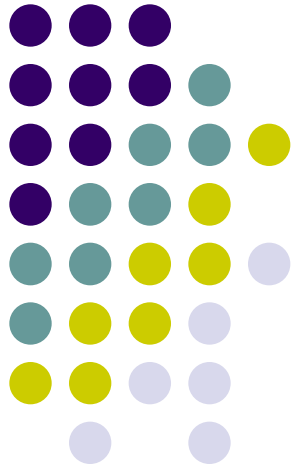
COPD – A COMMON COMORBIDITY IN LUNG CANCER



COPD - LUNG CANCER

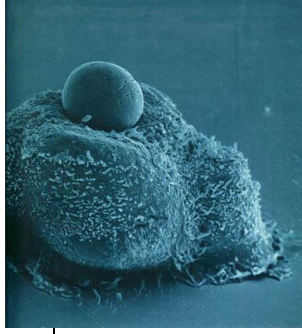
Two of the greatest challenges in pulmonary medicine

COPD is independently and closely related to Lung Cancer

Skillrud DM, Offord KP, Miller RD, et al. Higher risk of lung cancer in chronic obstructive pulmonary disease: a prospectiv matched controlled study. Ann Intern Med 1986; 105:503–507

R.P. Young, R.J. Hopkins, T. Christmas, P.N. Black, P. Metcalf, G.D. Gamble, COPD prevalence is increased in lung cancer, independent of age, sex and smoking history, Eur Respir J 2009; 34: 380–386

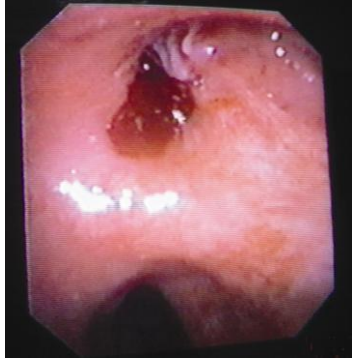
COPD - LUNG CANCER



- Lung cancer is the **number one cause of death from cancer worldwide**
- Approximately 85% of lung cancer occurs in **current or former smokers**
- Lung cancers frequently occur in patients with COPD

The correlation of emphysema or airway obstruction with the risk of lung cancer: a matched case-controlled study. K. Kishi, J.W. Gurney, D.R. Schroeder, P.D. Scanlon, Eur Respir J 2002; 19: 1093–1098.

COPD - LUNG CANCER



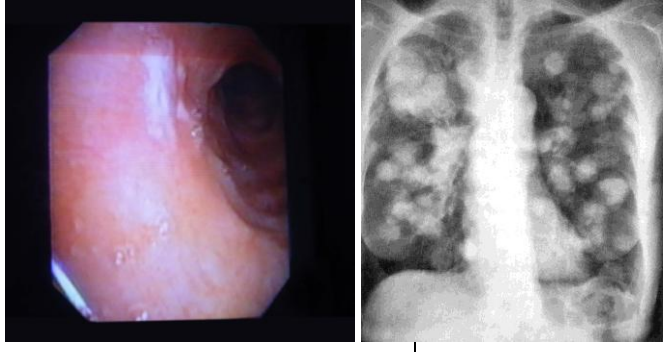
- **The risk of lung cancer** increases with age and amount of smoke exposure

- Cigarette smoke is the **common aetiological factor** for both lung cancer and COPD

- Smoking accounts for an estimated **80–90% of the risk of developing COPD**

The correlation of emphysema or airway obstruction with the risk of lung cancer: a matched case-controlled study. K. Kishi, J.W. Gurney, D.R. Schroeder, P.D. Scanlon, Eur Respir J 2002; 19: 1093–1098.

COPD - LUNG CANCER



- Several studies have shown that **airway obstruction** is associated with increased risk of **lung cancer independent of smoking** !

The correlation of emphysema or airway obstruction with the risk of lung cancer: a matched case-controlled study. K. Kishi, J.W. Gurney, D.R. Schroeder, P.D. Scanlon, Eur Respir J 2002; 19: 1093–1098.

Risk of lung cancer among COPD patients

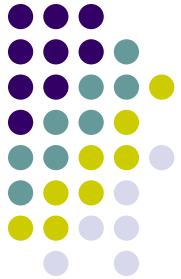
- Previously: 2 -fold increased risk associated with COPD

Wasswa-Kintu S, Gan WQ, Man SFP, et al., Relationship between reduced forced expiratory volume in one second and the risk of lung cancer: a systematic review and meta-analysis. Thorax 2005;60: 570–575

COPD - LUNG CANCER

Both diseases result from shared pathogenic mechanisms

Both diseases result from shared pathogenic mechanisms



- Smoking-related diseases
- Genetically-determined diseases
- Cluster in families
- Worsen with age

COPD – LUNG CANCER

- **Mortality studies** of patients with **COPD** suggest 20–30% die from lung cancer.

The Lung Health Study Research Group. Effect of inhaled triamcinolone on the decline in pulmonary function in chronic obstructive pulmonary disease. N Engl J Med 2000; 343: 1902–1909.

The most important underlying

Risk factor

for

Lung Cancer

is

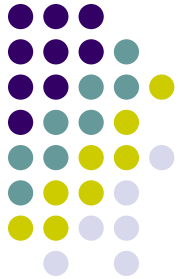
COPD

greater

than that attributed to

<u>smoking dose or age !</u>

SUMMARY



- Pathogenic mecanisms
- Genetics
- Smoking
- Airflow obstruction
- Endoscopy-COPD-lung cancer
- Conclusions

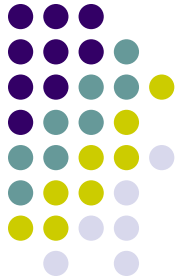
1.Pathogenic mecanisms

COPD and Risk of Lung Cancer in Population

- Every year, over **1 million people die from lung cancer worldwide**
- **Cigarette smoking** is the primary etiologic agent in **85–90% of all lung cancers**

Koshiol J, Rotunno M, Consonni D, Pesatori AC, De Matteis S, et al. (2009) Chronic Obstructive Pulmonary Disease and Altered Risk of Lung Cancer in a Population-Based Case-Control Study. PLoS ONE 4(10): e7380. doi:10.1371/journal.pone.0007380, Neeraj Vij, Johns Hopkins School of Medicine, October 8, 2009

COPD and Risk of Lung Cancer in Population



- **Only 10–15% of active smokers** develop lung cancer !!

