

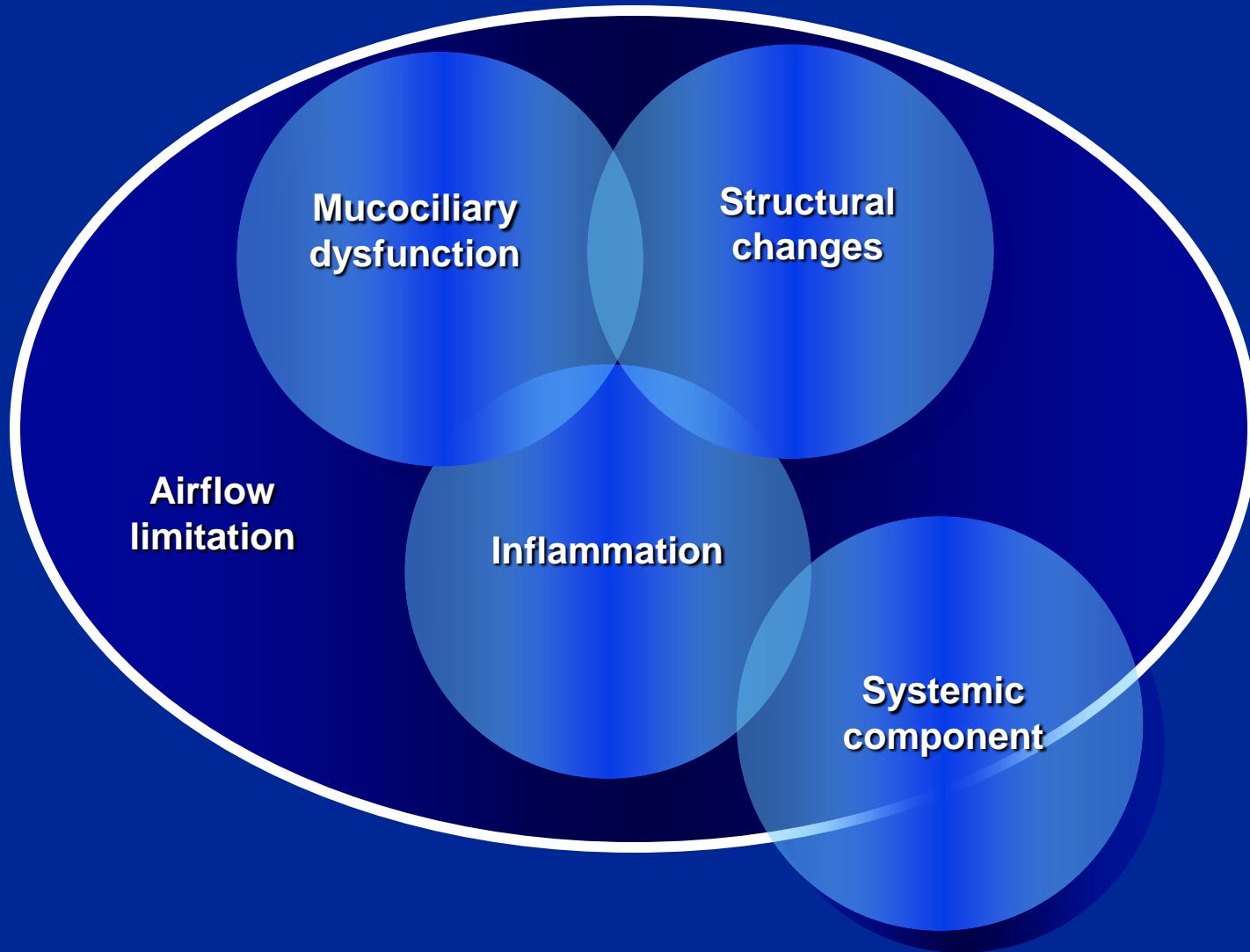
# **The Role of Inflammation in COPD**

# Objectives

- **Discuss the multicomponent nature of COPD**
- **Examine inflammation during an exacerbation**

# COPD Is a Multicomponent Disease

All Components, Including Inflammation, Are Important



# Definition of COPD

- “...a preventable and treatable disease state characterised by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and is associated with an abnormal **inflammatory** response of the lungs to noxious particles or gases, primarily caused by cigarette smoking. Although COPD affects the lungs, it also produces significant systemic consequences.”<sup>1</sup>
- According to GOLD, COPD is characterized by chronic **inflammation** throughout the airways, and the complications of COPD can be explained on the basis of underlying **inflammation** and the resulting pathology<sup>2</sup>

1. Celli, BR, et al. *Eur Respir J*. 2004;23:932-946.

2. *Global Initiative for Chronic Obstructive Lung Disease: Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, NHLBI/WHO workshop report. Bethesda, Md: National Heart, Lung, and Blood Institute; National Institutes of Health; April 2001 (updated 2005). NIH publication 2701.

