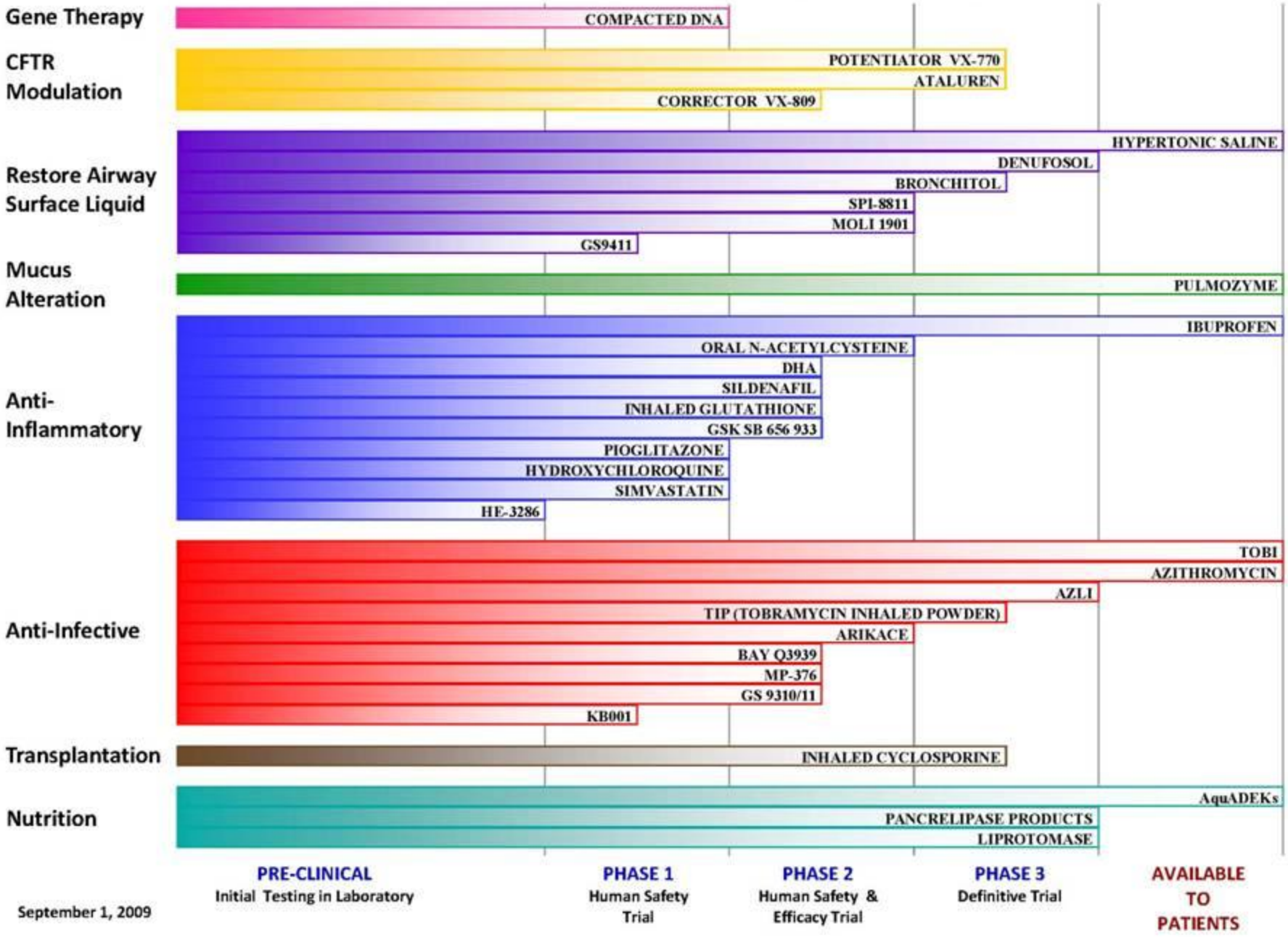
The Modern Management of Cystic Fibrosis

Gary Connett

CF Management

- Becoming increasingly complicated

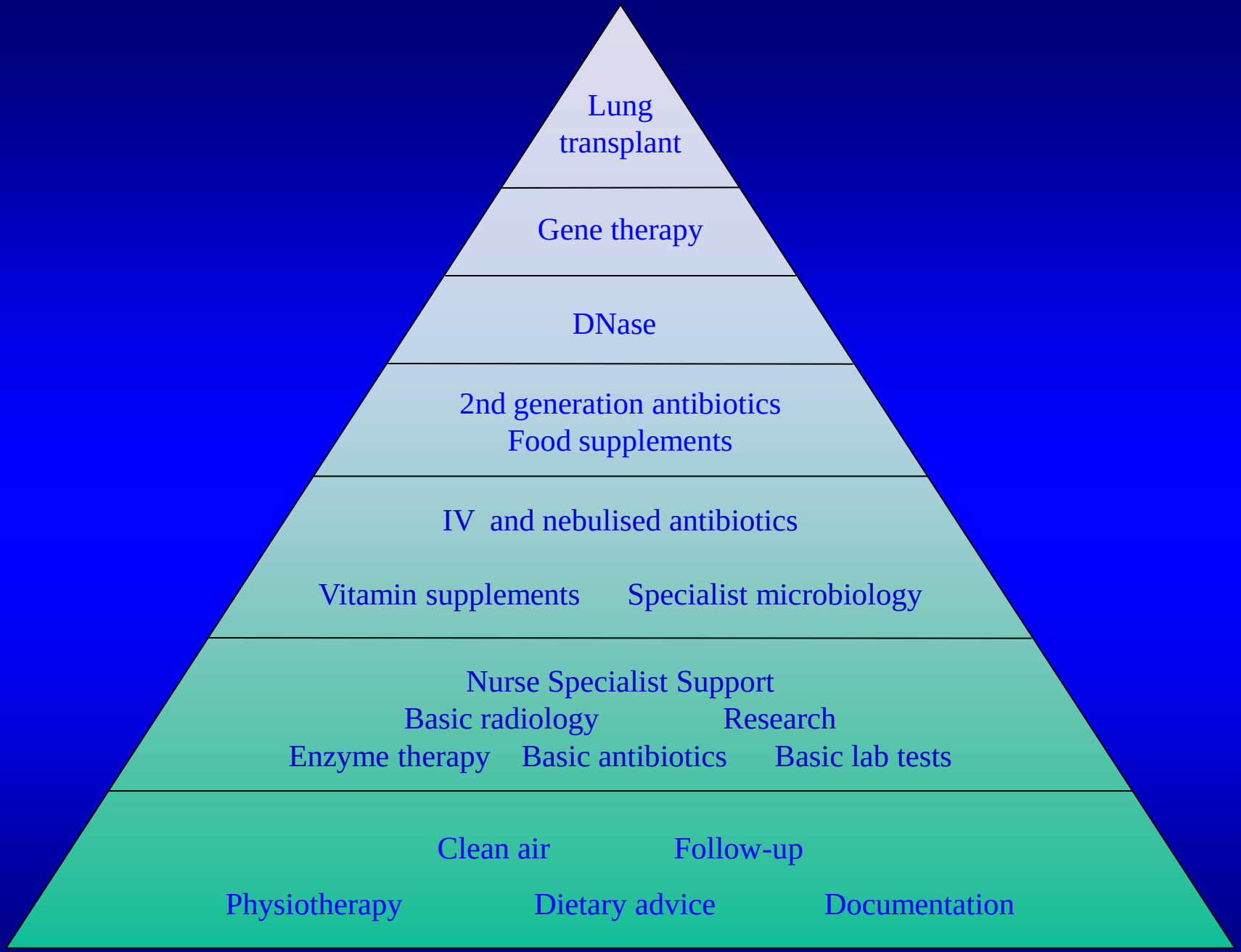
Cystic Fibrosis Foundation Therapeutics Pipeline

