

LUNG FUNCTION IN ASTHMA : RELATION TO CLINICS, CHALLENGE TESTS AND IMMUNOTHERAPY

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INTRODUCTION

Lung function in asthma must always be related to clinical evolution but also evaluated in relation to provocation tests, therapy and specific immunotherapy. In this review the correlation between clinical symptoms and lung function Peak expiratory flow (PEF), forced expiratory volume (FEV₁) and obstructive and restrictive patterns the effect of skin tests in bronchial obstruction, the correlation between bronchial challenges in the specific allergens or histamine, the clinical outcome of specific immunotherapy related to the initial lung function and the evolution of static and dynamic lung compliance during immunotherapy will be discussed.

All the points reviewed are based in personal results.

CLINICAL CLASSIFICATION OF ASTHMA, PFR AND FEV₁

■ **Background:** In the last few years the consensus on asthma, guidelines and GINA have introduced a classification based on clinical criteria, PFR or FEV₁ values and reversibility. However the relation of clinical classification with the functional data is not well defined.

■ **Purpose:** To correlate the clinical evaluation of asthma with the most usual parameters of larger and smaller airways bronchial obstruction, PFR and FEV₁.
n **Material and methods:** 153 patients have been studied by spirometry on absence of bronchodilator or anti inflammatory therapy in the last few days. Clinically, they were classified following the 2002 revised strategy for asthma management (NIH), 66 as mild intermittent, 61 mild persistent and 26 moderate persistent asthmas.

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■ **Results:** In mild intermittent asthma PFR was decreased in 53 patients (80,3%) and FEV₁ in 51 (77,2%). In mild persistent PFR and FEV₁ were decreased in 59 (96,7%). In medium persistent asthma PFR was decreased in 25 (96,0%) and FEV₁ in 24 (92%). The values of PFR and FEV₁ were statistically different in intermittent and persistent asthma. For PFR square chi X² = 8,91, p<0,01 and for FEV₁ X² = 9,0 p<0,01. In contrast there were no statistically differences between mild and moderate persistent asthmas. For PFR X² = 0,02 p<0,8 and for FEV₁ X² = 0,039, p<0,9 (tables 1, 2, 3, 4).

■ **Discussion:** The occurrence of 77,2% and 80,3% of decreased FEV₁ and PFR values in non dyspnea as reported by the patients. There were also no functional differences between patients in the different groups of

	Number of patients	Decreased EV	Decreased PEF
STEP 1			
Intermittent	66	51 (77,2%)	53 (80,3%)
STEP 2			
Mild Persistent	61	59 (96,7%)	59 (96,7%)
STEP 3			
Moderate Persistent	26	24 (92%)	25 (96%)
STEP 4			
Severe Persistent	0	0	0

Table 1 : Classification of Asthma.

■ Distribution of abnormal functional intermittent asthmas versus mild and moderate persistent

X² = 8,91 P< 0,01 for PEF
X² = 9,00 P< 0,01 for FEV₁

■ Mild persistent versus moderate

X² = 0,12 P< 0,8 for
X² = 0,039 P<0,9 for FEV₁

Table 2 : Statistical analysis.

	Guidelines	Present series
STEP 1		
Intermittent		
FEV ₁ > 80	100%	49%
Predicted		
PEF > 80%	100%	47%
Predicted		
STEP 2		
Mild Persistent		
FEV ₁ > 80%	100%	3,3%
Predicted		
PEF > 80%	100%	3,3%
Predicted		
STEP 3		
Moderate Persistent	100%	92%
FEV ₁ > 60%		
< 80%		
Predicted		
PEF > 60%	100%	96%
< 80%		

Table 3 : Comparison between proposal guidelines and present series.

persistent asthma. Clinical and functional data must be correlated, case by case in order to establish a correct classification of asthmatic patients and improve therapy and the relation between lung function and clinic reevaluate.

CORRELATION BETWEEN PFR, FEV₁, AND VENTILATORY DISFUNCTION IN ASTHMA

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■ **Background:** Peak expiratory flow rate (PFR) and forced expiratory volume in the first second (FEV₁) are currently used in functional evaluation of asthmatic patients but his degree of correlation in obstructive, restrictive and mixed spirometric ventilatory patterns are not well known.

■ **Purpose:** To evaluate if the correlation between PFR and FEV₁ 2 markers of global airways obstruction is comparable in asthmatic patients with obstruction restriction or both.

■ **Material and methods:** 152 asthmatic patients, 69 males, 83 females have been studied by spirometry with a Vitalograph Compact in absence of bronchodilatory or anti-inflammatory therapy. Patients

have been classified in 4 functional patterns according to VC, and FEV₁/CV: Normal: VC greater than 90% of expected value and FEV₁/VC greater than 70%, obstructive:VC greater than 90% and FEV₁/VC greater than 70% restrictive VC, less than 90% and FEV₁/VC greater than 70% and mixed VC less than 90% and FEV₁/VC greater than 70% and mixed VC less than 90% and FEV₁/VC less than 55% presenting a so called functional emphysema.