# Inflammation in COPD

- COPD is characterized by an increase in neutrophils, macrophages, and T-lymphocytes (specifically CD8+) in various parts of the lungs, which relate to the degree of airflow limitation
- Eosinophils may increase in some patients, particularly during exacerbations
- This inflammation pattern is markedly different from that seen in patients with asthma
- Inflammatory changes may persist after quitting smoking

The roles of inflammatory cells in COPD are not fully understood.

# Evaluation of the Role of Inflammation Across All Stages of COPD

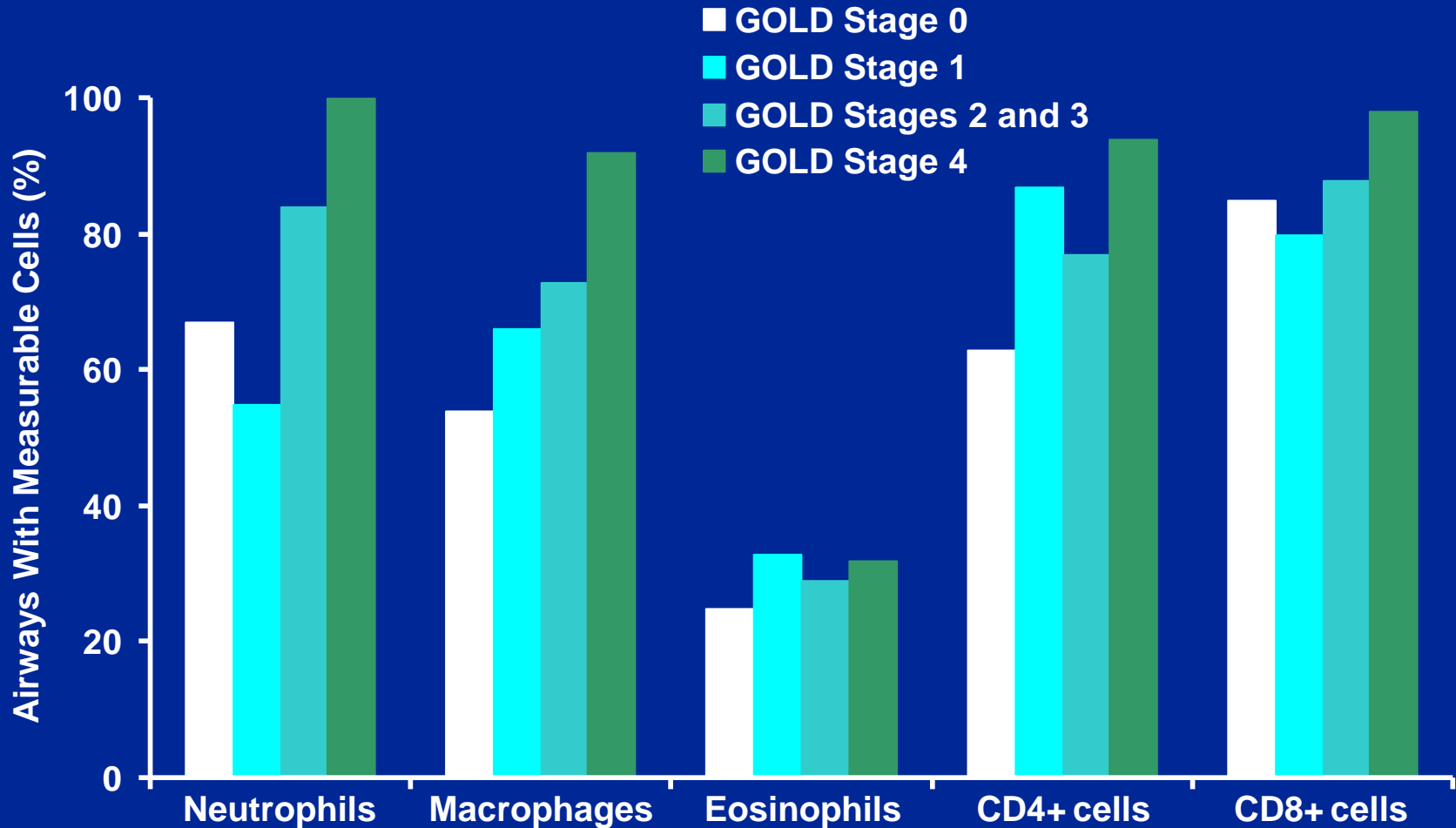
## Study Design

- The objective of this study was to evaluate the relationship between progression of COPD (as reflected by GOLD stage) and the pathological findings in small airways (<2 mm in internal diameter)
- Specimens/patient population: surgically resected lung tissue from 159 patients with various stages of COPD (according to GOLD classification)
  - Stage 0 n=39
  - Stage 1 n=39
  - Stage 2 n=22
  - Stage 3 n=16
  - Stage 4 n=43

