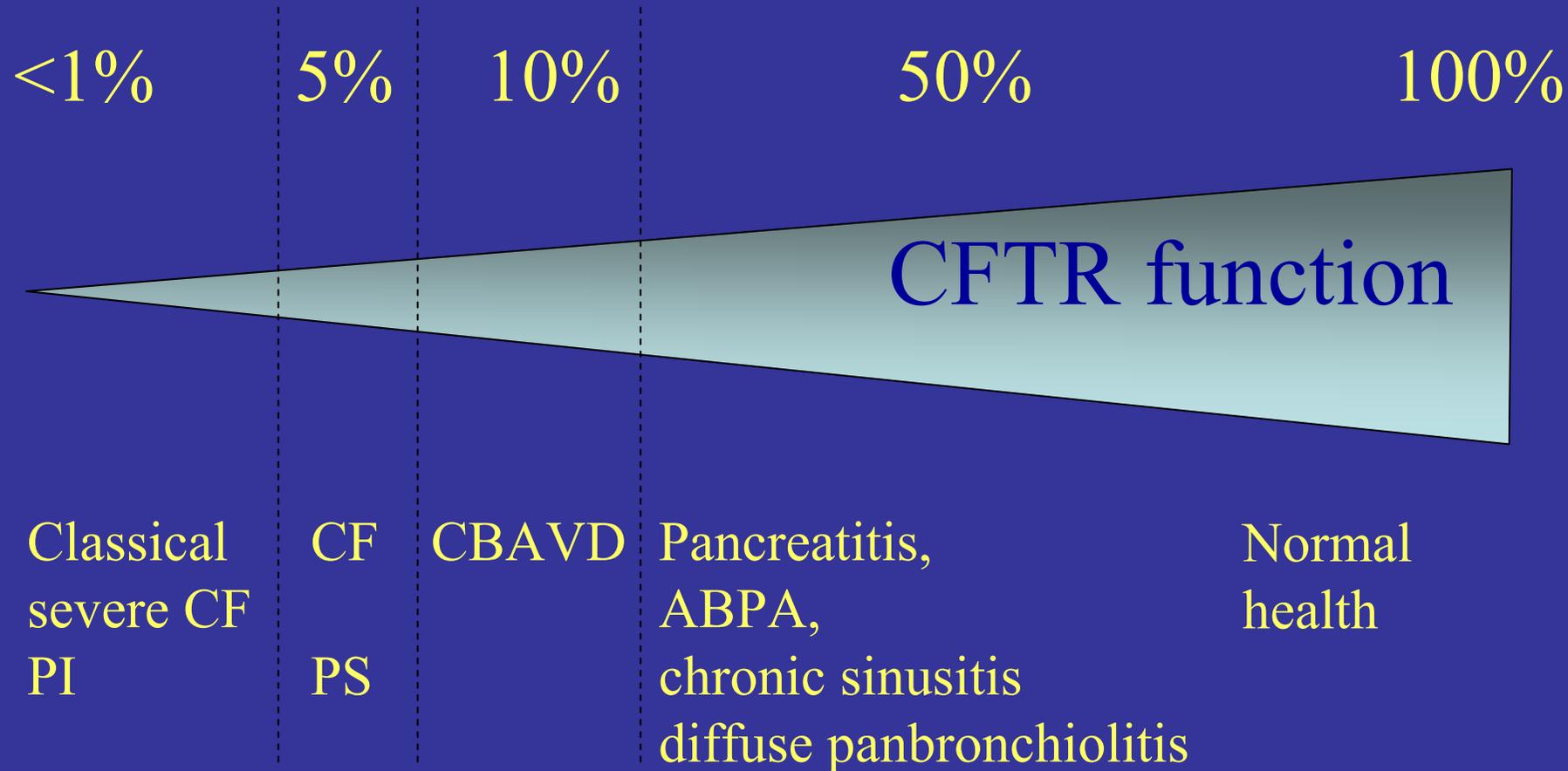
- Abnormal sweat test: *chemical pre-CF*
- Abnormal genotype: *genetic pre-CF*
- Abnormal PD: *electrical pre-CF*

CF with no CFTR Mutations



T for Two? 5T-7T-9T

- 9T – No problems
- 5T – Reduced CFTR, hinterland of disease-causing mutation
- 7T – yes and no, with reservations!