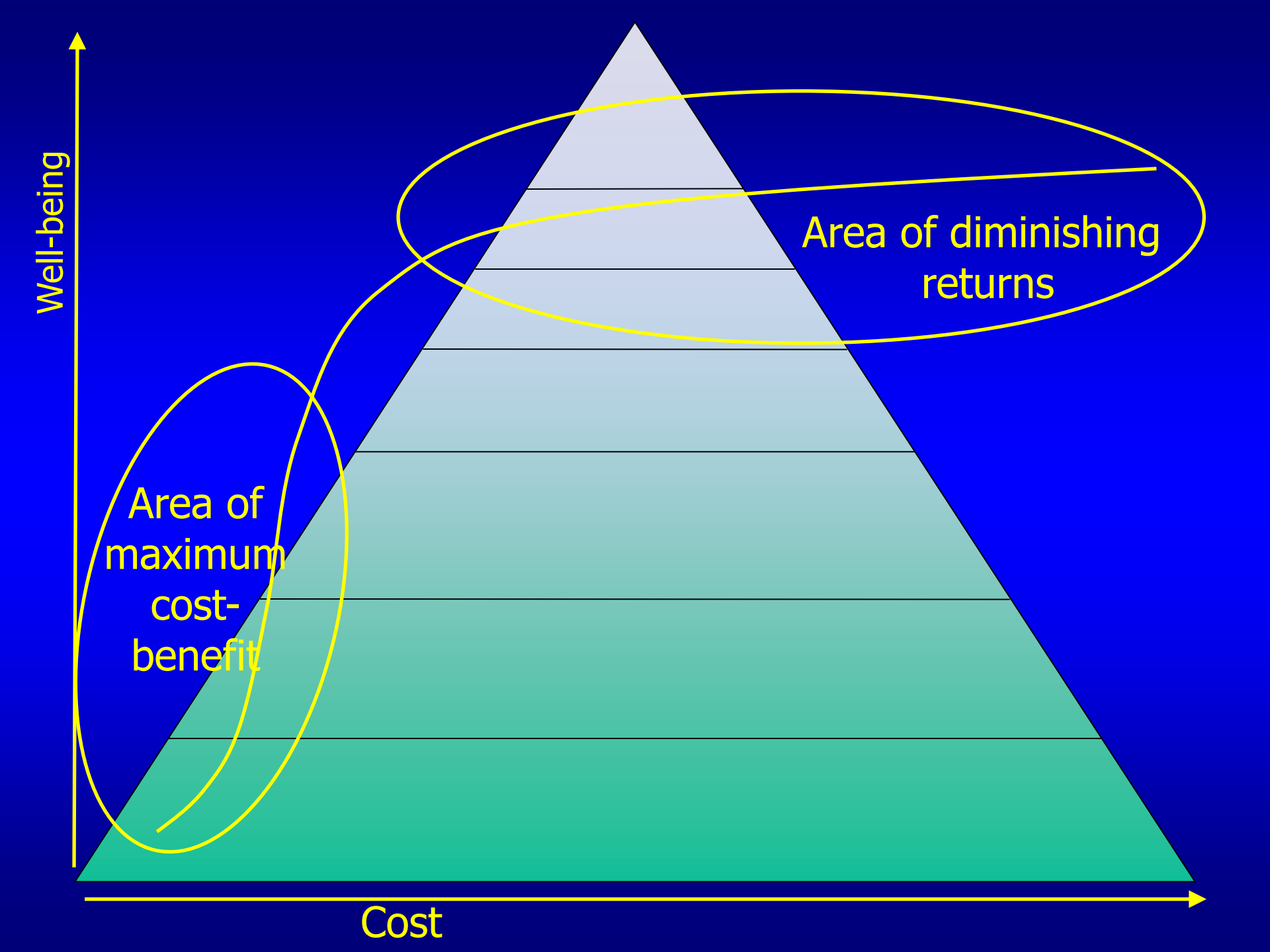


September 1, 2009

CF Management

- Adhering to some simple basic principles of care maximises returns


Lung transplant
Gene therapy
DNase
2nd generation antibiotics
Food supplements
IV and nebulised antibiotics
Vitamin supplements
Specialist microbiology
Nurse Specialist Support
Basic radiology
Research
Enzyme therapy
Basic antibiotics
Basic lab tests
Clean air
Follow-up
Physiotherapy
Dietary advice
Documentation
Diagnosis


Well-being
Area of diminishing returns
Area of maximum cost-benefit
Cost

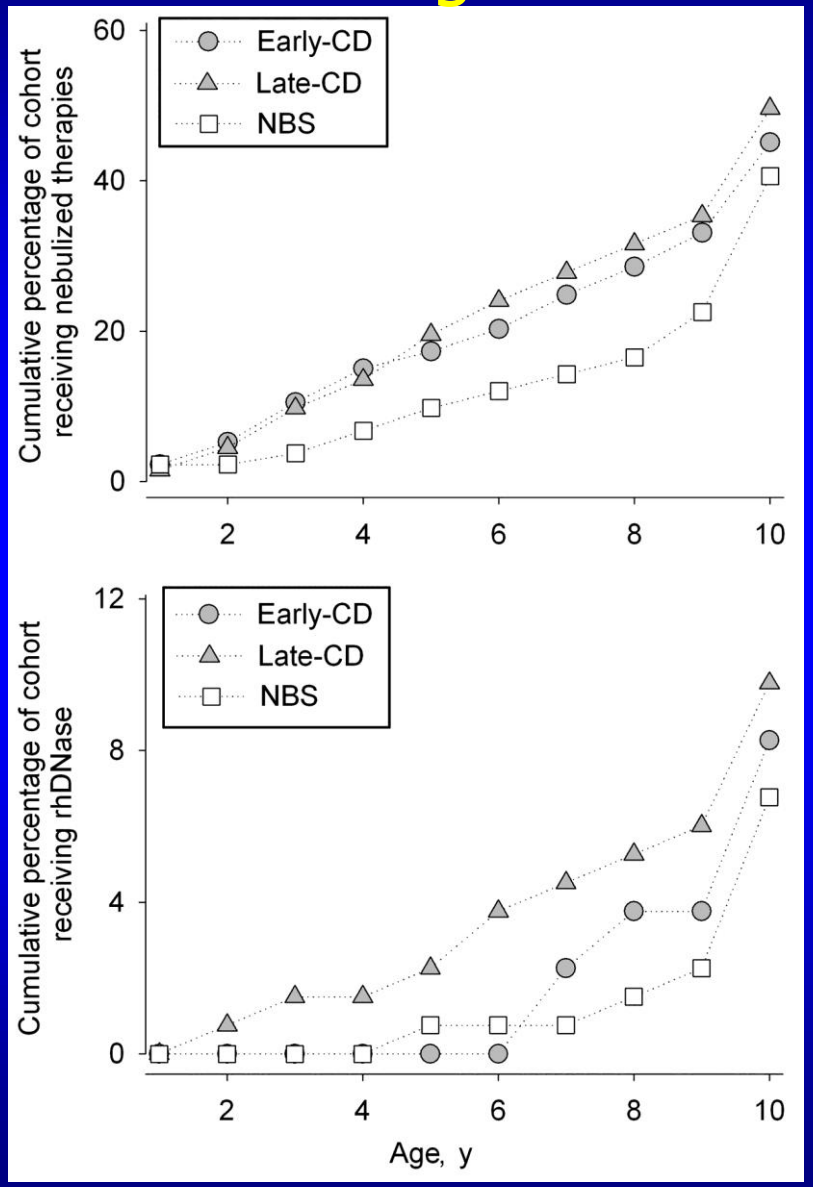
Modern Management

- Newborn screening
- Multidisciplinary team care
- Nutritional care
- Respiratory care

Newborn Screening

- Expensive?

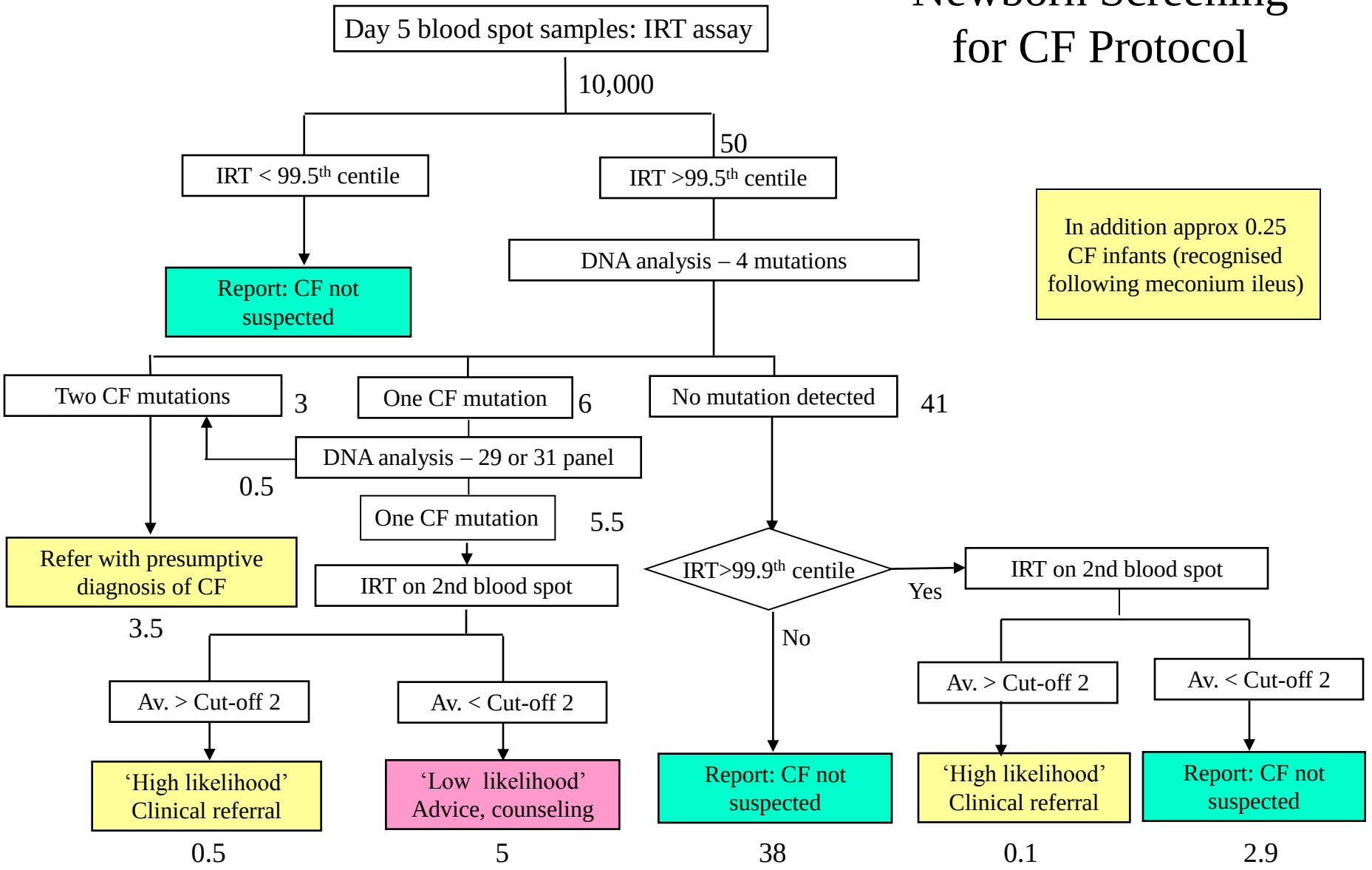
Early Versus Late Versus New Born Screening CF Diagnoses



Sims, E. J. et al. Pediatrics 2007;119:19-28

PEDIATRICS®

Newborn Screening for CF Protocol



New Born Screening in UK

- 2007-08 224 babies diagnosed
- 2008-09 213 babies diagnosed

Neonatal Cystic Fibrosis Screening in Latvia: a pilot project

- Immune reactive trypsinogen in new born dried blood spots
- > 80ng/ml – CFTR analysis on blood for DF508 and other common mutations

Baiba Lace et al Riga Stradins University, Dept of Medical Biology and Genetics

Neonatal Cystic Fibrosis Screening in Latvia: a pilot project

- Estimated frequency of CF 1:3250
- First infant in Latvia identified through new born screening

Baiba Lace et al Riga Stradins University, Dept of Medical Biology and Genetics

Numbers

UK

- 1 person in 25 carries the CF gene
- 7500 people have CF
- Every week five babies are born with CF

Latvia

- 1 in 28 carry the defective gene for CF
- If survival figures were the same in Latvia as the UK there would be 170-200 patients
- There should be 6-8 new cases of CF every year in Latvia

