CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Treatment Opportunities in a Heartsink Disease

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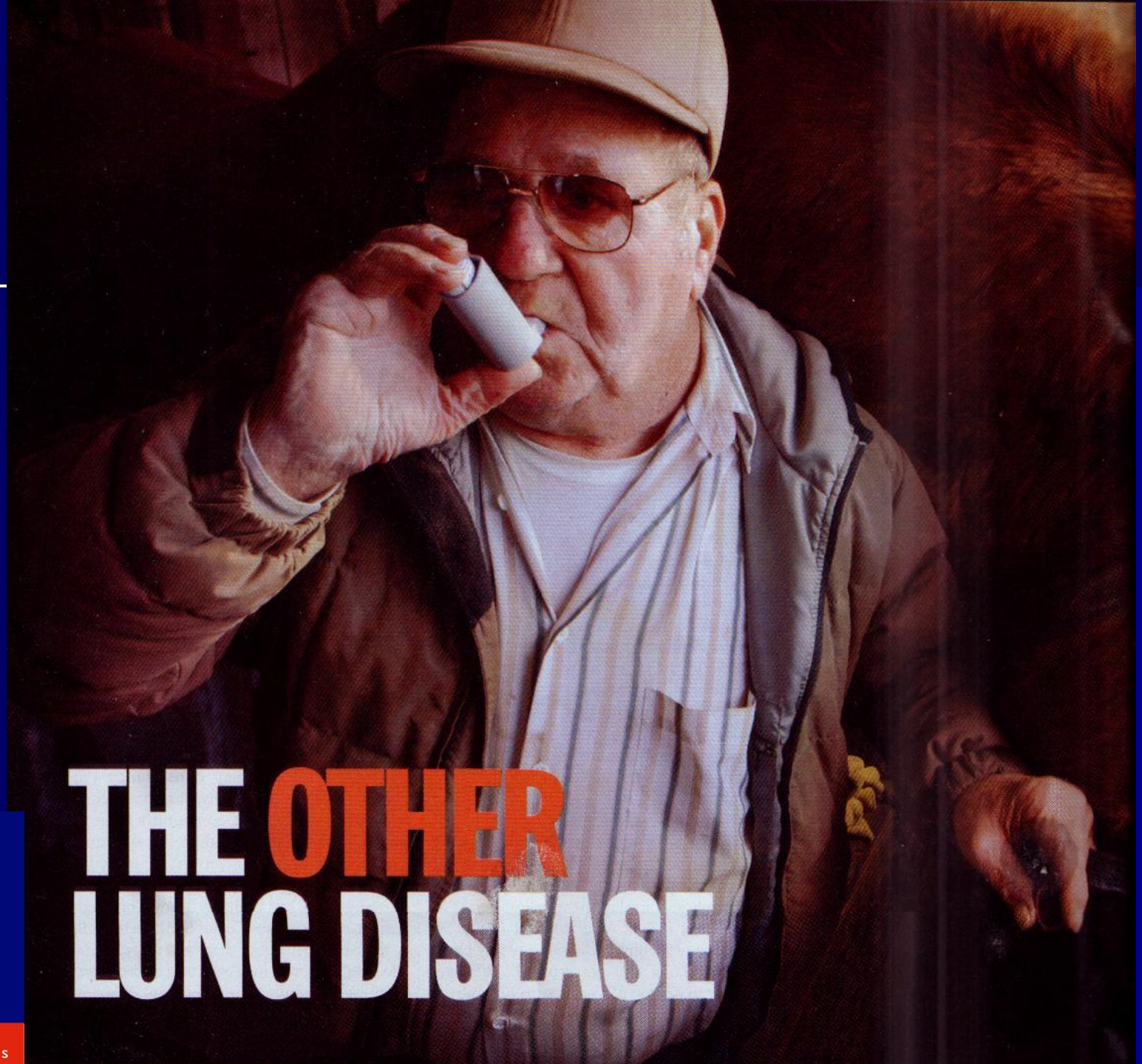