Adapted from Griesenbach *et al*, *Thorax* 1999

1-Diagnosis of CF: 2011

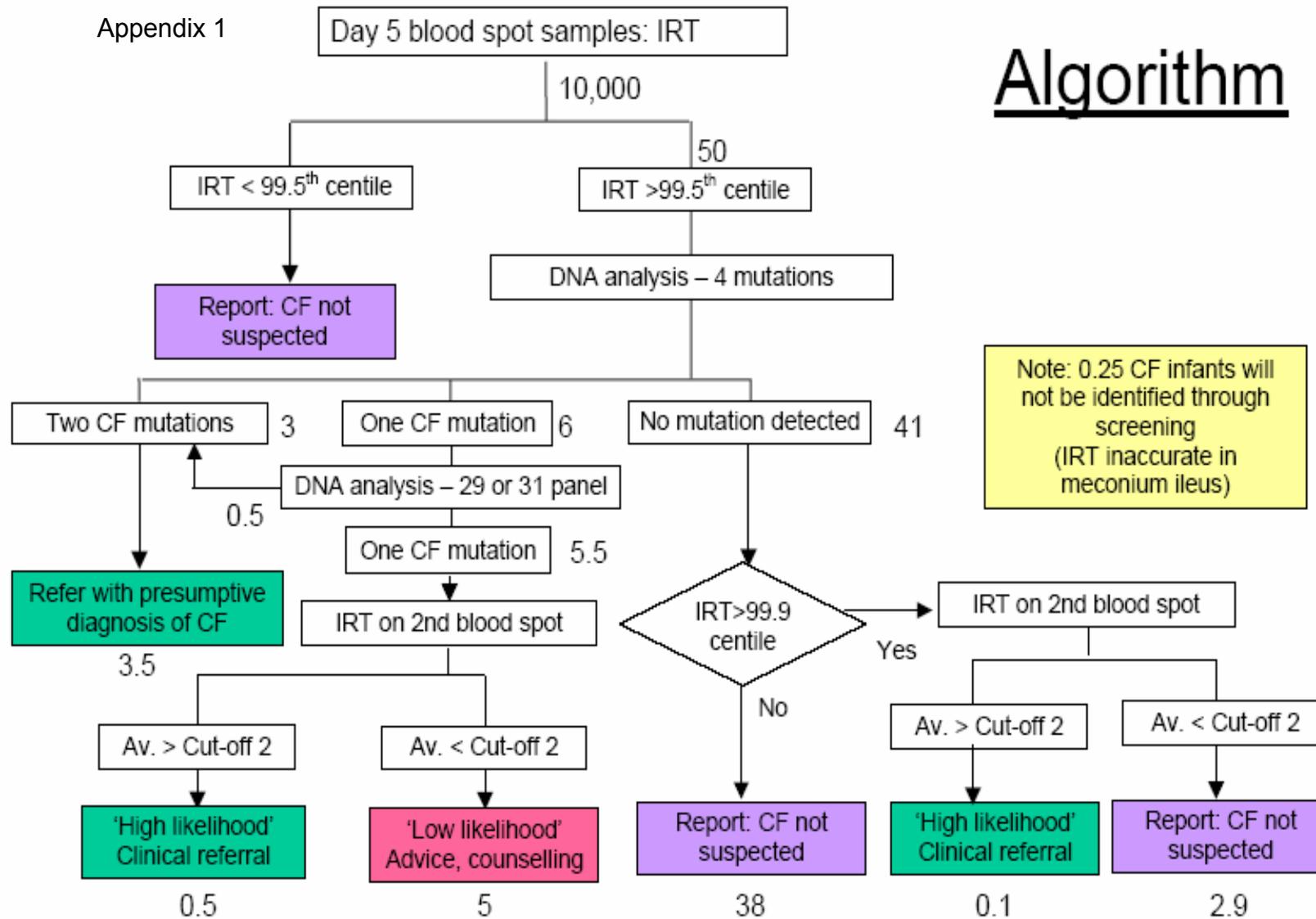
- Is and remains a *clinical* one primarily – compatible phenotype
- Laboratory tests confirmative only
- The more negative tests, and the more atypical the phenotype – consider alternative diagnoses, and test for them

2-Diagnosis of CF: 2011

- **Whatever the diagnosis, treat what you find, and look for trouble**
- **314/409 on USCF Registry with normal, equivocal or missing sweat test were diagnosed on clinical grounds alone.**
- **The clinician is alive and well!**