- Lung cancer is **the 7 th most common cause of cancer death** worldwide **in never smokers !!**

Koshiol J, Rotunno M, Consonni D, Pesatori AC, De Matteis S, et al. (2009) Chronic Obstructive Pulmonary Disease and Altered Risk of Lung Cancer in a Population-Based Case-Control Study. PLoS ONE 4(10): e7380. doi:10.1371/journal.pone.0007380, Neeraj Vij, Johns Hopkins School of Medicine, October 8, 2009

Pathogenic mecanisms

COPD

Exacerbations-Pulmonary infections

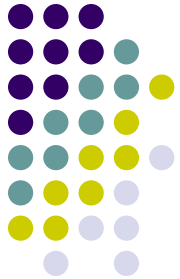
Inflammation

Lung carcinogenesis

Carcinogenesis in general

Koshiol J, Rotunno M, Consonni D, Pesatori AC, De Matteis S, et al. (2009) Chronic Obstructive Pulmonary Disease and Altered Risk of Lung Cancer in a Population-Based Case-Control Study. PLoS ONE 4(10): e7380. doi:10.1371/journal.pone.0007380, Neeraj Vij, Johns Hopkins School of Medicine, October 8, 2009

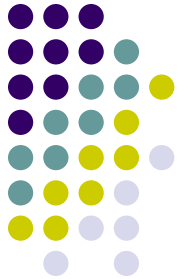
Lung carcinogenesis
Carcinogenesis in general



- reactive oxygen or nitrogen species
- increase cellular proliferation
- upregulating antiapoptotic pathways
- stimulating angiogenesis
- Infections -airway remodelling-enhance carcinogenesis

Koshiol J, Rotunno M, Consonni D, Pesatori AC, De Matteis S, et al. (2009) Chronic Obstructive Pulmonary Disease and Altered Risk of Lung Cancer in a Population-Based Case-Control Study. PLoS ONE 4(10): e7380. doi:10.1371/journal.pone.0007380, Neeraj Vij, Johns Hopkins School of Medicine, October 8, 2009

Shared pathogenic mechanisms



- Occupational toxins
- Community air pollution

→ Accumulated and damaging mutations

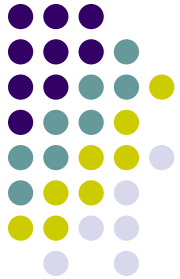
→ Inflame and destroy airways alveoli

→ Dysplastic and ultimately neoplastic changes

Koshiol J, Rotunno M, Consonni D, Pesatori AC, De Matteis S, et al. (2009) Chronic Obstructive Pulmonary Disease and Altered Risk of Lung Cancer in a Population-Based Case-Control Study. PLoS ONE 4(10): e7380. doi:10.1371/journal.pone.0007380, Neeraj Vij, Johns Hopkins School of Medicine, October 8, 2009

R.P. Young, R.J. Hopkins, T. Christmas, P.N. Black, P. Metcalf, G.D. Gamble, COPD prevalence is increased in lung cancer, independent of age, sex and smoking history, Eur Respir J 2009; 34: 380–386

Shared pathogenic mechanisms



- **Chronic inflammation** → role in the pathogenesis of lung cancer as a tumour promoter.

*Virchow R. Aetiologie der neoplastischen Geschwulste/ Pathogenie der neoplastischen Geschwulste. In: DieKrankhaften Geschwulste. Berlin, Verlag von August Hirschwald, **1863**; pp. 57–101.*

- Some **cytokines (IL-6, IL-8, IL-10):** can inhibit apoptosis, interfere with cellular repair and promote angiogenesis.

O'Byrne KJ, Dalgleish AG. Chronic immune activation and inflammation as the cause of malignancy. Br J Cancer 2001;85: 473–483

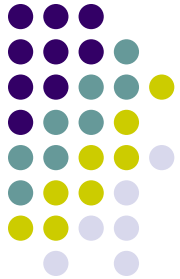
Shared pathogenic mechanisms

- These **cytokines** have also been implicated in COPD progression.

- Activation of nuclear **(NF)-kB transcription factor** may have major relevance for cancer and COPD.

Wright JG, Christman JW. The role of nuclear factor kappa B in the pathogenesis of pulmonary diseases: implications for therapy. Am J Respir Med 2003; 2: 211–219.

Shared pathogenic mechanisms

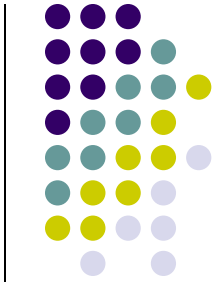


- **COPD** patients have impaired mucociliary clearance.

Rogers DF. Mucociliary dysfunction in COPD: effect of current pharmacotherapeutic options. Pulm Pharmacol Ther 2005; 18: 1–8.

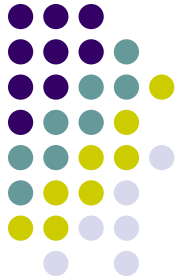
- **Reduced mucociliary clearance from the lungs** may increase risk cancer?

D.D. Sin, N.R. Anthonisen, J.B. Soriano, A.G. Agusti, Mortality in COPD: role of comorbidities, Eur Respir J 2006; 28: 1245–1257



2. Genetics

Genetically-determined diseases



- A shared genetic susceptibility to ***chronic smoking*-induced *inflammation***.

Schwartz AG, Ruckdeschel JC. Familial lung cancer: genetic susceptibility and relationship to chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2006; 173: 16–22

Gwilt CR, Donnelly LE, Rogers DF. The non-neuronal cholinergic system in the airways: an unappreciated regulatory role inpulmonary inflammation? Pharmacol Ther 2007; 115: 208–222.

- Genetic variant in the **α 5subunit of the nicotinic acetylcholine receptor gene.**

Young RP, Hopkins RJ, Hay BJ, et al. Lung cancer gene associated with COPD: triple whammy or possible confounding effect? Eur Respir J 2008; 32: 1158–1164.

Hung RJ, McKay JD, Gaborieau V, et al. A susceptibility locus for lung cancer maps to nicotinic acetylcholine receptor subunit genes on 15q25. Nature 2008; 452: 633–637

.

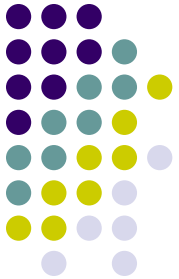
Genetically-determined diseases

- Functional significance and susceptibility to COPD and to lung cancer.

Carlisle DL, Hopkins TM, Gaither-Davis A, et al. Nicotine signals through muscle-type and neuronal nicotinic acetylcholine receptors in both human bronchial epithelial cells and airway fibrosis. Respir Res 2004; 5: 27–42.