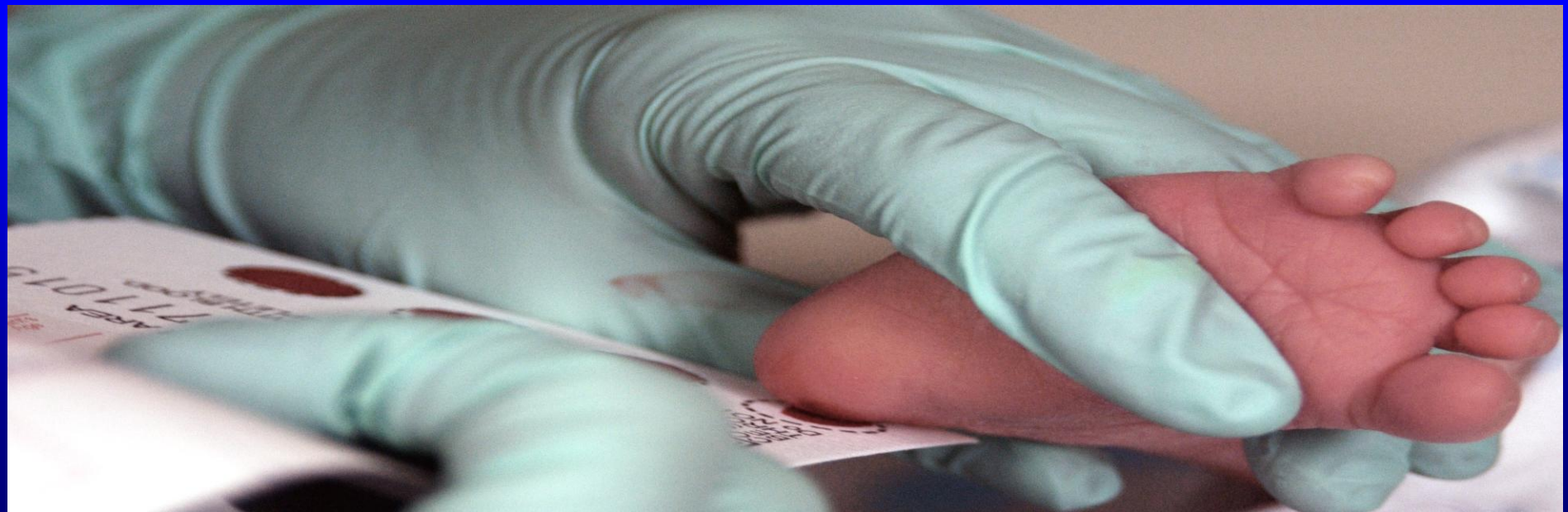
Existing CF Service

30 patients attending the National Clinic

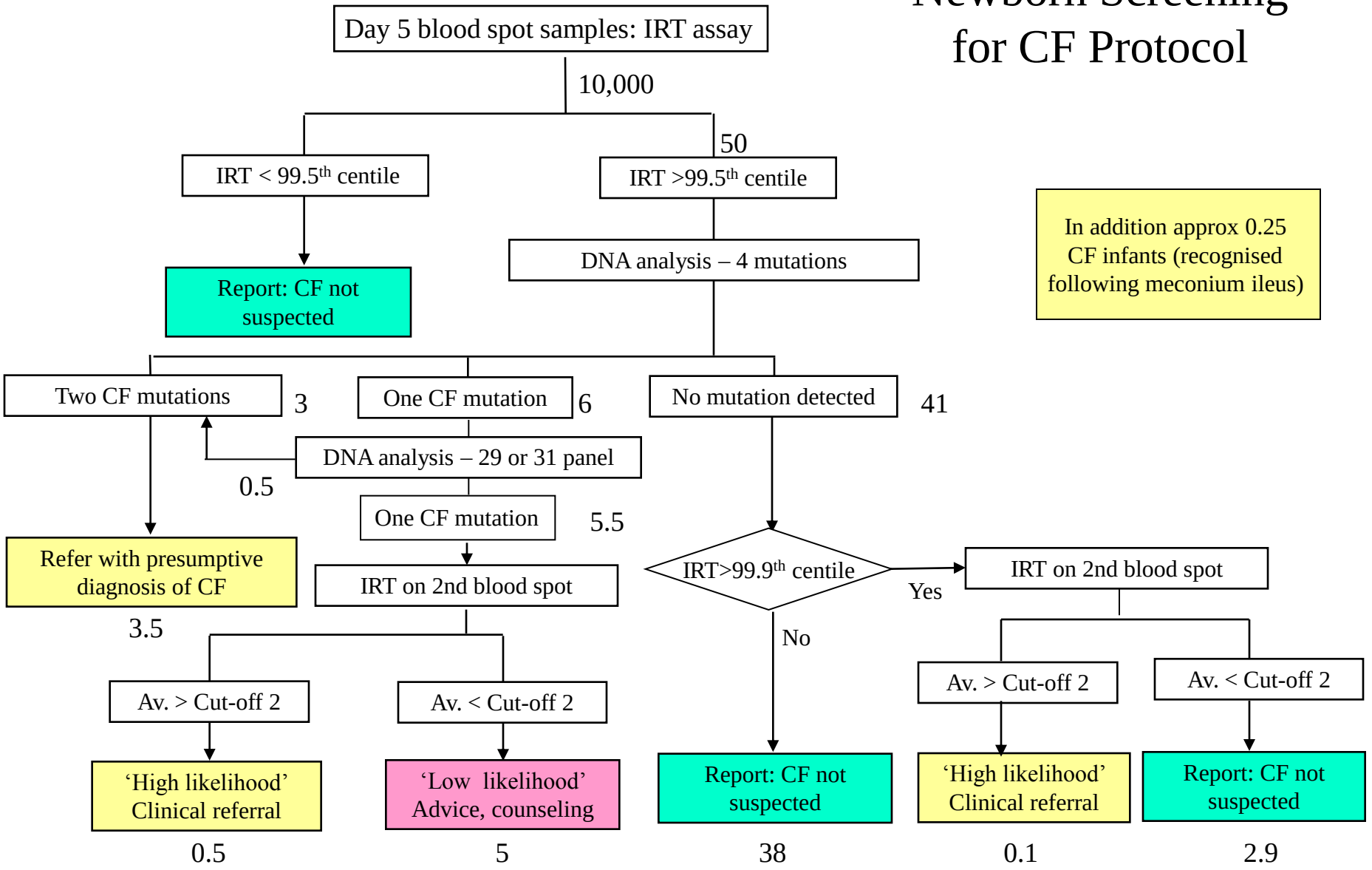
- At least 90-100 children should be attending CF services

Problems - False positives

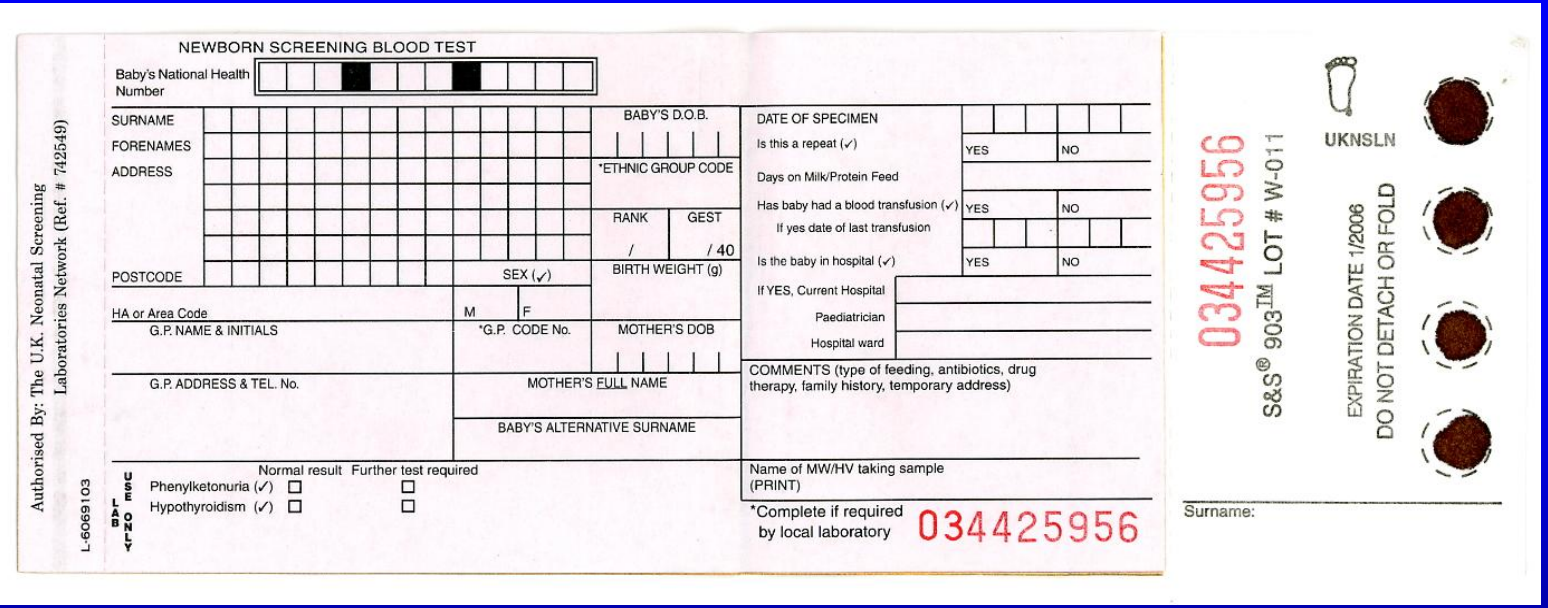
- 2914 cases in 2007-8 and 3551 in 2008-09 had raised initial IRT >99.5th centile but lower IRT on repeat testing. (0.5% of tests).
- Probable faecal contamination?



Newborn Screening for CF Protocol



Mistakes Happen



NEWBORN SCREENING BLOOD TEST

Baby's National Health Number

SURNAME

FORENAMES

ADDRESS

POSTCODE

HA or Area Code

G.P. NAME & INITIALS

G.P. ADDRESS & TEL. No.

BABY'S D.O.B.

*ETHNIC GROUP CODE

RANK / GEST / 40

SEX (✓) M F

BIRTH WEIGHT (g)

*G.P. CODE No.