Appendix 1

Algorithm



CF. The next big things

• CF Related Diabetes

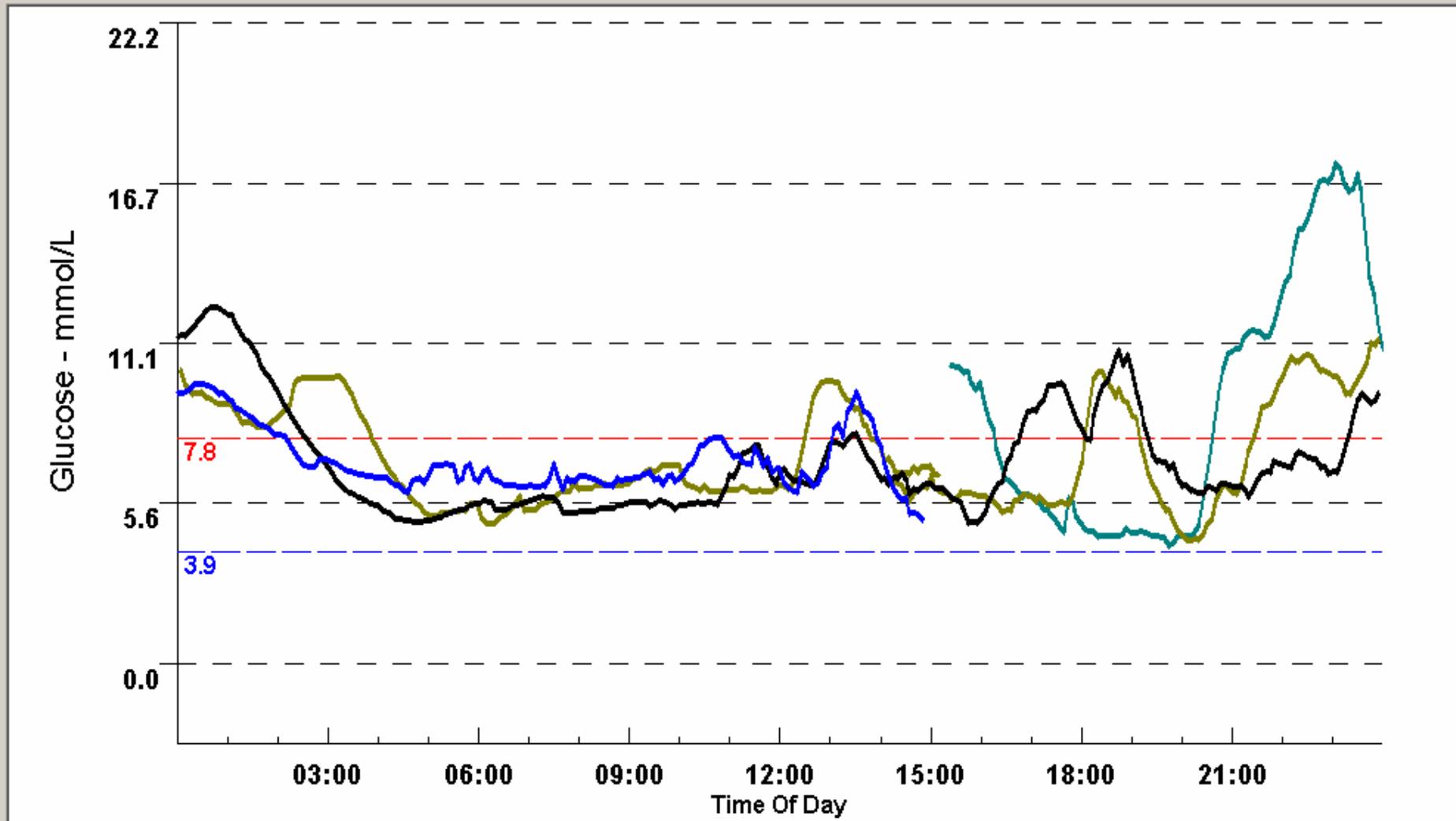
- Non tuberculous mycobacteria especially M. Abscessus.
- Aspergillus and allergic bronchopulmonary aspergillosis (ABPA)
- Osteoporosis and use of water soluble Vitamin K