- Susceptibility through **overlapping pathogenic pathways**, such as those underlying smoking-induced inflammation

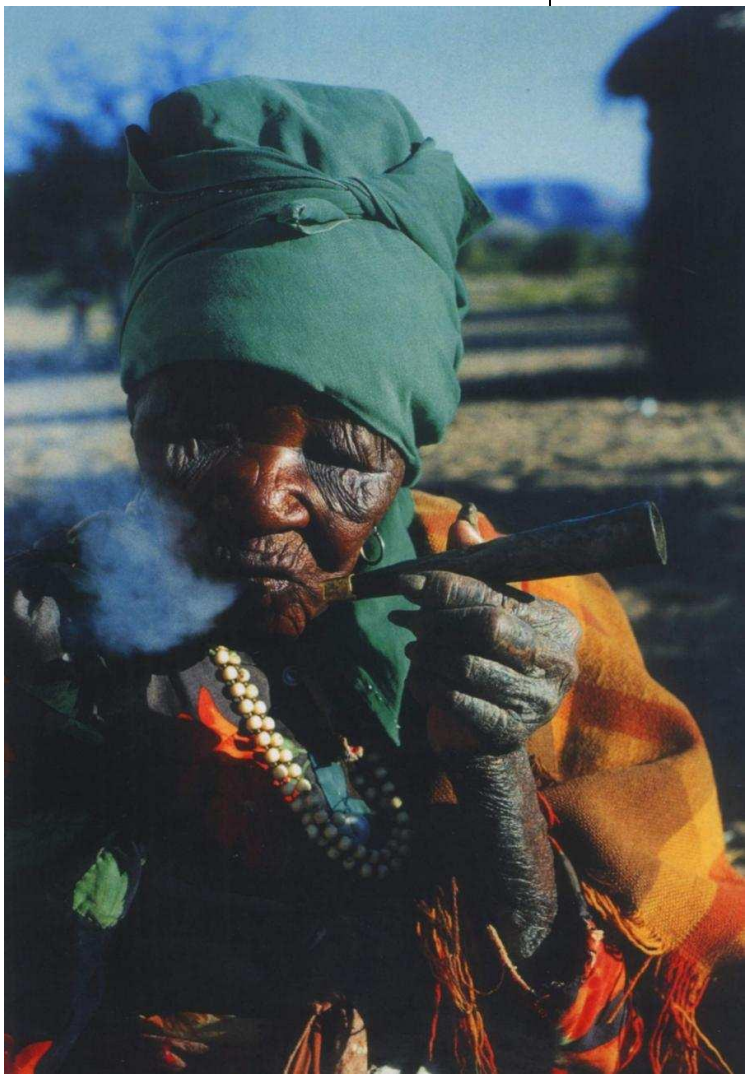
Brody JS, Spira A. Chronic obstructive pulmonary disease, inflammation, and lung cancer. Proc Am Thorac Soc 2006; 3: 535–538.



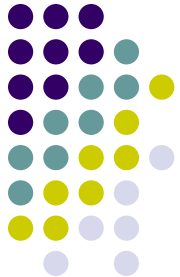
3.Smoking

Smoking-related diseases

- Smoking exposure is found in **85–90%** of those diagnosed with either COPD or lung cancer



Smoking - Lung Cancer



- Only 10–15% of chronic smokers get lung cancer !

  Mattson ME, Pollack ES, Cullen JW. What are the odds that smoking will kill you? Am J Pub Health 1987; 77: 425–431.

- Host susceptibility factors have been implicated

- Key risk factors: age, smoking history, family history and impaired lung function

  Alberg AL, Brock MV, Samet JM. Epidemiology of lung cancer: looking to the future. J Clin Oncol 2005; 23: 3175–3185

COPD – LUNG CANCER

COPD – LUNG CANCER

MORE THAN A SHARED SMOKING HISTORY?

Risk of lung cancer among COPD patients

- Six-fold higher

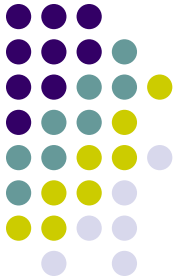
R.P. Young, R.J. Hopkins, T. Christmas, P.N. Black, P. Metcalf, G.D. Gamble, COPD prevalence is increased in lung cancer, independent of age, sex and smoking history, Eur Respir J 2009; 34: 380-386

TABLE 1 Summary of characteristics of the lung cancer cases and control smokers before and after matching

Parameter	Unmatched cohorts		Matched cohorts		p-value#
	Control smokers	Lung cancer	Control smokers	Lung cancer	
Subjects n	654	446	301	301	
Males %	57	53	53	53	
Age yrs	59±10	69±10	64±9	65±9	0.23
Height cm	170±0.09	167±0.08	168±0.09	168±0.08	0.58
Weight kg	80±16	69±15	78±15	71±16	<0.001
Smoking history					
Age started smoking yrs	18±4	17±4	18±4	18±4	0.62
Cigarettes day^{-1}	17±9	20±10	20±7	19±9	0.33
Current smokers %	24	35	22	39	<0.001
Pack-yrs	35±20	41±25	38±18	38±18	0.93
Lung function					
FEV$_1$ L	2.84±0.82	1.86±0.69	2.56±0.80	1.90±0.69	<0.001
FEV$_1$ % pred	97±18	73±23	96±20	71±23	<0.001
FEV$_1$/FVC %	81±9	64±13	80±10	64±13	<0.001
Prevalence of COPD %					
GOLD 1+	10	60	15	65	<0.001
GOLD 2+	6	51	8	50	<0.001
GOLD 3+	1.2	14	1.3	15	<0.001
History of comorbidities %					
Chronic bronchitis	5	18	6	16	<0.001
Asthma	12	12	11	13	0.45

Data are presented as mean±so, unless otherwise stated. FEV$_1$: forced expiratory volume in 1 s; % pred: % predicted; FVC: forced vital capacity; COPD: chronic obstructive pulmonary disease; GOLD: Global Initiative for Chronic Obstructive Lung Disease. #: comparison for matched cohorts only.

COPD – LUNG CANCER



- Smoking-induced airway inflammation typically **persists** in those smokers with COPD for **many years after quitting smoking.**

Ind PW. COPD progression and airway inflammation: uncoupled by smoking cessation. Eur Respir J 2005; 26: 764–766

- 50% of lung cancer cases are found in **ex-smokers**

Young RP, Hopkins RJ, Hay BJ, et al. Lung cancer gene associated with COPD: triple whammy or possible confounding effect? Eur Respir J 2008; 32: 1158–1164

Yang P, Allen MS, Aubry MC, et al. Clinical features of 5,628 primary lung cancer patients; experience at Mayo clinic from 1997 to 2003. Chest 2005; 128: 452–462

COPD and squamous cell carcinoma

- Squamous cell carcinoma has a stronger association with **tobacco smoking** than other nonsmall cell lung cancers (NSCLC)