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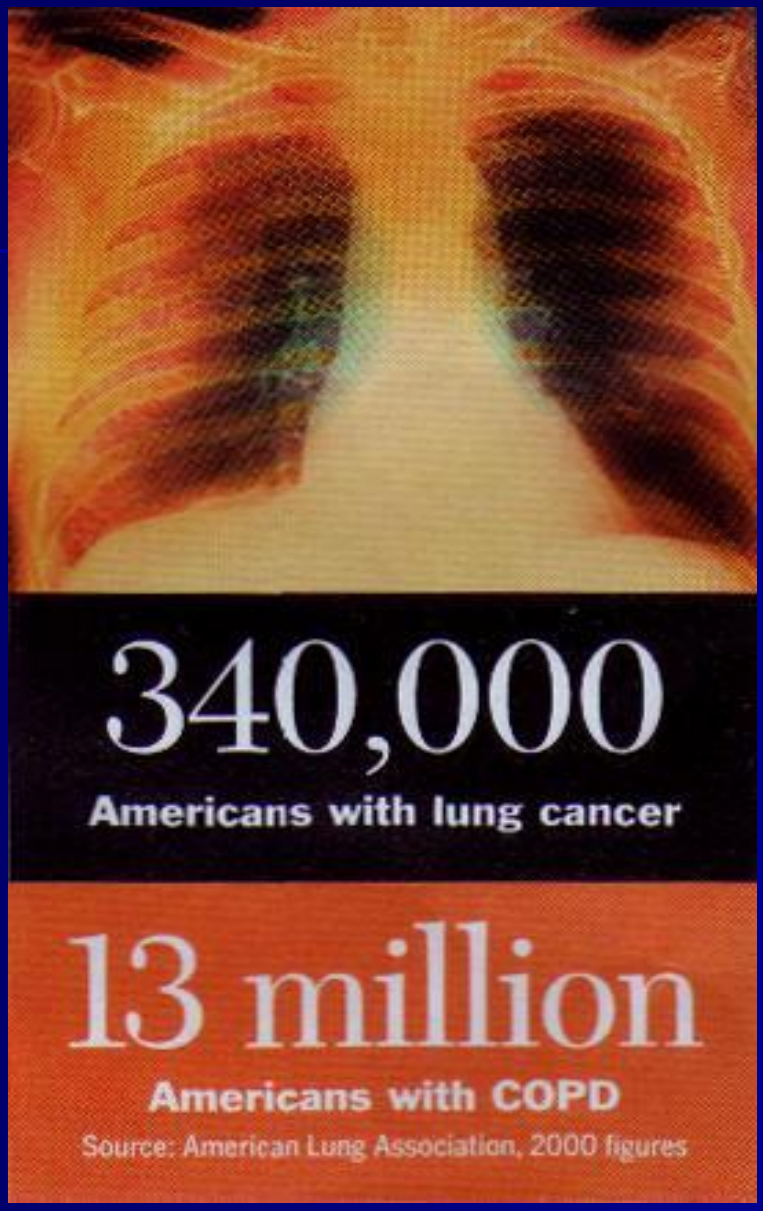


COPD – Treatment Opportunities

Target of treatment

- To improve quality of life
- To improve lung function
- To prevent deterioration
- To prevent exacerbations
- To reduce shortness of breath
- To decrease mortality