■ **Results:** According to these criteria 15 patients were normal, 44 restrictive, 15 obstructive and 78 mixed. In all the group the correlation between PFR

and FEV₁ was statically significant (P<001) but the correlation coefficient variable. In functionally normal patients r = + 0,74 in restrictive patients + 0,67 in obstructive + 0,66 in mixed + 0,84 and in the subgroup with functional emphysema + 0,96. For this sub-group the correlation coefficient R allows to define FEV₁ = 91 + 5,6 PFR. n Discussion: The report between the two most usual assays of global bronchial obstruction depends on the balance between restriction, (either by interstitial fibrosis or hyperinflation) and obstruction and is more close when a more marked obstruction coexist with a restrictive pattern (functional emphysema). In practice PFR has the same value that FEV₁ only in more severe cases of ventilatory failure. The dispersion of values and the standard error of regression don't allow to correlate both data in most patients.

STEP 1	
Intermittent	51%
FEV ₁ >80%	
Predicted	
PEF >80%	53%
Predicted	
STEP 2	
Mild persistent	6,7%
FEV ₁ >80%	
Predicted	
PEF >8%	96,7%
Predicted	
STEP 3	
Moderate	8%
Persistent	
FEV ₁ >6%	
Predicted<0%	
PEF>60%<80%	4%

Table 4 : Discordance between guidelines and present series.

EFFECT OF SKIN TESTS IN BRONCHIAL OBSTRUCTION

■ **Background:** The effect of skin tests on bronchial obstruction is generally considered irrelevant but objective data are scarce.

■ **Purpose:** To evaluate the effect of skin tests on bronchial obstruction.

■ **Material and methods:** Spirometry has been done before and 20 min. after allergy skin tests. Skin

prick tests (SPT) have been done in 206 patients -166 allergic to house dust mites and 40 non allergic asthmatic controls. In this group SPT never caused, as confirmed generally in practice, a significant change in FEV₁ or FEV₁/VC. Intradermal skin tests have been done with 0,01 ml of house dust mites extract Bencard) in 17 asthmatic patients 4 non atopic controls and 13 allergic to house dust mites.

■ **Results:** In the 4 non allergic patients no changes in VC, FEV₁ or FEV₁/VC have been observed after intra dermal skin tests. In the allergic patients two different patterns have been observed. In 4 patients where intradermal skin tests to house dust mites were slightly positive no spirometric changes have been found. One out of these four patients presented before tests an initial restrictive pattern with VC at 71% of expected value. The other allergic patients presented changes in FEV₁ and/or FEV₁/VC triggered by intradermal skin tests. All these patients have clear positive skin tests to house dust mites (3+). A variation of FEV₁/VC greater than 10% has been achieved in 6 out of 9 patients the mean decrease of these report being 12,2%, the range 7-21% square chi statistic analysis show (P<0,05) that spirographic decreases were correlated with stronger skin tests.

■ **Discussion:** These results show that skin tests at least intra dermal can trigger bronchial obstructions even without clinical symptoms and great care must be taken in asthmatic patients during most aggressive skin tests.

CORRELATION BETWEEN BRONCHIAL PROVOCATION TESTS WITH ALLERGENS AND HISTAMINE

■ **Background:** Bronchial challenges are currently done in allergic asthma with allergen, histamine or metacholine. Bronchial reactivity to allergens and histamine can probably be variable.

■ **Purpose:** To evaluate if the dose of allergen and histamine triggering a significant bronchial obstruction are always correlated in asthmatic patients.

■ **Material and methods:** A Vitalograph model Compact has been used throughout the study. Allergen challenge has been done with an aqueous solution of house dust mite. Bronchial challenges with placebo (sodium chloride) histamine or allergens have been done in all patients. For the provocations with histamine or allergens the threshold dose, inducing a decrease in FEV₁ greater than 15% has been determined in

all the cases, as well for histamine as for allergens. A second challenge has been done in all patients with a supra-threshold dose of histamine or allergen corresponding to the double of the threshold.

■ **Results:** 30 provocations have been done in 10 patients either with histamine or allergen. 6 were allergic and 4 non allergic. The threshold dose for histamine were between 5 and 25 ug in allergic patients and 250 and 500 ug. In non allergic patients. In allergic patients after histamine threshold challenge mean decrease was for FEV₁ 19,2% and for FEV₁/VC 17,3%. For supra-threshold dose FEV₁ decreases 37,8% and FEV₁/VC 32,8%. After allergen challenge FEV₁ decreases 20,3% and FEV₁/VC 15,8%. With supra threshold doses FEV₁ decreases 28,6% and FEV₁/VC 29,3%. In 4 non allergic patients there was no changes after allergen challenge. A good correlation in constriction induced by histamine or allergen either for threshold or supra threshold doses (p<0.001) was observed but not between the threshold doses of histamine and allergen.