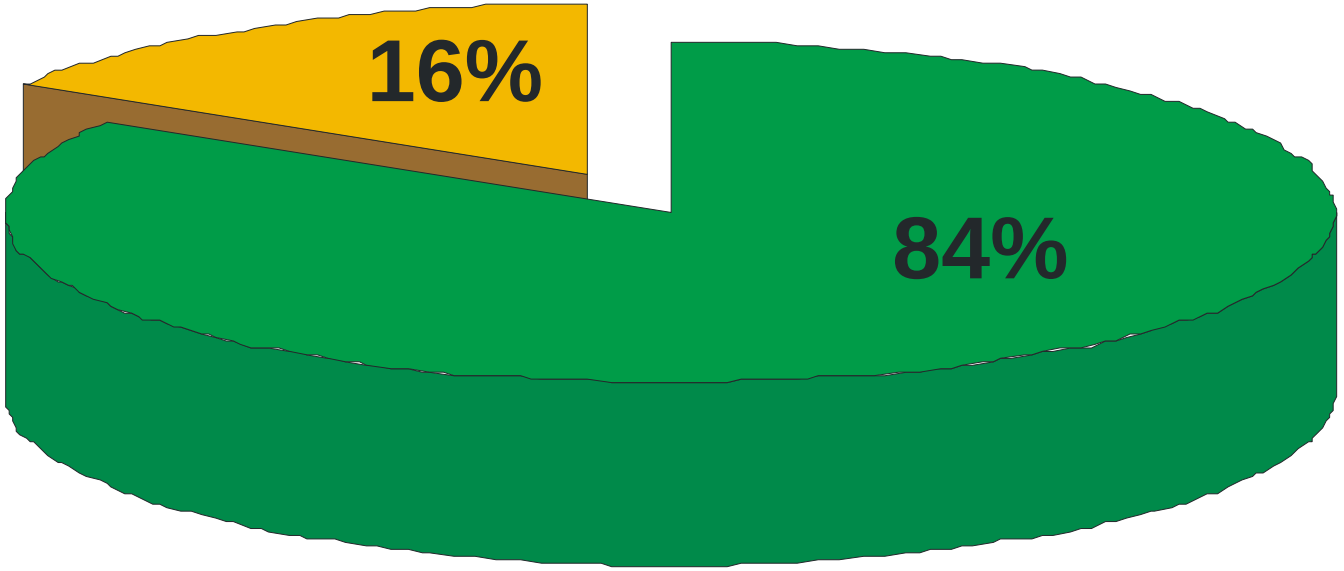
- COPD is a risk factor for the **squamous cell carcinoma** histological subtype in **smokers with surgically resectable** NSCLC.

- Chronic bronchitis is a risk factor for the **adenocarcinoma histological subtype.**

A Papi, G Casoni, G Caramori, I Guzzinati, P Boschetto, F Ravenna, N Calia, S Petruzzelli,L Corbetta, G Cavallesco, E Forini, M Saetta, A Ciaccia, L M Fabbri, COPD increases the risk of squamous histological subtype in smokers who develop non-small cell lung carcinoma, Thorax 2004;59:679–681.