COPD – Treatment Opportunities

Causative elements

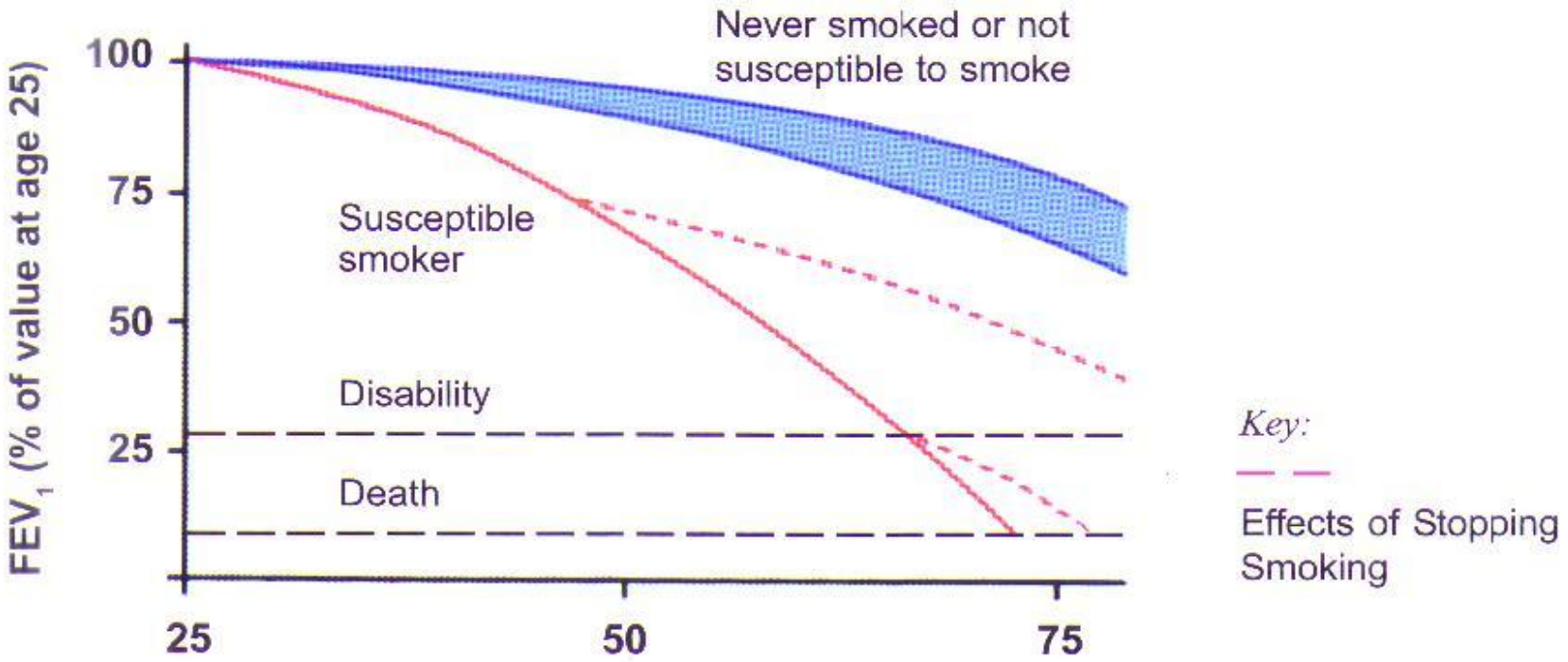
- Oxidative stress associated with neutrophil infiltration
- Elastin breakdown
- Narrowing of small airways – inflammation and scarring
- Increase in goblet cell size and number.

COPD – Treatment Opportunities

The common denominator is cigarette smoke.

Natural History [2]

Illustration of effects of smoking on rate of decline in FEV_1



COPD – Treatment Opportunities

Other Causes

- Burning of biomass fuels
- Industrial pollution
- Mining – coal, silica etc
- Car exhaust pollution.

AIR POLLUTION

Air pollution resulting from the burning of wood and other biomass fuels is estimated to kill two million women and children each year.

GOLD 2006

COPD – Treatment Opportunities

Opportunity # 1

- Smoking cessation
- Adequate ventilation if exposed to biomass burning – Cooking.
- Avoidance of exposure to industrial pollution etc
- Adequate breathing protection.

COPD – Treatment Opportunities

Opportunity # 1

- Influenza Vaccination
- Pneumococcal Vaccination.