MOTHER'S DOB

MOTHER'S FULL NAME

BABY'S ALTERNATIVE SURNAME

DATE OF SPECIMEN

Is this a repeat (✓) YES NO

Days on Milk/Protein Feed

Has baby had a blood transfusion (✓) YES NO

If yes date of last transfusion

Is the baby in hospital (✓) YES NO

If YES, Current Hospital

Paediatrician

Hospital ward

COMMENTS (type of feeding, antibiotics, drug therapy, family history, temporary address)

Name of MW/HV taking sample (PRINT)

*Complete if required by local laboratory 034425956

LAB USE ONLY

Normal result Further test required

Phenylketonuria (✓) ☐ ☐

Hypothyroidism (✓) ☐ ☐

Authorised By: The U.K. Neonatal Screening Laboratories Network (Ref. # 742549)

L-6069103

034425956

S&S® 903™ LOT # W-011

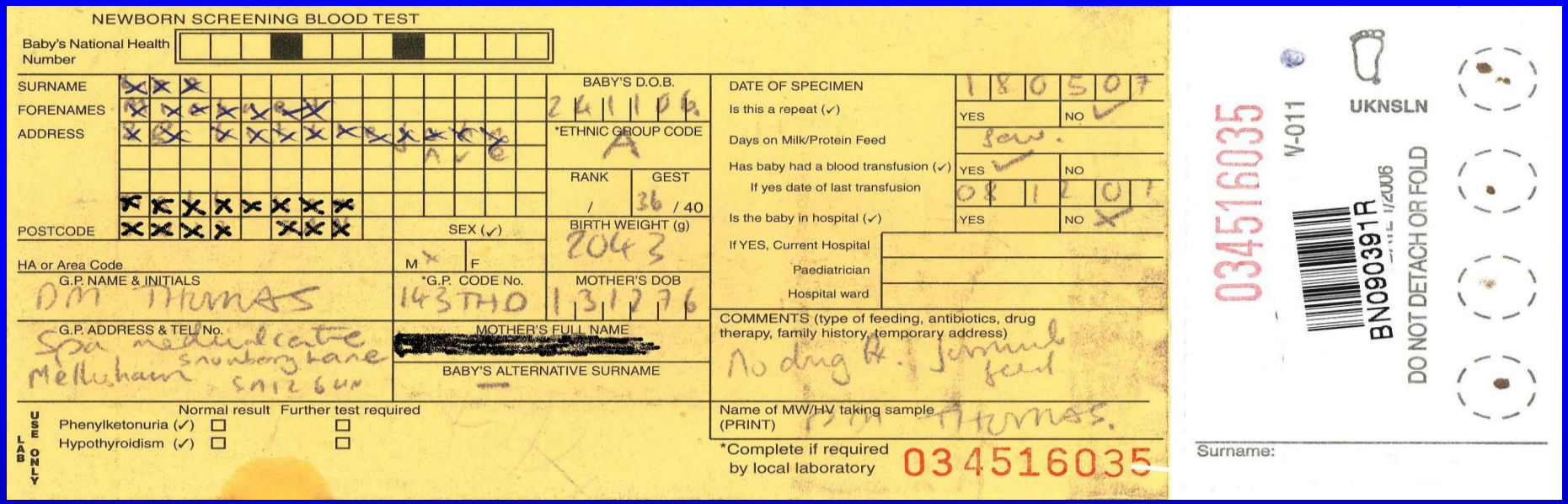
UKNSLN

EXPIRATION DATE 1/2006

DO NOT DETACH OR FOLD

Surname:

Mistakes Happen



NEWBORN SCREENING BLOOD TEST

Baby's National Health Number

SURNAME

FORENAMES

ADDRESS

POSTCODE

HA or Area Code

G.P. NAME & INITIALS

DM THOMAS

G.P. ADDRESS & TEL. No.

Spa Medical Centre
Snowberry Lane
Melksham
SN12 6UP

BABY'S D.O.B.

*ETHNIC GROUP CODE

A

RANK / GEST 36 / 40

SEX (✓) M F

BIRTH WEIGHT (g) 2043

*G.P. CODE No. 143THO

MOTHER'S DOB 13/12/76

MOTHER'S FULL NAME

BABY'S ALTERNATIVE SURNAME

DATE OF SPECIMEN 18/05/07

Is this a repeat (✓) YES NO ✓

Days on Milk/Protein Feed 5ew.

Has baby had a blood transfusion (✓) YES ✓ NO

If yes date of last transfusion 08/12/07

Is the baby in hospital (✓) YES NO ✓

If YES, Current Hospital

Paediatrician

Hospital ward

COMMENTS (type of feeding, antibiotics, drug therapy, family history, temporary address)

No drug Hx. Formula fed

Name of MW/HV taking sample (PRINT) DM THOMAS.

*Complete if required by local laboratory 034516035

LAB USE ONLY

	Normal result	Further test required
Phenylketonuria (✓)	☐	☐
Hypothyroidism (✓)	☐	☐

034516035

V-011

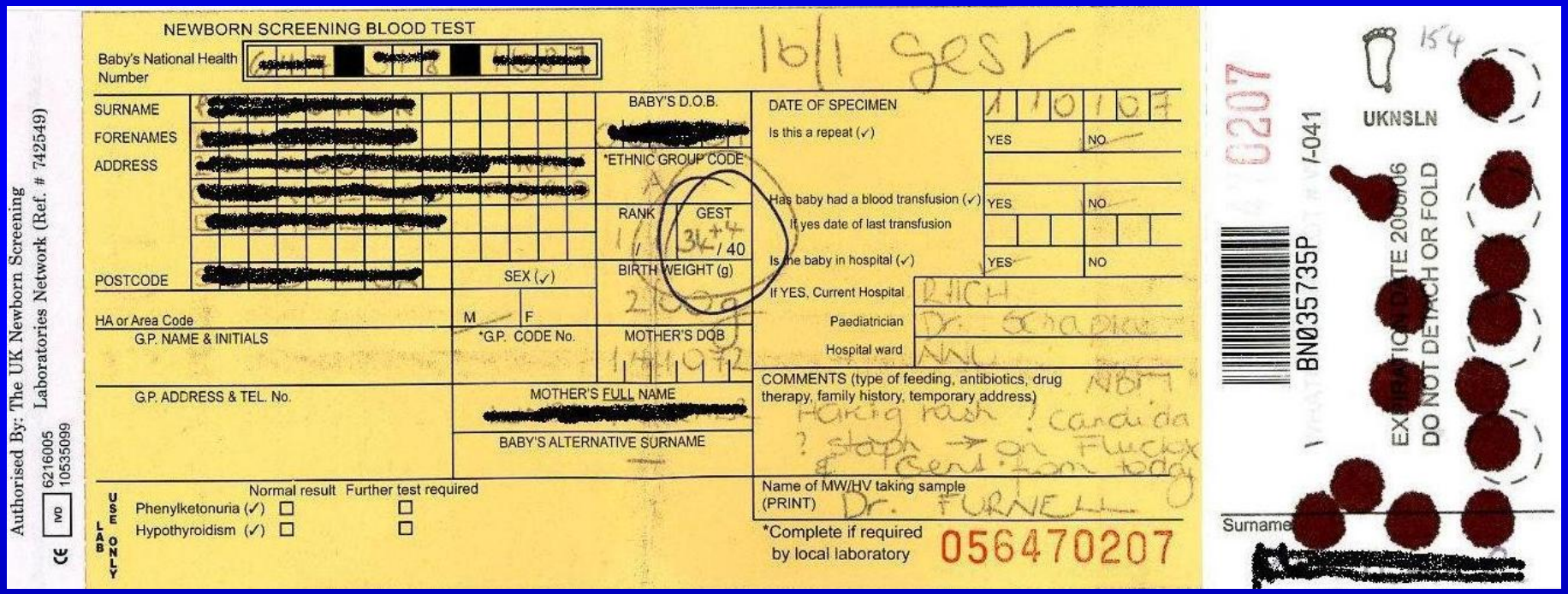
UKNSLN

BN090391R

DO NOT DETACH OR FOLD

Surname:

Mistakes Happen



NEWBORN SCREENING BLOOD TEST

Baby's National Health Number

16/1 gest

SURNAME

FORENAMES

ADDRESS

POSTCODE

HA or Area Code

G.P. NAME & INITIALS

G.P. ADDRESS & TEL. No.

BABY'S D.O.B.

*ETHNIC GROUP CODE

RANK

GEST 34+4 / 40

SEX (✓) M F

BIRTH WEIGHT (g) 2

*G.P. CODE No.

MOTHER'S DOB

MOTHER'S FULL NAME

BABY'S ALTERNATIVE SURNAME

DATE OF SPECIMEN 1/10/07

Is this a repeat (✓) YES NO

Has baby had a blood transfusion (✓) YES NO

If yes date of last transfusion

Is the baby in hospital (✓) YES NO

If YES, Current Hospital RHCH

Paediatrician Dr. Chapple

Hospital ward NNU

COMMENTS (type of feeding, antibiotics, drug therapy, family history, temporary address)

NBM

Having rash ? Candida

? staph → on Flucloxacillin

Sent from today

Name of MW/HV taking sample (PRINT) Dr. FURNELL

*Complete if required by local laboratory 056470207

LAB USE ONLY

Normal result Further test required

Phenylketonuria (✓) ☐ ☐

Hypothyroidism (✓) ☐ ☐

Authorised By: The UK Newborn Screening Laboratories Network (Ref. # 742549)