Bronchoscopies - “Marius Nasta” Institute
1999-2000-2001
8856 cases -lung cancer

1417 non-smokers



7439 smokers

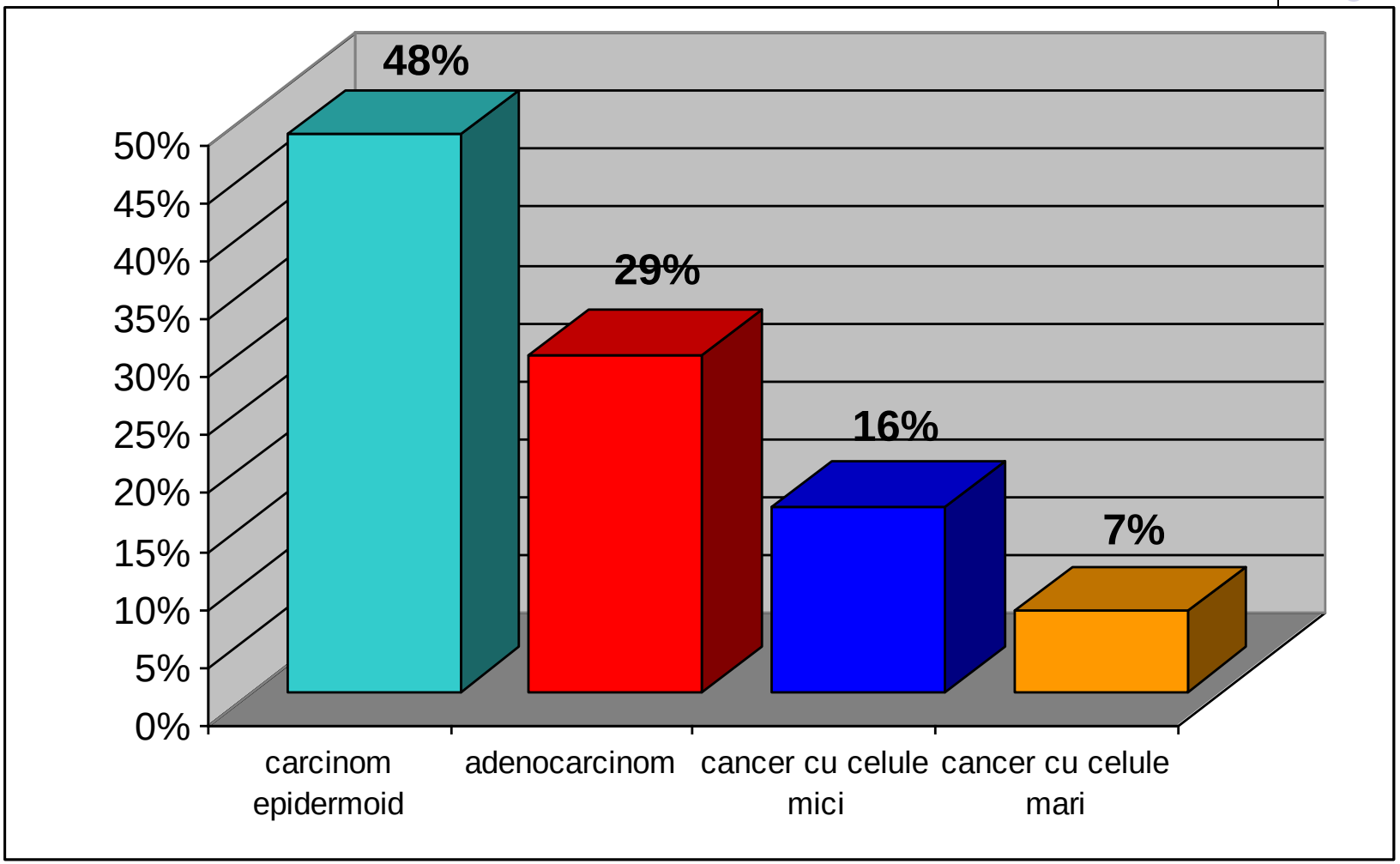
smokers ≥ 10 p/ years

R Ulmeanu, CT- bronchoscopy corel. in lung cancer, 2006

7792 cases -lung cancer

1999 – 2000 – 2001

"MARIUS NASTA“ Institute



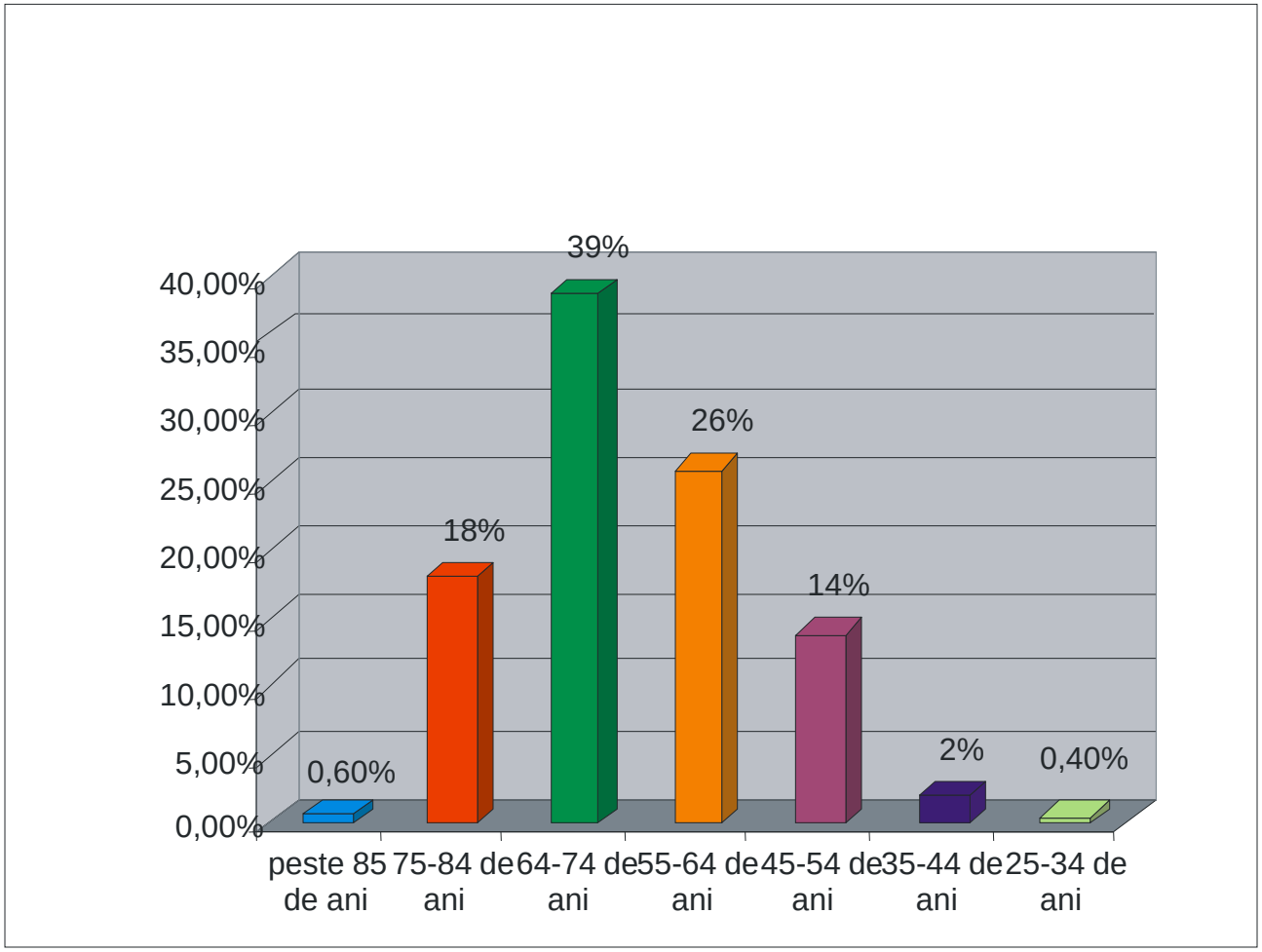
R Ulmeanu, CT- bronchoscopy corel. in lung cancer, 2006

Lung Cancer- 7792 patients

SMOKERS $\geq$ 10 pack/ yrs

AGE OVER 45 YEARS

PRESENCE OF RESPIRATORY SIMPTOMATOLOGY



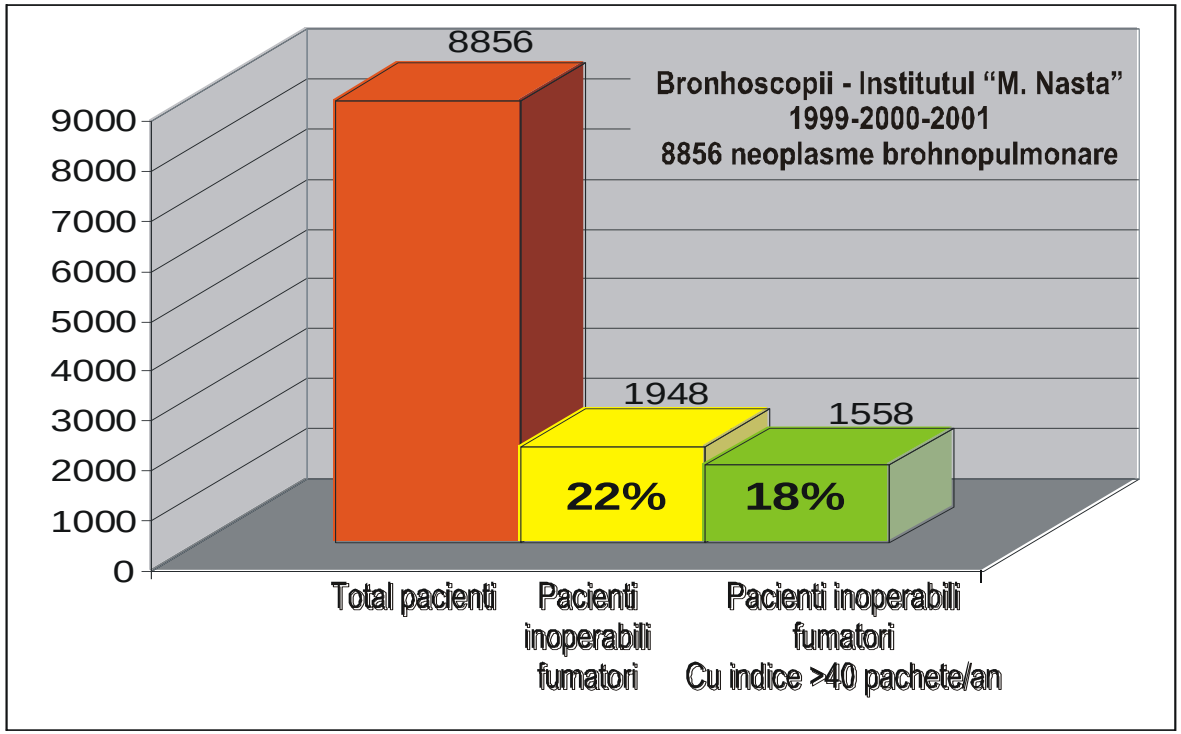
R Ulmeanu, CT- bronchoscopy corel. in lung cancer, 2006