# Baseline Characteristics

	GOLD Stage 0 (At Risk) (39)		GOLD Stage 1 (Mild) (39)		GOLD Stage 2 (Moderate) (22)		GOLD Stage 3 (Severe) (16)		GOLD Stage 4 (Very Severe) (43)	
FEV <sub>1</sub> % predicted	98.1	1.7	93.0	1.3	67.5	1.5	35.0	1.0	21.9	0.6
FEV <sub>1</sub> /FVC (% of FVC)	0.78		0.65		0.58		0.35		0.30	
	0.009		0.006		0.016		0.014		0.008	
<b>Smoking history</b>										
Pack-years	40	13	50	5	51	6	60	5	67	5
Current (No. of pts)	22		22		14		0		0	
Former	17		15		8		12		43	
Years since quitting	6	2	4	1	5	2	9	2	9	1
Unknown	0		2		0		4		0	
No. of airways examined per patient	10	1	9	1	7	1	7	1	13	2

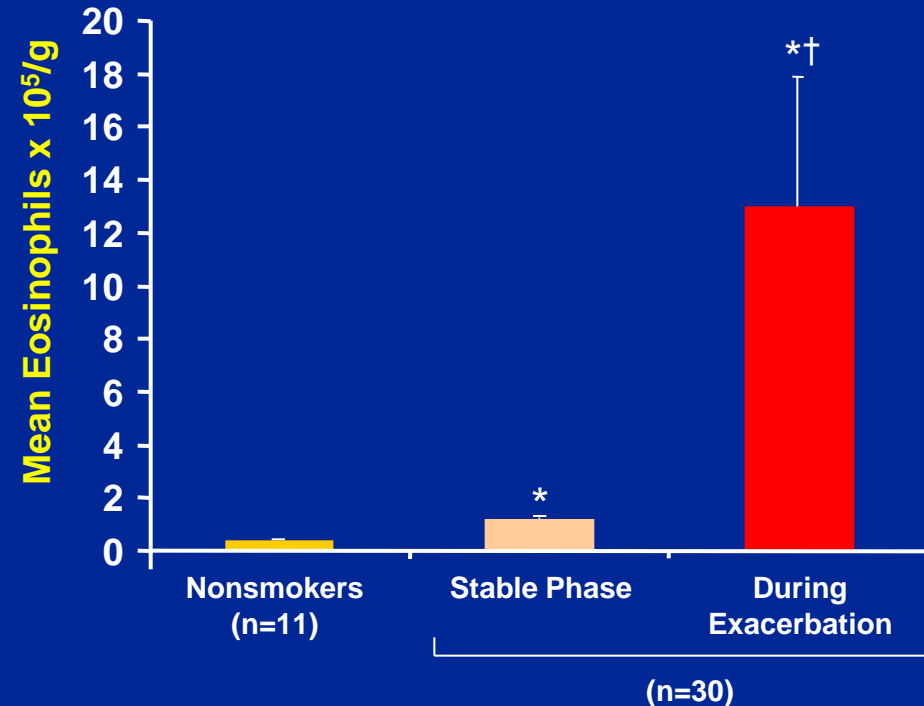
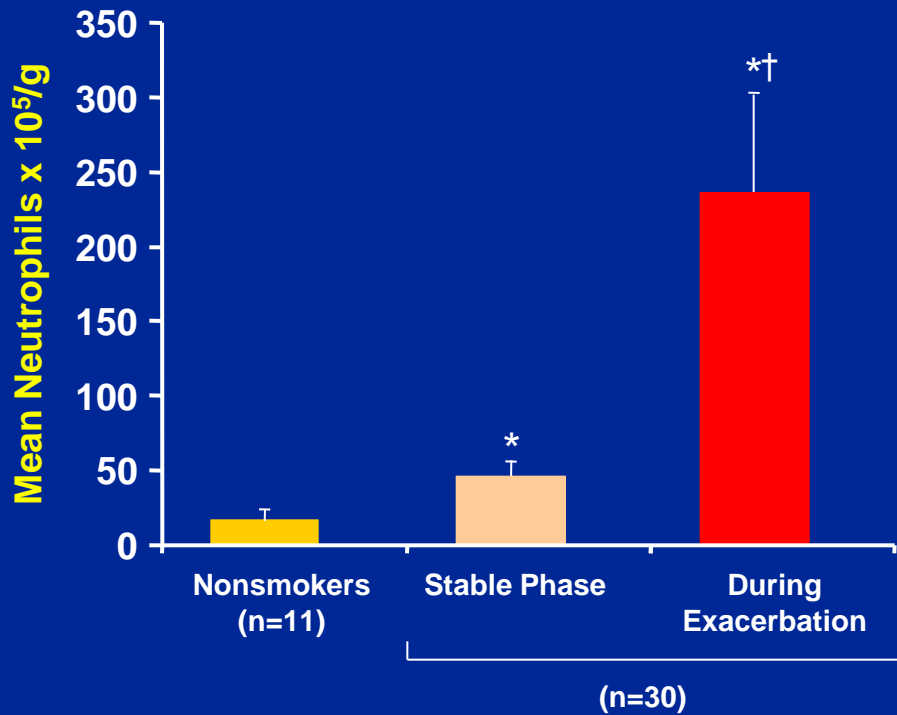
# Inflammation in COPD Occurs Even in the Early Stages