IVD 6216005 10535099

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0207

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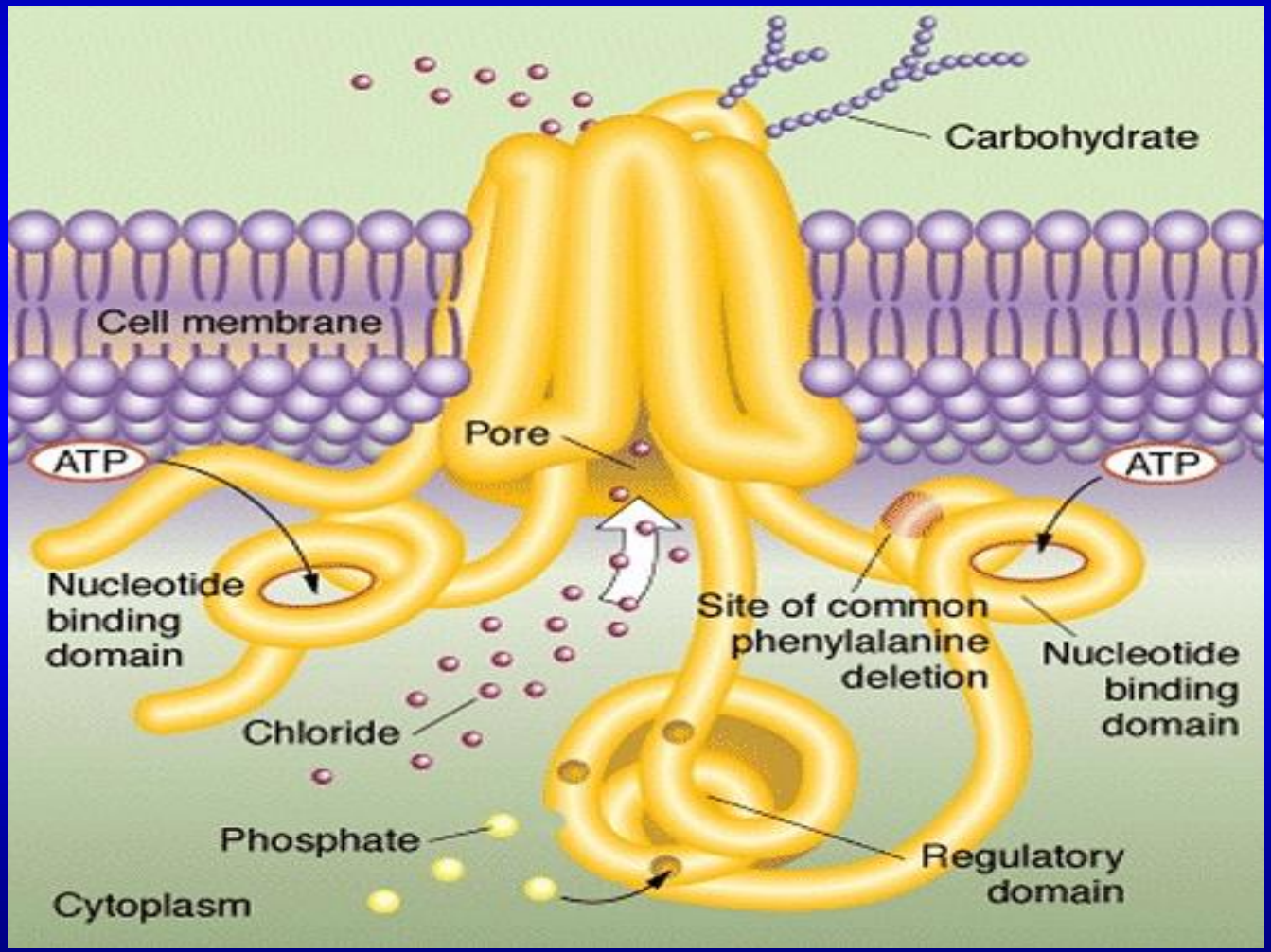
UKNSLN

DO NOT DETACH OR FOLD

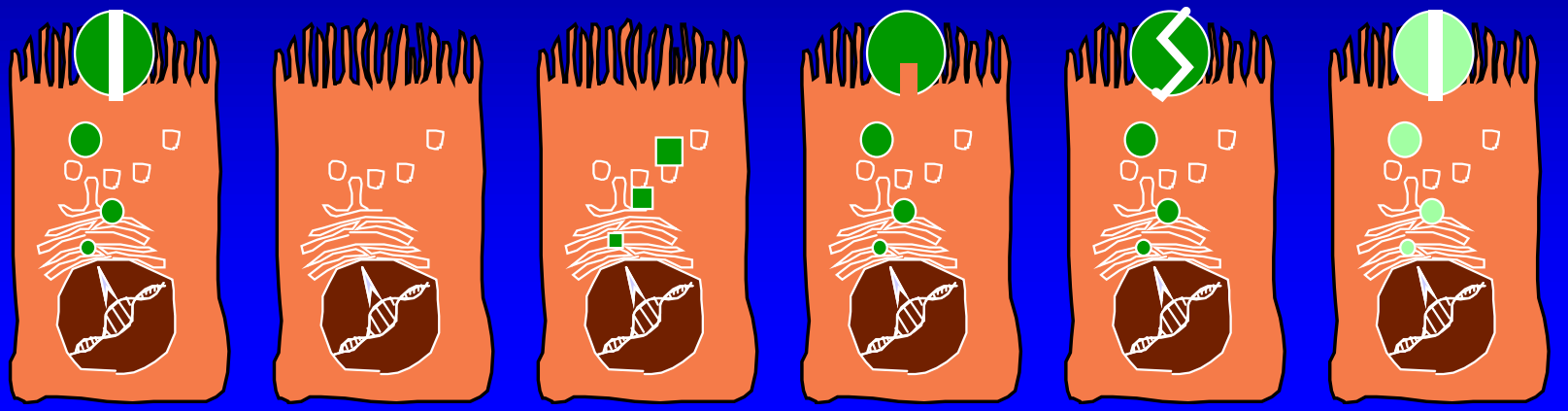
Surname

CFTR



CFTR sits across the membrane of a cell. The CFTR protein is a channel that opens and closes to allow the passage of chloride ions across the epithelial surface.

CFTR Mutations



Every CF Child is Different

- CF care packages need to be tailored to the individual according to their symptoms and circumstances

The CF Team

Good CF care has the following components…

- A dedicated multidisciplinary team with involvement from the following health care professionals:
  - doctors
  - nurse specialists
  - physiotherapists
  - dieticians
  - psychologists
  - pharmacists

The CF Team

- Agreed standards of care
- A system for regular monitoring and review
- Back up from other specialist services

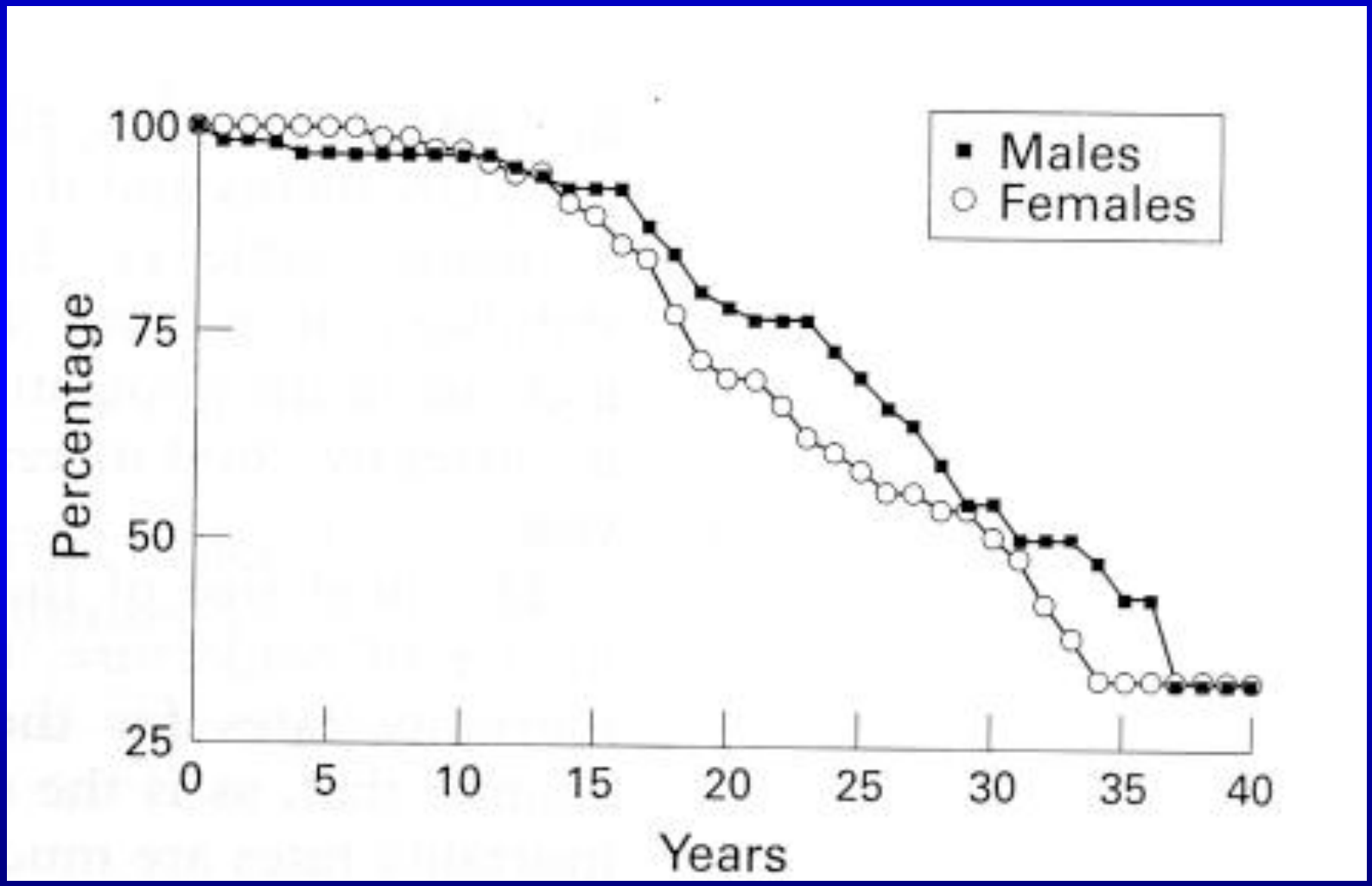
The CF Team

- CF teams are one of the best examples of multidisciplinary care working in the best interests of patients.
- In most cases CF teams are headed up by a respiratory consultant paediatrician
- CF teams meet regularly to share information and to plan the care of their patients.