7792 patients

MAJOR RISK- LUNG CANCER

INOPERABLE STAGE - MOMENT OF DIAGNOSIS

"BIG" SMOKERS $\geq$ 40 pack/ yrs



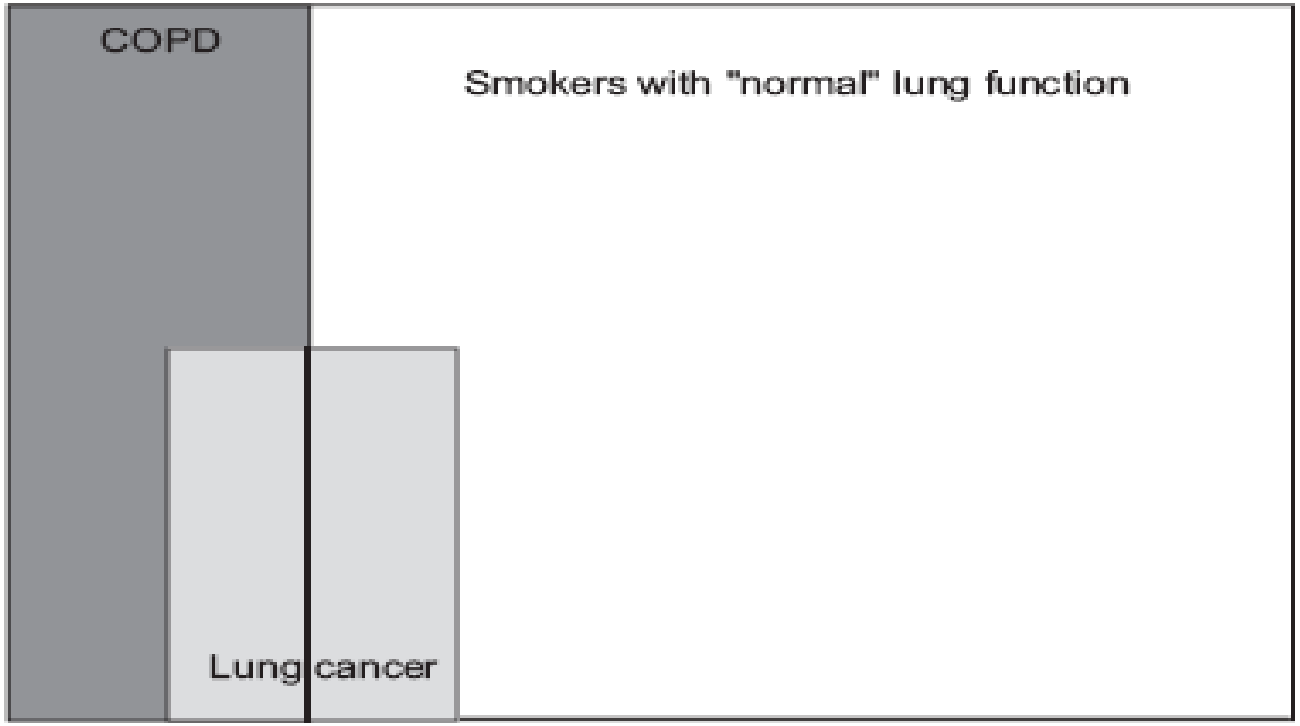
R Ulmeanu, CT- bronchoscopy corel. in lung cancer, 2006

4. Airflow obstruction

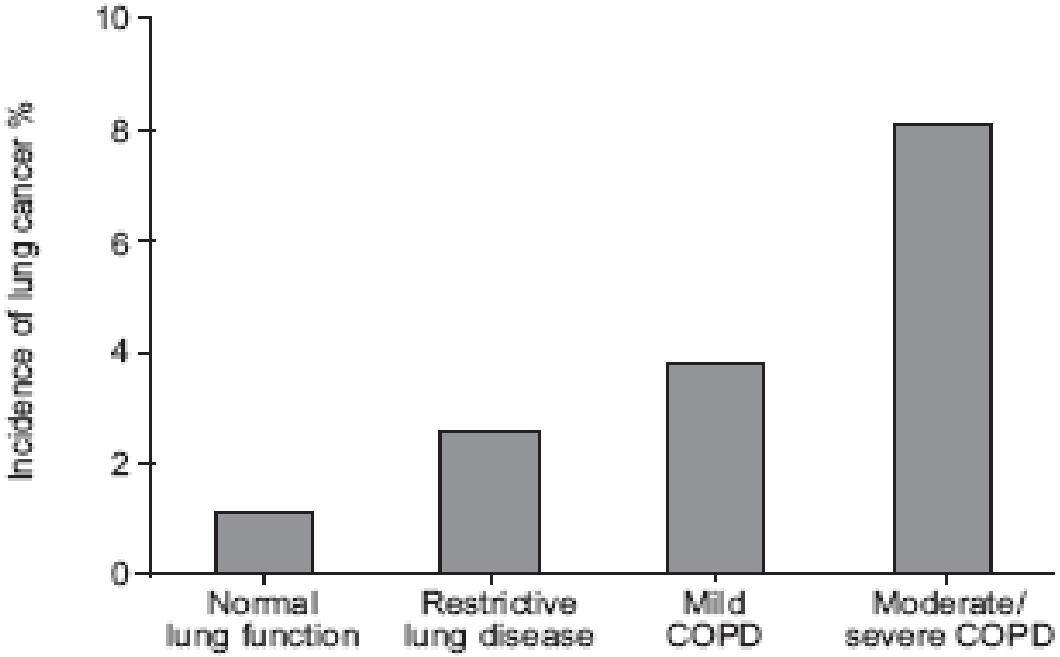
> 50% of lung cancer cases have coexisting moderate-to-severe COPD

A disproportionate number of lung cancer cases occur in smokers with pre-existing COPD compared with those with normal (or near normal) lung function !

R.P. Young, R.J. Hopkins, T. Christmas, P.N. Black, P. Metcalf, G.D. Gamble, COPD prevalence is increased in lung cancer, independent of age, sex and smoking history, Eur Respir J 2009; 34: 380–386



An inverse correlation between the degree of airflow obstruction and lung cancer risk



Mannino DM, Aguayo SM, Petty TL, Redd SC. Low lung function and incident lung cancer in the United States: data from the First National Health and Nutrition Examination Survey follow-up. Arch Intern Med 2003; 163: 1475 1480.

Lung function and COPD prevalence according to stage and histology

- **No relationship- stage**
- Prevalence slightly higher in **squamous cell lung cancers and small cell**

R.P. Young, R.J. Hopkins, T. Christmas, P.N. Black, P. Metcalf, G.D. Gamble, COPD prevalence is increased in lung cancer, independent of age, sex and smoking history, Eur Respir J 2009; 34: 380–386

TABLE 2 Lung function and chronic obstructive pulmonary disease (COPD) prevalence according to stage and histology in the lung cancer cohort#

Lung cancer histology¶	Subjects n	Staging+	Spirometry				COPD prevalence GOLD 2+ %
			FEV1 L	FEV1 % pred	FVC L	FEV1/FVC %	
Small cell§	78		1.88±0.46	72±17	2.95±0.71	64±7	53
	26	Limited	1.81±0.63	72±19	2.86±0.77	63±12	50
	52	Extensive	1.92±0.44	73±17	3.00±0.71	64±7	54
Nonsmall cell/	100	Stage 1	1.89±0.72	78±27	2.87±0.83	66±15	46
	34	Stage 2	1.77±0.43	71±19	2.68±0.71	67±13	42
	107	Stage 3	2.11±0.33	76±10	3.23±0.52	65±14	46
	103	Stage 4	1.93±0.87	70±25	2.97±0.67	65±11	48
Histological subtype							
Adenocarcinoma	191		1.96±0.65	77±26	2.96±0.44	66±13	45
Squamous	108		1.85±0.29	70±22	2.93±0.47	63±12	51
Nonsmall	45		1.78±0.55	71±19	2.89±0.87	62±11	47

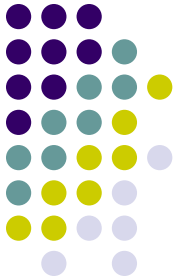
The airflow obstruction

- **Moderate or severe airflow obstruction**: significant predictor of incident lung cancer.