# Evaluation of Airway Inflammation During an Exacerbation of COPD

- 68 outpatients with COPD were followed over 2-3 years
- A COPD exacerbation was defined as worsening of 2 or more major symptoms (dyspnea, sputum purulence, sputum volume) or 1 major and 1 minor symptom (sore throat, colds, fever without other cause, and increased cough or wheeze) for 2 or more consecutive days
- Sputum samples were taken during a stable phase and during an exacerbation when possible
  - Stable phase was defined as a stable condition  $\geq 3$  months without evidence of an infection
- For comparison, sputum samples were also obtained from 11 nonsmoking individuals

# Sputum Neutrophils and Eosinophils Significantly Increased During an Exacerbation



Results of nonsmokers from a stable phase and during an exacerbation in patients who developed an exacerbation during the study.

\* $P < 0.01$  vs nonsmokers.

† $P < 0.05$  vs stable phase.

Fujimoto K, et al. *Eur Respir J.* 2005;25:640-646.

# Evaluation of Incidence of Symptom- and Healthcare-defined Exacerbations

## Objective:

- To investigate the incidence of chronic obstructive pulmonary disease (COPD) exacerbations in primary care

## Study Design:

- Prospective, 12-month observational study in primary care setting with patients who have a diagnosis of COPD
- Patients recorded information on symptoms, quality of life, and use of healthcare services in daily diaries:
  - Symptom-defined exacerbations: Patients recorded an increase in major and minor symptoms. Exacerbation defined as a symptom score of at least 2 for 2 consecutive days, with no score for at least 2 of these symptoms in the preceding 5 days
  - Healthcare-defined exacerbations: Defined as the need to take antibiotics and/or oral corticosteroids (OCS) for chest problems
- Overall, 201 patients completed at least 1 diary card during the study and 127 completed diary cards covering  $\geq 80\%$  of the year
- Mean baseline FEV<sub>1</sub> was 50% of predicted

# Majority of COPD Patients Experience Exacerbations

- In a 12-month study, 77% of patients had at least 1 exacerbation\*

	Type of exacerbation dependent on definition	
	Symptom-defined	Healthcare-defined
Total number of exacerbations experienced	296	351
Mean yearly rate of exacerbations	2.3	2.8
Patients experiencing 0 exacerbations, n (%)	29 (23)	29 (23)
Patients experiencing 1-2 exacerbations, n (%)	56 (44)	41 (32)
Patients experiencing 3 or more exacerbations, n (%)	42 (33)	57 (45)

\*Based on 127 of 201 subjects who completed diary cards covering  $\geq 80\%$  of the year.

O'Reilly J, et al. *Prim Care Respir J*. 2006;15:346-353.

# Summary: Inflammation and Exacerbations in COPD

- COPD is a multi-component chronic disease characterized by chronic inflammation<sup>1,2</sup>
- Inflammation occurs at all stages of COPD<sup>3</sup>
- Evidence supports that exacerbations are acute inflammatory events superimposed on the chronic inflammation characteristic of COPD<sup>4,5</sup>
- Exacerbations are defined as an acute change in dyspnea, cough, and/or sputum sufficient enough to warrant therapy change<sup>6</sup>
- 77% of patients reported having at least 1 exacerbation<sup>6\*</sup>

\*Based on diary records of symptom-defined and healthcare-defined exacerbations.

1. Rodríguez-Roisin R. *COPD: J COPD*. 2005;2:253-262.
2. *Global Initiative for Chronic Obstructive Lung Disease: Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, NHLBI/WHO workshop report. Bethesda, Md:National Heart, Lung, and Blood Institute; National Institutes of Health; April 2001 (updated 2005). NIH publication 2701.
3. Hogg JC, et al. *N Engl J Med*. 2004;350:2645-2653.
4. Fujimoto K, et al. *Eur Respir J*. 2005;25:640-646.
5. Anzueto A, et al. *Proc Am Thorac Soc*. 2007;4:554-564.
6. O'Reilly J, et al. *Prim Care Respir J*. 2006;15:346-353.