Sensor Modal Day

Legend

Close



Click sensor plot line to read data value

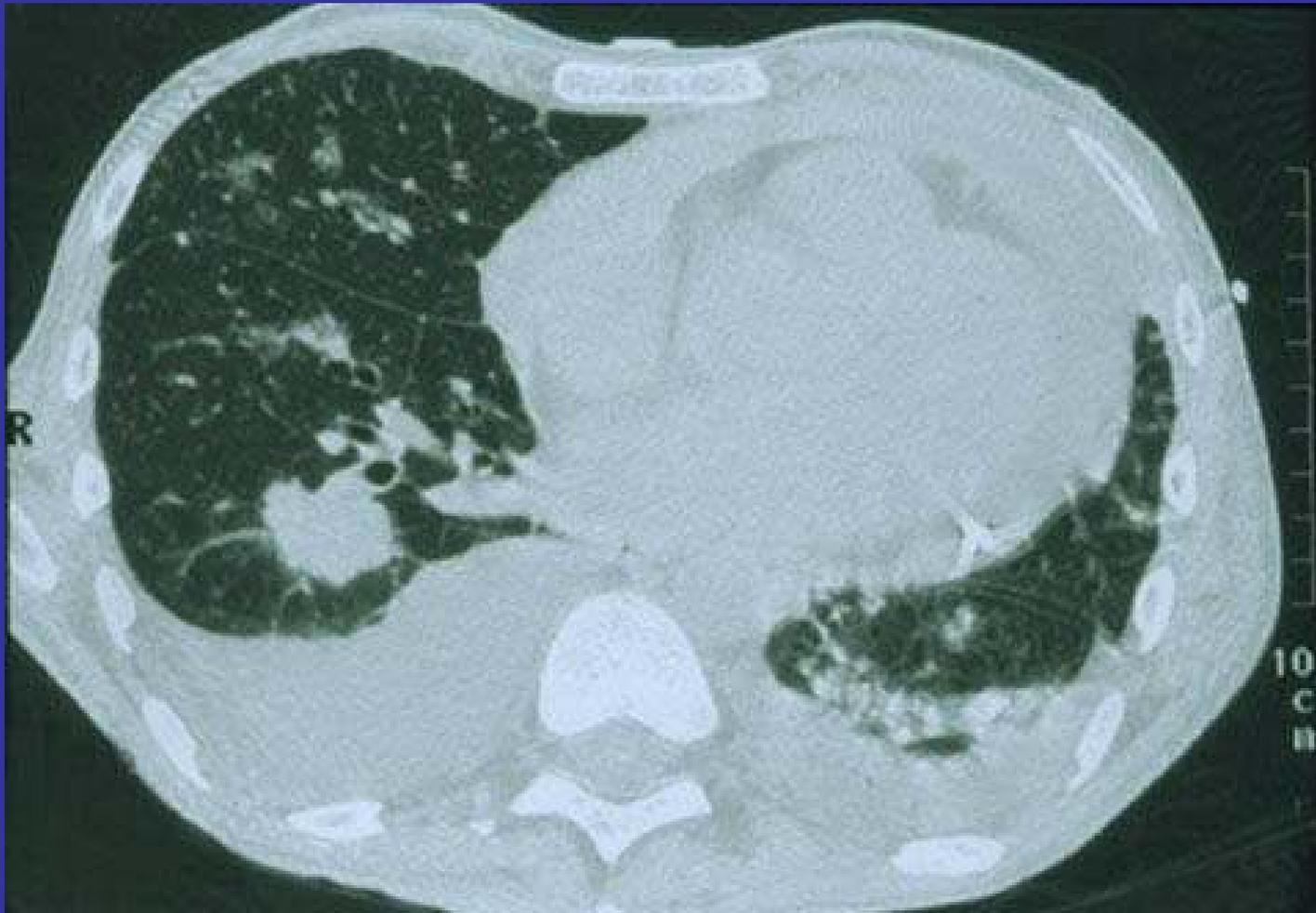
Diagnosis of CFRD

- An AFTERNOON, UNSTARVED oral glucose tolerance test.