Mannino DM, Aguayo SM, Petty TL: Low lung function and incident lung cancer in the United States. Arch Intern Med 2003;113:1475-1480

- Lung cancer may itself cause an obstructive effect on spirometry.

The airflow obstruction



- Impaired lung function is more important than age or smoking exposure (pack-yrs)!

- Even in **nonsmokers,** impaired lung function is associated with an **increased risk of lung cancer!**

Turner MC, Chen Y, Krewski D, et al. Chronic obstructive pulmonary disease is associated with lung cancer mortality in a prospective study of never smokers. Am J Respir Crit Care Med 2007; 176: 285–290.

Anthonisen NR. Prognosis in chronic obstructive pulmonary disease: results from multicenter clinical trials. Am Rev Respir Dis1999; 140: S95–S99.

Emphysema - Lung cancer

- **Emphysema** (30–40% of long-term smokers) **related to lung cancer** independently of sex, age, smoking habits and airflow obstruction.

de Torres JP, Bastarrika G, Wisnivesky JP, et al. Assessing the relationship between lung cancer risk and emphysema detected on low-dose CT of the chest. Chest 2007; 132: 1932–1938.

Wilson DO, Weissfeld JL, Balkan A, et al. Association of radiographic emphysema and airflow obstruction with lung cancer. Am J Respir Crit Care Med 2008; 178: 738–744

Emphysema - Lung cancer

- Asymptomatic lung cancers in 2–5% of patients with severe emphysema **evaluated CT for lung volume reduction surgery.**

Rozenshtein A, White CS, Austin JHM, Roinney BM, Protopapas Z, Krasna MJ. Incidental lung carcinoma detected at CT in patients selected for lung volume reduction surgery to treat severe pulmonary emphysema.Radiology 1998; 207: 487–490.

- Lung cancer patients are significantly more likely to carry **the mutated a1-antitrypsin allele than the general population**.

Yang P, Wentzlaff KA, Katzmann JA, et al. Alpha 1-antitrypsin deficiency allele carriers among lung cancer patients. Cancer Epidemiol Biomakers Prev 1999; 8: 461–465.

Emphysema - Lung cancer

- **Bronchoalveolar stem cells (BASC)** proliferate to replace damaged alveolar cells

A. Bourdin, P-R. Burgel, P. Chanez, G. Garcia, T. Perez, N. Rochee, Recent advances in COPD: pathophysiology, respiratory physiology and clinical aspects, including comorbidities, Eur Respir Rev 2009; 18: 114, 198–212

- Abnormal **BASC proliferation** due to carcinogens present in cigarette smoke may result in lung cancer.

Houghton AM, Mouded M, Shapiro SD. Common origins of lung cancer and COPD. Nat Med 2008; 14: 1023–1024.

5. Endoscopy-COPD-lung cancer

Endoscopy-COPD-lung cancer

a. Detection of precancerous bronchial lesions

b.Palliate inoperable lung cancer

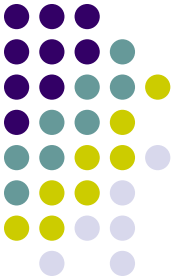
Advances in endoscopic technology

-improved the detection of precancerous bronchial lesions

-associated with the occurence of proximal squamous cell lung cancer (SCC) in high-risk individuals

Suzana Bota, Jean-Bernard Auliac, Christophe Paris, Josette Métayer, Richard Sesboüé, Georges Nouvet, and Luc Thiberville, Follow-up of Bronchial Precancerous Lesions and Carcinoma in Situ Using Fluorescence Endoscopy, American Journal Of Respiratory And Critical Care Medicine Vol 164, 2001, p 1688-1693

Distribution and Outcome of Preneoplastic Lesions in Bronchial Epithelium



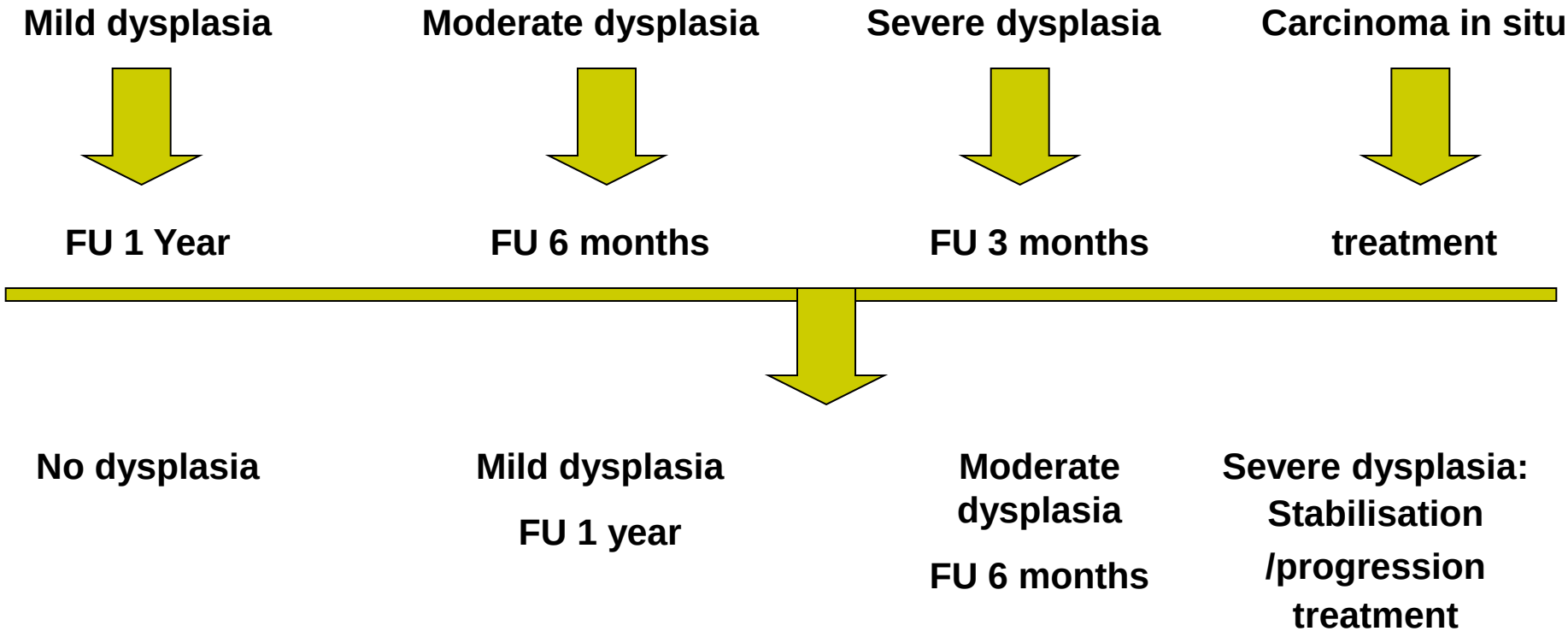
Various risk factors such as:

- smoking history
- past history of cancer
- chronic obstructive pulmonary disease.