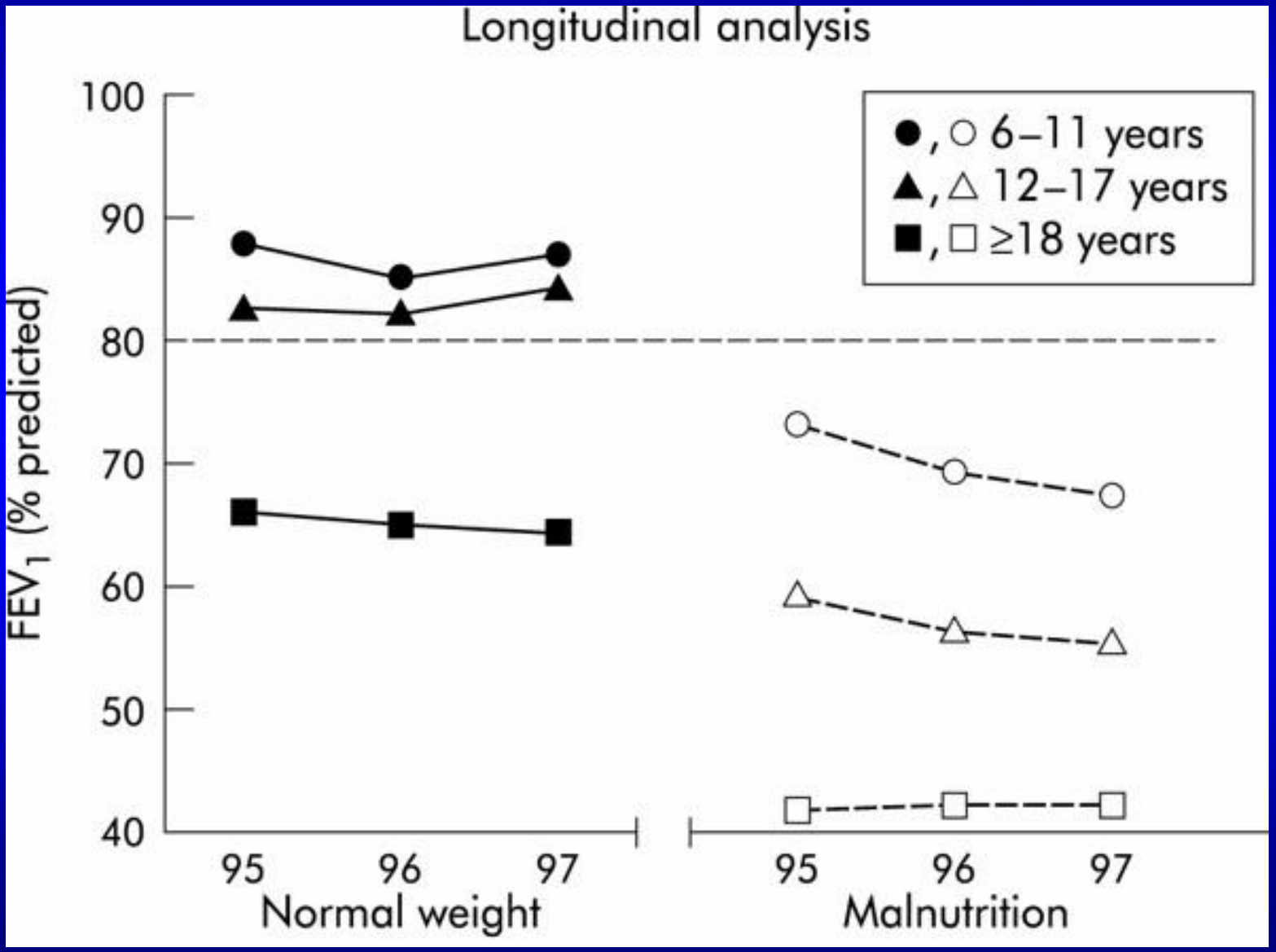
CF Statistics

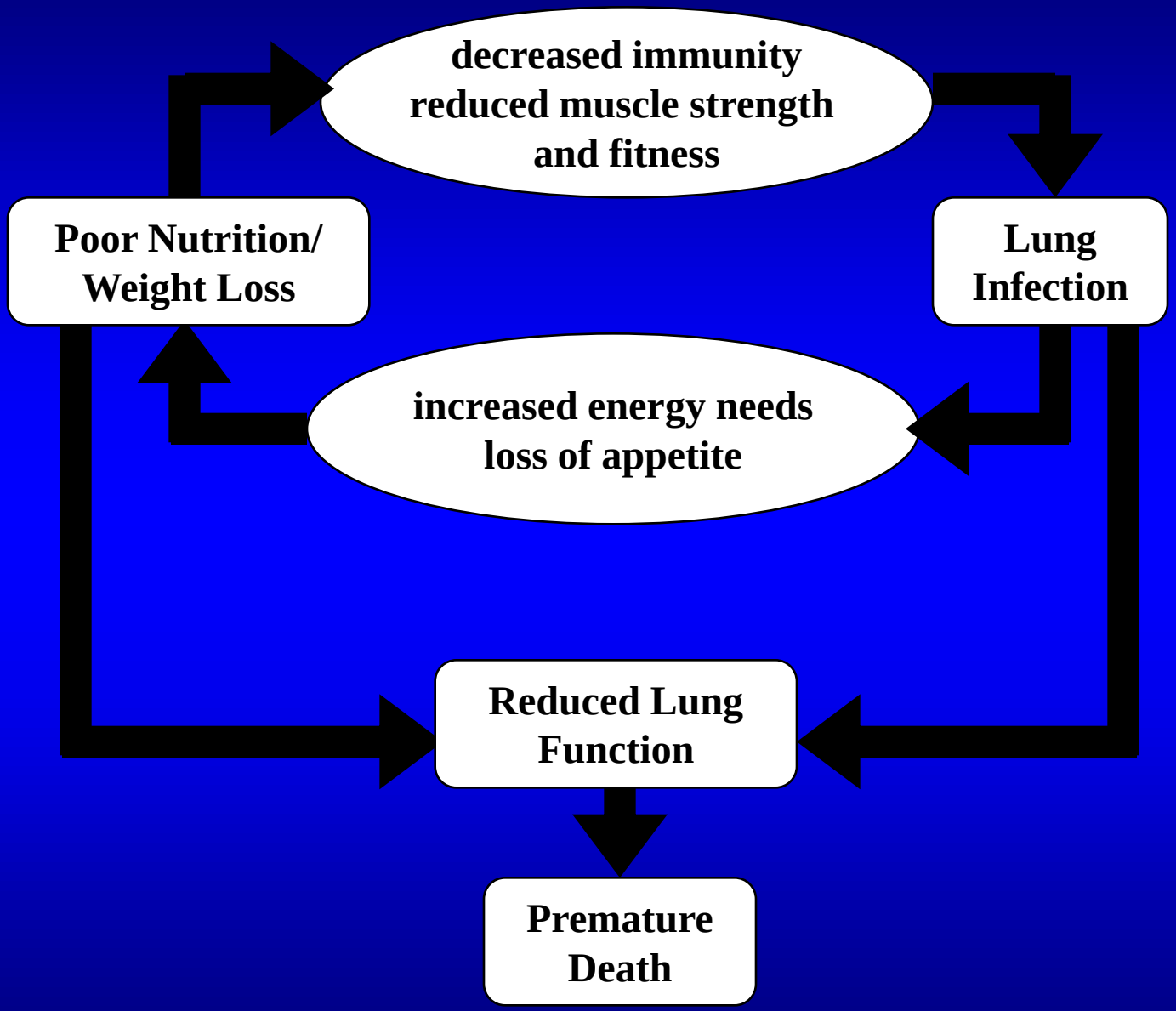
- In 1964, the average life expectancy for a child with CF was just 5 years.
- In 2006, median life expectancy is around 31 Years.

UK figures for Median Survival against age



longitudinal data from the National database of CF patients in Germany.




decreased immunity
reduced muscle strength
and fitness
Poor Nutrition/
Weight Loss
Lung
Infection
increased energy needs
loss of appetite
Reduced Lung
Function
Premature
Death

Individuals with CF usually need a greater fat intake (35-40% of ingested calories versus < 30%) to achieve a high energy intake

Nutritional Management

- Patients should eat a normal to high fat diet
- Pancreatic enzymes should be given in sufficient doses to achieve a normal bowel habit and abolish GI symptoms
- If this is not easily achieved a proton pump inhibitor should be given routinely

Micronutrients

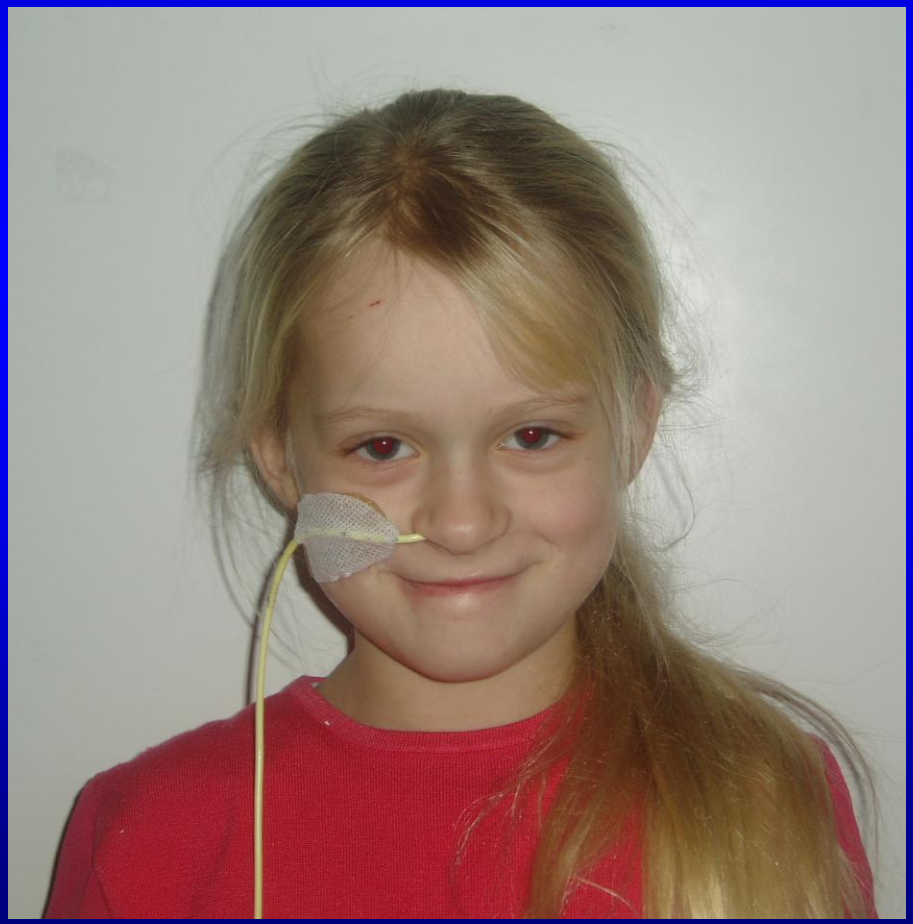
- The fat soluble vitamins A, D, E and sometimes also K should be given as oral supplements.

- Minerals and electrolytes such as Calcium for bone growth and Sodium to replace increased losses in sweat might also beneeded.