■ **Discussion:** These results confirm that bronchial obstruction can be triggered by allergens and mediators that the sensitivity of FEV₁ and FEV₁/VC for evaluation are roughly comparable after challenge and points to a better sensitivity of a supra threshold dose of allergen or mediators. Allergen and histamine challenges don't give the same information.

CLINICAL OUTCOME OF ASTHMA SPECIFIC IMMUNOTHERAPY AND SPIROMETRIC PATTERNS

■ **Background:** The relationship between spirometry pattern and outcome of specific immunotherapy (SIT) is not well known.

■ **Objectives:** To study the evolution of atopic asthma treated by SIT on the bases of the initial spirometric pattern.

■ **Material and Methods:** 35 asthmatic patients, 17 males and 18 females, 18 to 50 treated with (SIT). Spirometry has been done in absence of any bronchodilator or anti-inflammatory therapy. 16 patients presented an obstructive ventilatory pattern, 11 a restrictive pattern and 8 a mixed obstructive-restrictive pattern. SIT has been done during 12 to 24 months (mean 18). Results have been classified as very good (disappearance of asthma symptoms), good (decrease in the number and severity of asthma crisis) and null (no improvement) SIT was done for HDM in all cases.

■ **Results:** In obstructive group mean VC 2423 before SIT (-38% expected) 3000 after SIT (+21%) FEV₁ 973 (-64%) before, 1824 after (+108%), FEV₁/CV HO before, 71 after. In the restrictive group VC 2413 before (-39%) 2523 after (+45%) FEV₁/CV81 (+16%) before and 79 (-1%) after. In the mixed group VC 2496 before (-35%) 2693 after (+3%) FEV₁ 1643 before (-36%) 1847 after (+12%) FEV₁ 65 before (-7%) 69 after (+6%). Clinically in the obstructive group 1 very good, 13 good and 2 failures. In the same group FEV₁ was normalized in 4 cases, improved in 1 unchanged in 1. In the restrictive group very good in 1 case, improved in 10, and 0 failures. FEV₁ was normal in 2 cases, 1 improved in 3, unchanged in 6. In the mixed group, clinically 2 very good results, 5 good, 0 failures. FEV₁ was improved in 6 cases and without change in 2.

■ **Discussion:** Clinical results of SIT at mean term seems not to be correlated to initial spirographic evaluation, very good and good results are equally distributed between 3 spirographic patterns. FEV₁ improvement seems to be better correlated to clinical outcome. Spirography could add useful data to SIT outcome.

EVOLUTION OF STATIC AND DYNAMIC LUNG COMPLIANCE IN ASTHMATIC PATIENTS DURING IMMUNOTHERAPY

■ **Background:** SIT can act on bronchial inflammation and in lung compliance.

■ **Objective:** To evaluate the evolution of ventilatory mechanics during in asthma.

■ **Material and methods:** 35 asthmatic patients. 17 males, 18 females aged 18 to 50 have been studied. Spirometry in all patients. Static and dynamic compliances evaluated before and after SIT in absence of bronchodilators or antiinflammatory drugs the last 3 days SIT has been done during 1 to 2 years (mean 18 months) by systemic route with HDM extracts.

■ **Results:** Patients have been divided in 3 groups according to spirometry 16 with obstructive, 11 pure restrictive and 8 combined. In the obstructive group (16 patients) before SIT mean static compliance was 0,064 v.r.l./cm OH2 (-47% of expected value) and mean dynamic compliance 0,43 v.r.l./m OH2 (59%). After SIT static compliance was 0,150 v.r.l./cm OH2 (+134%)

,01) and dynamic compliance 0,136 v.r.l./cm OH2 (+216%) (p>0,01). In the restrictive group before SIT mean static compliance 0,067 v.r.l./cm OH2 (-45%) and dynamic compliance 0,070 v.r.l./c OH2 (-52%). After SIT mean static compliance 0,090 v.r.l./cm OH2 (+34%) and dynamic compliance 0,073 v.r.l./cm OH2 (+12%). In combined mean static compliance was 0,113 v.r.l./cm OH2 (-6%) and dynamic compliance 0,09 v.r.l./cm OH2 (-26%). After SIT static compliance was 0,097 v.r.l./cm OH2 (-14%) and dynamic compliance 0,089 v.r.l./cm OH2.

■ **Discussion:** The improvement of lung compliance static as well as dynamic was significant in obstructive patients. In the other patients there was no significant changes in lung compliances either static or dynamic. These results suggest that SIT could act in bronchial elastic properties. The fibrosis or remodelling were already established, this effect is no longer observed. SIT must be started before chronic inflammation.

■ **Conclusions:** Evaluation of lung function in asthma must be done in a dynamic way considering the clinical and functional aspects case by case. Lung function can be disturbed by provocation tests even by intradermal skin tests. The evaluation of lung function before immunotherapy could be an useful method to choose the patients where the probability of improvement if greater.

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