1. *Suzana Bota, Jean-Bernard Auliac, Christophe Paris, Josette Métayer, Richard Sesboüé, Georges Nouvet, and Luc Thiberville, Follow-up of Bronchial Precancerous Lesions and Carcinoma in Situ Using Fluorescence Endoscopy, American Journal Of Respiratory And Critical Care Medicine Vol 164, 2001, p 1688-1693*
2. *Breuer R, Pasic A, Smit E, Esther van Vliet, Vonk A Noordegraaf, Elle J. Risse, Pieter E. Postmus, and Thomas G. Sutedja1 The Natural Course of Preneoplastic Lesions in Bronchial Epithelium Clinical Cancer Research Vol. 11, 537–543,2005*
3. *American Cancer Society Guidelines for the Early Detection of Cancer, 2009*
4. *A. McWilliams, B. Lam and T. Sutedja, Early proximal lung cancer diagnosis and treatment, Eur Respir J 2009; 33: 656–665*
5. *Kunst P, With blue light into the depth, Annual Congress of ERS, Vienna 2009,*

Early proximal lung cancer Algorithm – Diagnosis and treatment

Fluorescence brochoscopy (FUB)



Suzana Bota, Jean-Bernard Auliac, Christophe Paris, Josette Métayer, Richard Sesboüé, Georges Nouvet, and Luc Thiberville, Follow-up of Bronchial Precancerous Lesions and Carcinoma in Situ Using Fluorescence Endoscopy, American Journal Of Respiratory And Critical Care Medicine Vol 164, 2001, p 1688-1693

Endoscopy-COPD-lung cancer

a. Detection of precancerous bronchial lesions

b.Palliate innoperable lung cancer

LUNG CANCER

INITIAL DIAGNOSIS

75% INOPERABLE

William Lunn, Obstruction of central airways: evaluation and management", in Michael J. Simoff, Daniel H. Sterman, Armin Ernst, Thoracic Endoscopy – Advances in Interventional Pulmonology, 2007, 22: 323-329

LUNG CANCER

75% CASES

SIGNIFICANT NEED

<u>TREATMENT OPTIONS</u>

TO PALLIATE THIS SYMPTOMS

William Lunn, Obstruction of central airways: evaluation and management", in Michael J. Simoff, Daniel H. Sterman, Armin Ernst, Thoracic Endoscopy – Advances in Interventional Pulmonology, 2007, 22: 323-329

Lung cancer

OBSTRUCTION > 50% OF NORMAL LUMEN

compulsory association

ENDOSCOPY

CHIMIOTHERAPY

RADIOTHERAPY

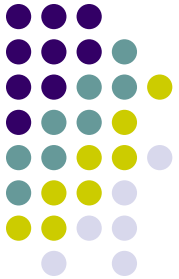
COPD

Exacerbations-Pulmonary infections

Inflammation

Lung carcinogenesis

Carcinogenesis in general



6.CONCLUSIONS

- COPD (or airflow limitation) closely associated with lung cancer, independent of smoking exposure dose and age

- The magnitude of the association is much greater than generally appreciated

40–70% of lung cancer cases have coexisting COPD.

R.P. Young, R.J. Hopkins, T. Christmas, P.N. Black, P. Metcalf, G.D. Gamble, COPD prevalence is increased in lung cancer, independent of age, sex and smoking history, Eur Respir J 2009; 34: 380–386

- The risk of lung cancer among those with COPD may be closer **to six-fold higher**, **much greater** than the estimated two-fold increased risk previously associated with COPD

R.P. Young, R.J. Hopkins, T. Christmas, P.N. Black, P. Metcalf, G.D. Gamble, COPD prevalence is increased in lung cancer, independent of age, sex and smoking history, Eur Respir J 2009; 34: 380–386

- The routine use of spirometry in smokers.
- Identify those with COPD.

Young RP, Hopkins RJ, Gamble GD, et al. A gene based risk score identifies smokers and ex-smokers at high risk of lung cancer. Respirology 2008; 13: Suppl. 2, TP143.

Young RP, Hopkins RJ, Eaton TE. Forced expiratory volume in one second: not just a lung function test but a marker of premature death from all causes. Eur Respir J 2007; 30: 616–622.

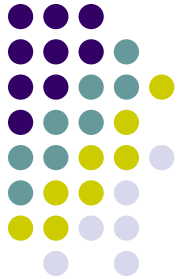
- Identify those with potential clinical benefits in smoking cessation

Taylor KL, Cox LS, Zinke N, et al. Lung cancer screening as a teachable moment for smoking cessation. Lung Cancer 2007; 56:125–134
Bednarek M, Gorecka D, Wielgomas J, et al. Smokers with airway obstruction are more likely to quit smoking. Thorax 2006; 61: 869–873.

- Early diagnostic work-up for lung cancer, targeted bronchoscopy,CT screening

Bechtel JJ, Kelley WA, Coons TA, et al. Lung cancer detection in patients with airflow obstruction identified in a primary care outpatient practice. Chest 2005; 127: 1140–1145.

Future challenges



- Explaining the similarities between COPD and lung cancer, possibly at a genetic and molecular level.

- Design and conduct of clinical trials to improve the outcome of both diseases.

*Thomas L. Petty, Are COPD and Lung Cancer Two Manifestations of the Same Disease**?** Chest 2005;128;1895-1897*

- The chromosome 15q25 locus: an important role in COPD

Pillai SG, Shianna K, Ge D, et al. Genome-wide association study of chronic obstructive pulmonary disease (COPD) in a case control population from Norway. American Thoracic Society, Toronto. Am J Respir Crit Care Med 2008; 177: A776

- A disproportionate number of lung cancer cases - from patients with pre-existing COPD

R.P. Young, R.J. Hopkins, T. Christmas, P.N. Black, P. Metcalf, G.D. Gamble, COPD prevalence is increased in lung cancer, independent of age, sex and smoking history, Eur Respir J 2009; 34: 380–386

- 1 in 16 smokers with ‘‘normal’’ lung function get lung cancer

R.P. Young, R.J. Hopkins, T. Christmas, P.N. Black, P. Metcalf, G.D. Gamble, COPD prevalence is increased in lung cancer, independent of age, sex and smoking history, Eur Respir J 2009; 34: 380–386

- 1 in 4 patients with COPD get lung cancer

R.P. Young, R.J. Hopkins, T. Christmas, P.N. Black, P. Metcalf, G.D. Gamble, COPD prevalence is increased in lung cancer, independent of age, sex and smoking history, Eur Respir J 2009; 34: 380–386

Future challenges

- A new target for novel treatments