COPD – Treatment Opportunities

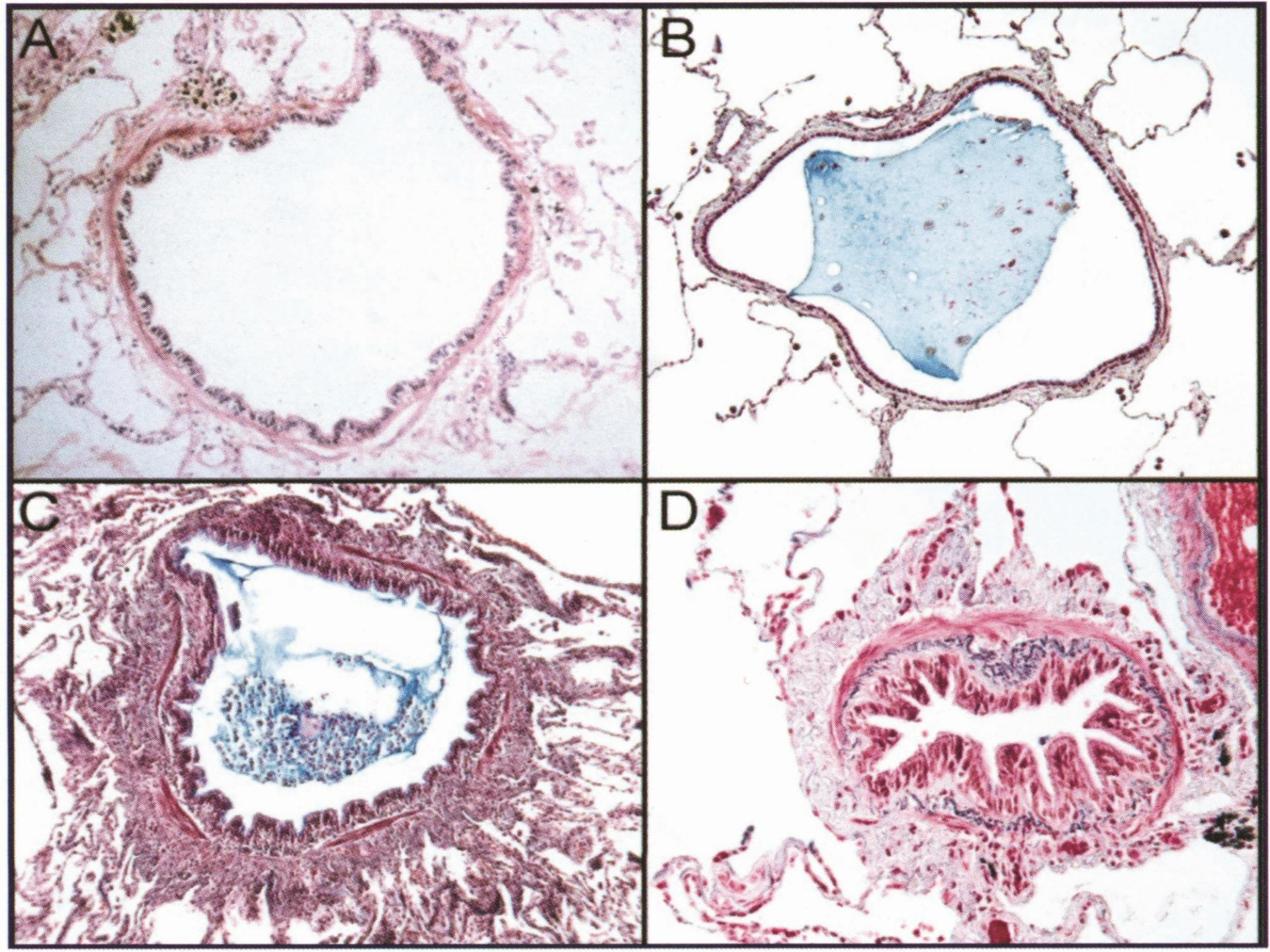
COPD - a chronic inflammatory disease – large numbers of

- neutrophils,
- macrophages,
- CD8 T lymphocytes

COPD – Treatment Opportunities

Inflammation leads to

- Fibrosis
- Small airway narrowing
- Decrease in FEV1.


A
B
C
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COPD – Treatment Opportunities

Difficulties

- Diagnosis
- Progression - outcome

COPD – Treatment Opportunities

Diagnosis

- Symptoms
- Spirometry

Progression of symptoms with increase in airway wall thickness, decrease in surface area, resulting in decrease in FEV1.

COPD Diagnosis

HISTORY	COPD	ASTHMA
Smoker or ex smoker	Nearly always	Variable
"Chesty Childhood"	Infrequent	Often
Chronic Cough and Sputum	Common	Infrequent
Breathlessness	Gradual and Progressive	Intermittent

COPD Diagnosis

INVESTIGATION	COPD	ASTHMA
FEV1	Always Reduced	Variable
Daily Variations in PEFR	Minimal	"Morning dip + day to day
Objective Response to SABA	Nil / Partial	Partial / Complete
Objective Response to Corticosteroid Trial	Partial Response in 10 - 20%	Good Response in Majority

COPD – Treatment Opportunities

Outcome

- Impossible to predict progression or outcome of disease in patient with Gold stage 0.