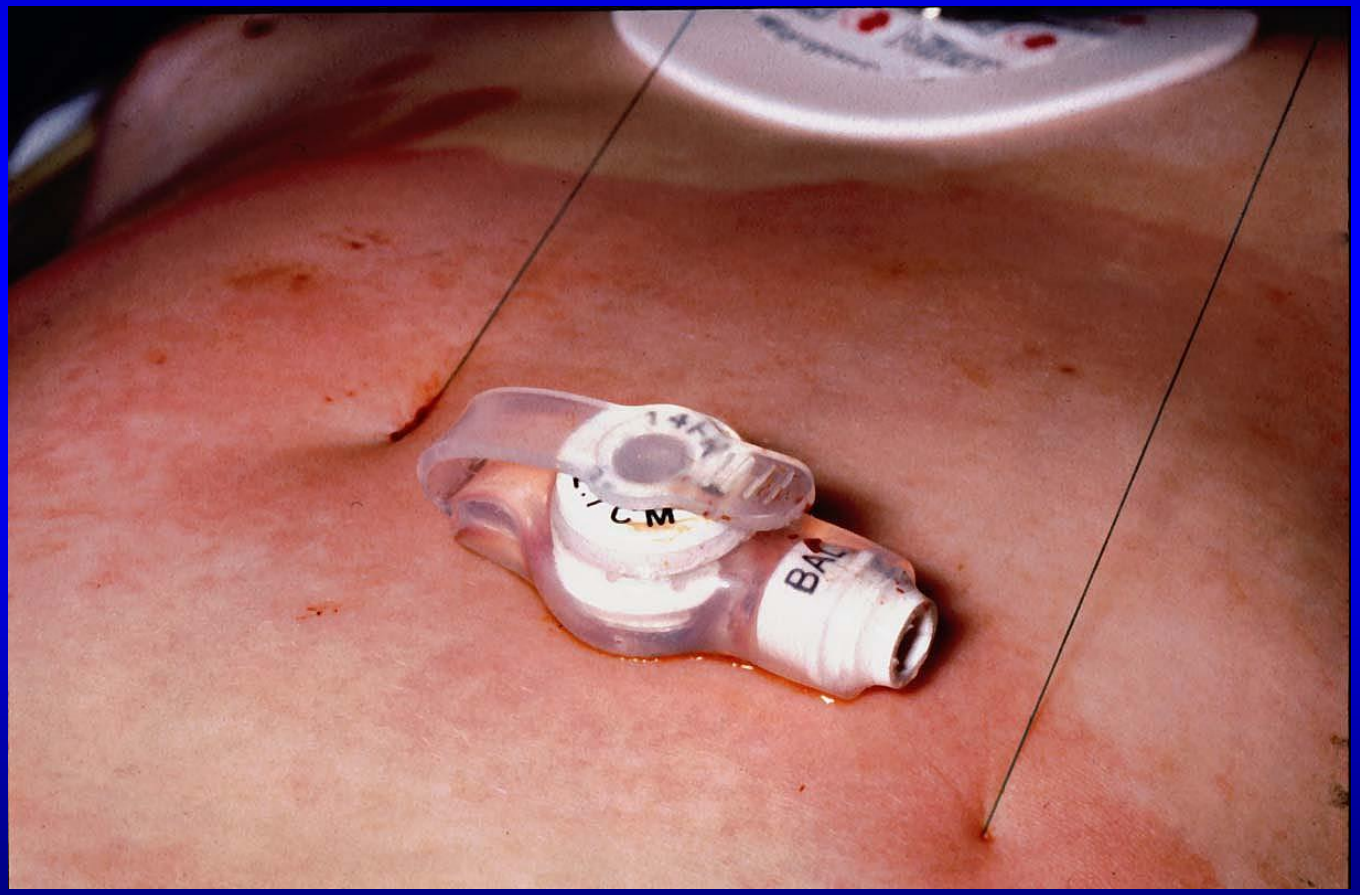
Supplements

- Oral Supplements such as calorie powders and emulsions, nutritionally fortified high calorie milk shakes and high glucose fruit juices are used to increase calorie intake during times of illness.

Occasionally when children do not have enough appetite to eat adequately, feeds should be given "enterally" through the use of a naso-gastric tube.



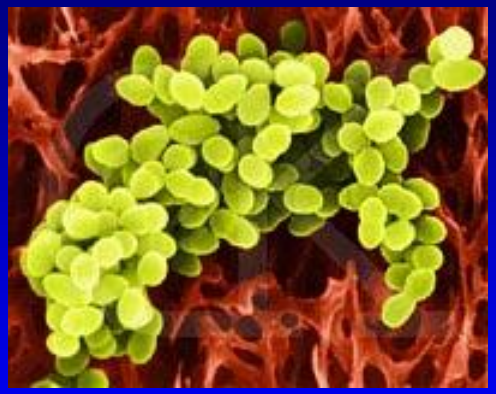
When long term enteral feeding is necessary a tube called a gastrostomy is placed directly into the stomach through the abdominal wall. The patient is usually fed by slow infusion overnight.



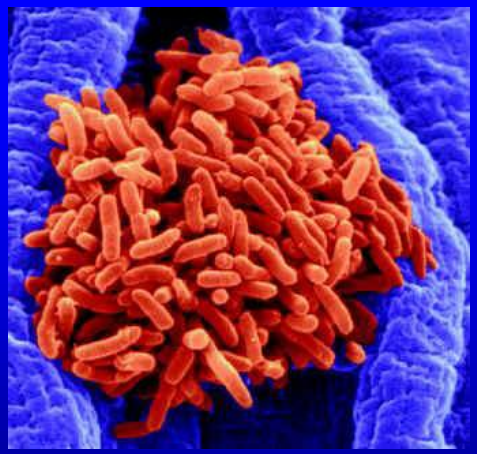
Respiratory Care Issues

Respiratory complications are prevented as far as possible by the following measures….

1. Regular swabs to detect and treat early any infection with bacteria such as *staphylococcus* and *pseudomonas.*



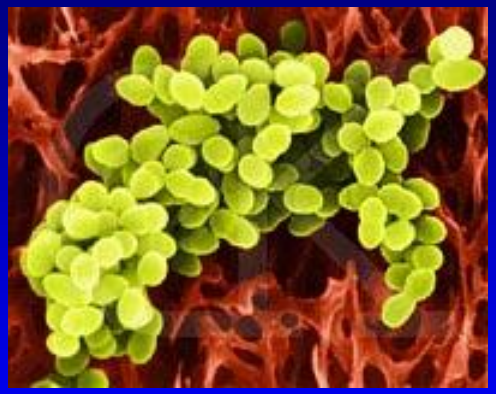
Staphylococcus



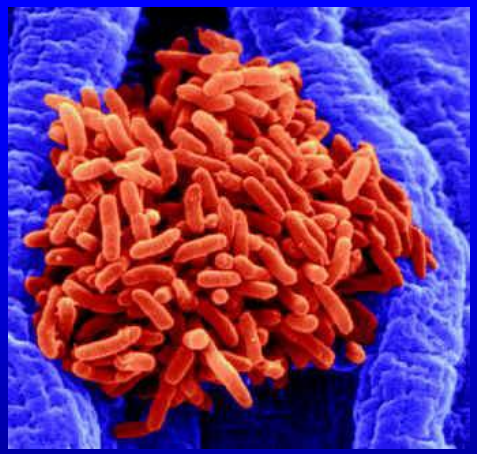
Pseudomonas

Respiratory complications are prevented as far as possible by the following measures….

2. Prompt treatment of any respiratory exacerbations with appropriate antibiotics.



Staphylococcus



Pseudomonas

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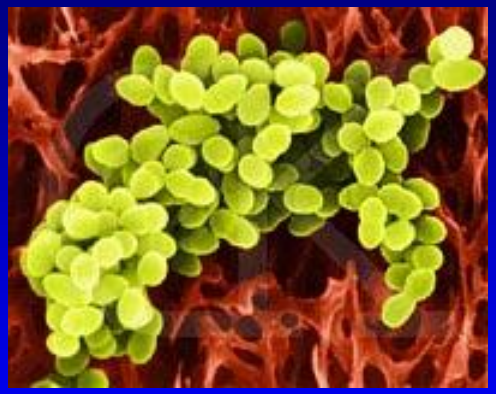
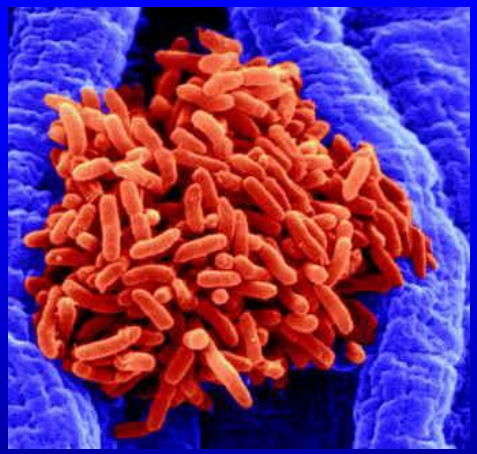