CF. The next big things

- CF Related Diabetes
- Non tuberculous mycobacteria especially M. Abscessus.
- Aspergillus and allergic bronchopulmonary aspergillosis (ABPA)
- Osteoporosis and use of water soluble Vitamin K

NTM



NTM Treatment

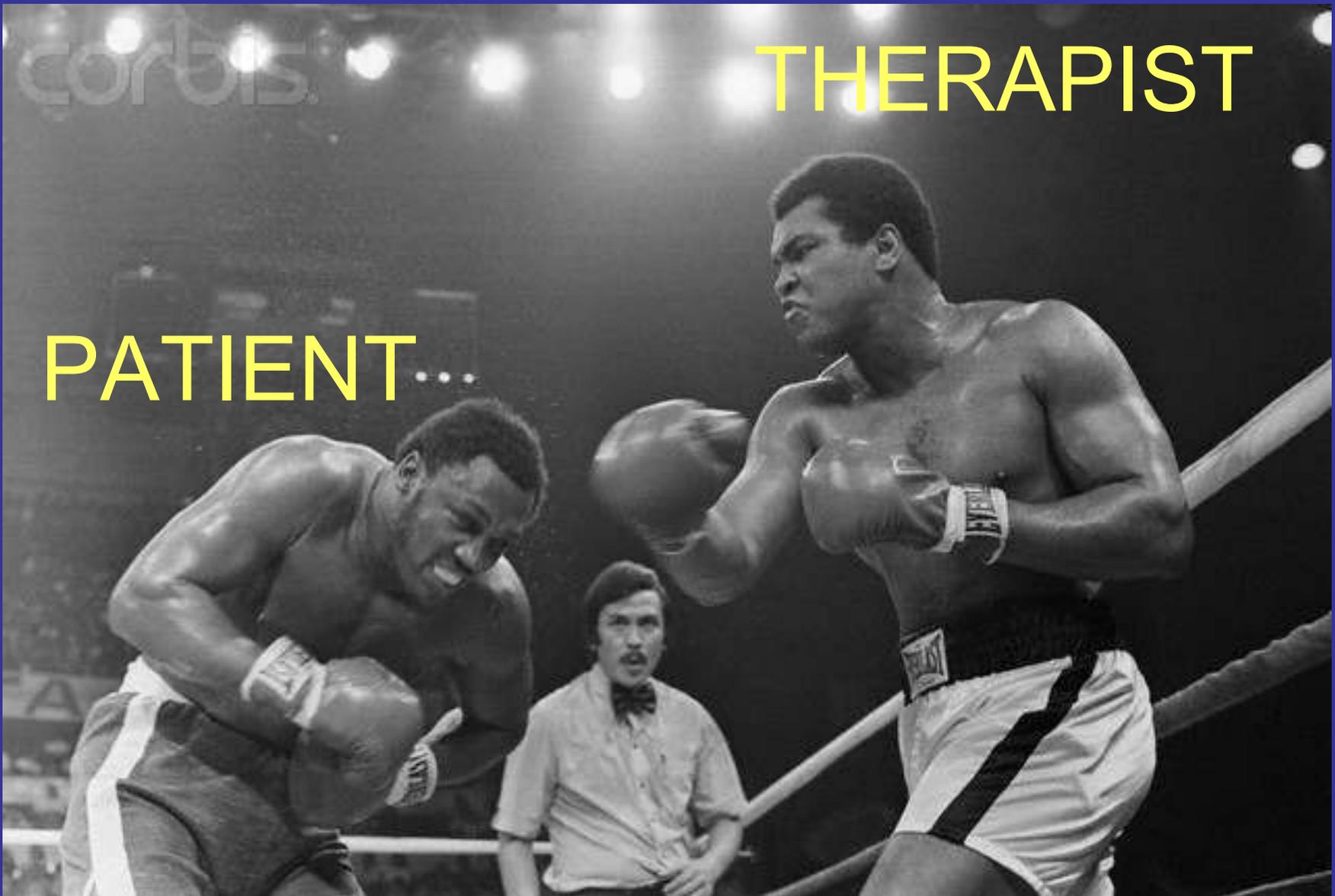
- 3 weeks IV amikacin, meropenem and ceftazidime plus oral clarithromycin
- Then 2 years of oral clarithromycin and ciprofloxacin and nebulised amikacin and meropenem

Aspergillus and ABPA

- Tortuous
- Use Itraconazole 200mg TWO times a day give with coca cola.
- Pulsed iv methyl prednisolone 10mg/kg twice day for 3 days is better than oral prednisolone, better result, fewer side effects

And finally.....

- What is the role of the doctor in an Multidisciplinary team?
- Or.....
- How to make an average person look really good?!



corbis

THERAPIST

PATIENT

ME!



ME PARENT

- Surround yourself with really good people
- To become unnecessary!