COPD – Treatment Opportunities

Comorbidities

- Comorbities increase with progression of the disease – decreased lung function, reduced exercise tolerance, muscle catabolism

COPD – Treatment Opportunities

Opportunity # 2

Bronchodilatation

The cornerstone of treatment

COPD – Treatment Opportunities

Bronchodilator choice

- Short acting beta agonist
- Long Acting beta agonist
- Anticholinergic – long or short acting
- Combination
- Theophylline

COPD – Treatment Opportunities

Bronchodilator Choice

Consider

- Price
- Effectiveness including side effects
- Individual Properties.

COPD – Treatment Opportunities

Tiotropium (Spiriva)

- Long term maintainence
- Previous trial (Sample or Atrovent)
- Grade 4 or 5 MRC dyspnoea scale
- Smoking and influenza addressed.
- FEV1 60% or less predicted.

COPD – Treatment Opportunities

Tiotropium

- Available for moderate to severe COPD.
- Reduction in exacerbations
- Reduction in sputum production
- No increase in pneumonia

COPD – Treatment Opportunities

Treatment of Inflammation

- Inflammatory basis of asthma known since the time of Osler (1900)
- Emphasis of treatment for 70 years was bronchodilatation
- Inflammation not targeted till mid 1960's.

COPD – Treatment Opportunities

Inhaled Corticosteroids in COPD

- Ineffective in neutrophil induced inflammation

However

- IHCs in significant COPD have been shown to reduce exacerbation rate.

COPD – Treatment Opportunities

Importance of Exacerbations

- While lung function steadily declines with age, it declines more rapidly in sufferers of COPD.
- With each exacerbation, lung function never quite returns to the previous state

COPD – Treatment Opportunities

Exacerbations

- If exacerbations can be reduced, deterioration in lung function may be reduced.
- This seems to only be relevant in GOLD stage 3 and 4.
- IHC use associated with increased survival

Van Schayck & Reid 2006

COPD – Treatment Opportunities

INHALED CORTICOSTEROIDS – 2011

- There is increasing evidence that IHCs may influence disease outcome in **severe** COPD
- Used in higher doses than in asthma (500µg bd fluticasone or 800µg bd budesonide)
- Reduce number of exacerbations which can cause progressive deterioration of lung function, but increase incidence of pneumonia. (TORCH 207)
- Increasing evidence that combination IHC and LABA have symbiotic action and are more effective together than when used separately.

COPD – Treatment Opportunities

Opportunity # 3

- Inhaled corticosteroids in selected patients.
- As effective as tiotropium
- Increase in incidence of pneumonia
- Reduction in exacerbations
- No change in mortality. (TORCH 2007)

COPD – Treatment Opportunities

Opportunity # 4 - Theophylline

- Some patients may benefit
- Now 3rd line treatment
- Narrow therapeutic window and potential for toxicity.
- Start low – go slow
- Blood levels after 1 week on increased dose till plateau reached
- Levels should be maintained 40 – 60 microl / L.

COPD – Treatment Opportunities

Opportunity # 5

REHABILITATION

- Exercise training - Walking
- Nutrition
- Education

GOALS

- Reduce symptoms
- Improve quality of life

COPD – Treatment Opportunities

Opportunity # 6

- Oxygen
- Long term oxygen increases survival.

  Goal to > PO2 to 60mmHg.

  Suitable only for stage 4 disease if PaO_2 is <55mm Hg.
- Lung reduction Surgery
- Lung transplant.

COPD – Treatment Opportunities

Opportunity # 7

EXACERBATIONS

- Antibiotics for infective episodes
- Regular bronchodilatation
- Glucocorticoids

COPD – Palliative Care

- A new concept with application to COPD
- The disease is incurable and has a terminal phase
- Concept needs careful planning, a team approach, with team consensus.
- Needs frank, pragmatic, sensitive approach.

COPD – Treatment Opportunities

The Future

- Inhibition of inflammation
  - Phosphodiesterase inhibition. Theophylline is a non targeted PDE inhibitor
  - Leukotriene B4 Inhibitors
  - Chemokine Inhibitors
  - Tumour Necrosis Factor Inhibitors.
  - Interleukin -10 – (A cytokine with anti-inflammatory actions