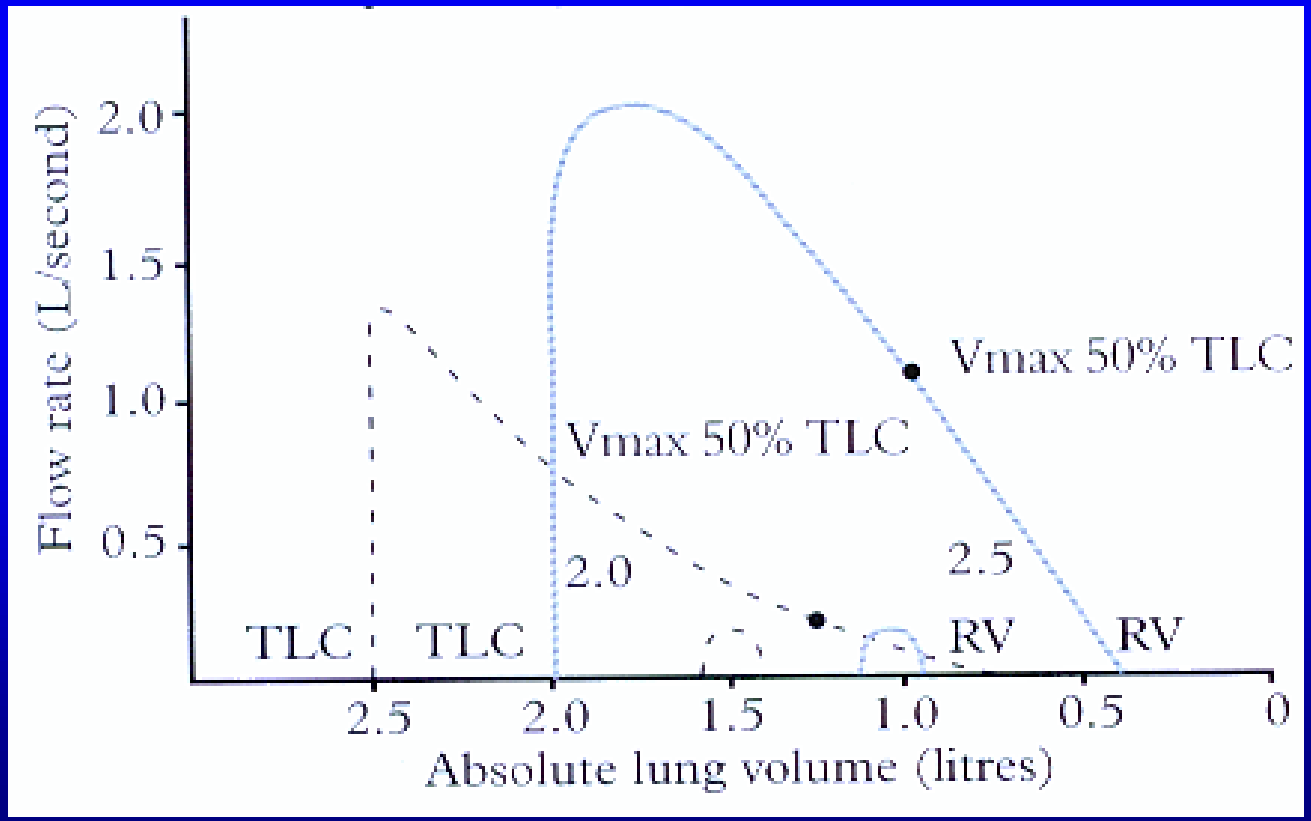
Staphylococcus

3. Regular physiotherapy to clear abnormal secretions from the airways.



Pseudomonas

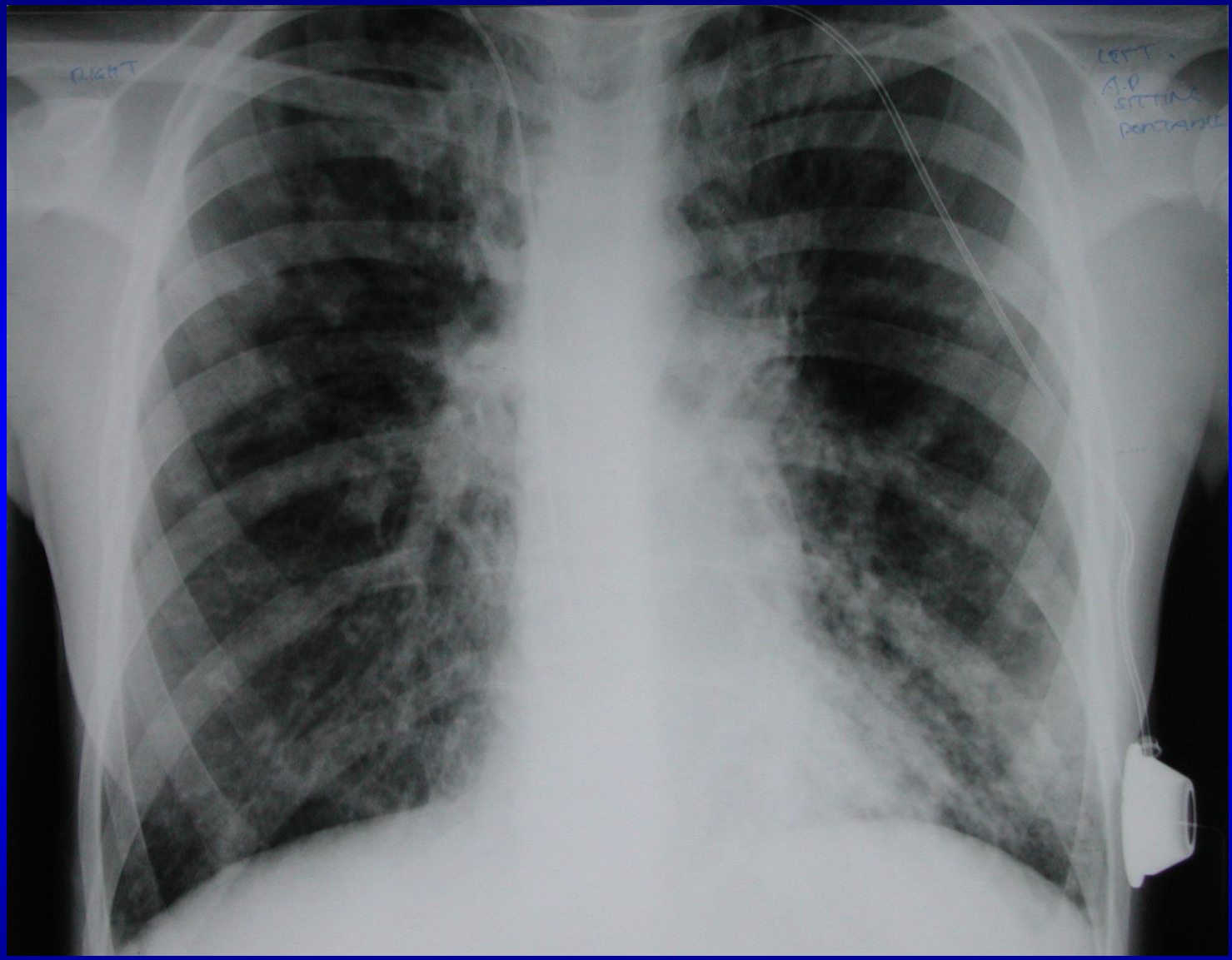
Lung function is the best predictor of long term survival and should be measured regularly. As the disease progresses, patients become hyperinflated and their expiratory flow rates decline because of airways obstruction.



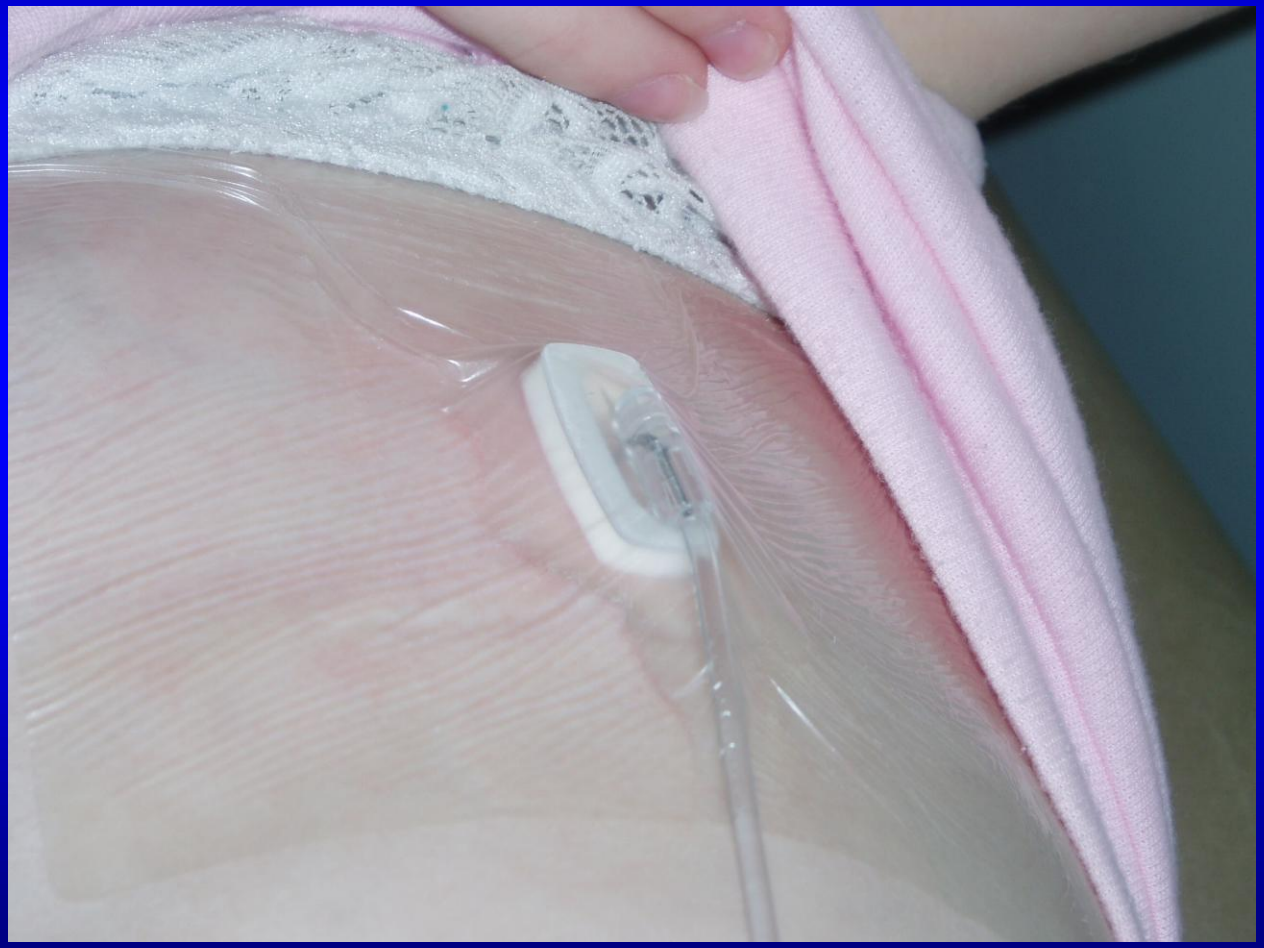
Nebulised Hypertonic Saline

6-7% solutions can be used as an adjunct to physiotherapy to clear secretions by increasing the water content of the fluid layer lining the airways.

Hypertonic saline can be used to induce sputum samples in children who are not able to expectorate airway secretions


RIGHT

Those needing frequent courses of intravenous antibiotics benefit from a totally implanted central venous access



Most important Factors

- Early Diagnosis
- Regular team follow up
- Prevention of malnutrition
- Regular physiotherapy
- Regular microbiology to detect and treat lung infection