# REVIEW OF LITERATURE

# REVIEW OF LITERATURE

## 1. Physiologic basis of pulmonary function testing:

Today, pulmonary function tests occupy a central role in investigations of the respiratory system. They provide an objective and quantifiable evaluation of lung function. But their shortcomings cannot be overlooked, for most of the respiratory diseases are defined in terms of structure (emphysema) or symptoms (asthma) Their indications may be classified into those for diagnostic and screening purposes and those for pre-operative evaluation.

**(a) Diagnostic:** They are used to evaluate and monitor diseases that affect heart and lung function, to monitor the effects of environmental, occupational, and drug exposures, to assess risks of surgery, and to assist in evaluations performed before employment or for insurance purposes Pulmonary function tests can identify abnormalities of lung function that might otherwise be overlooked and can exclude the possibility of some respiratory disorders such as chronic obstructive pulmonary disease (Crapo, 1994) Physicians cannot identify obstructive or restrictive patterns from history taking alone [Hepper N G et al, 1969; Russell N J et al, 1986, Gentry S E et al, 1983].

**(b) Screening and monitoring:** There is little evidence to support a policy of screening the general population with spirometry (ATS, 1983). Some subgroups are at higher risk of lung disease, screening and monitoring are more appropriate for them (ATS, 1983) (Hankinson, 1986) Serial measurements of lung function (monitoring) may be useful in tracking pulmonary expressions of diseases. Monitoring lung function allows the physician to identify and quantify involvement in such diseases For example, serial measurement of Vital Capacity (VC) may help a physician quantify a patient's response to therapeutic agents in congestive heart failure In the Framingham Study, decreases in VC were better predictors of heart failure than symptoms, examinations or radiographic findings (Kannel WB et al, 1974). Improvements in vital capacity may also indicate recovery from congestive heart failure (Light R W, 1983)

**Interpretation of lung function tests:** Test quality remains the most important concern in lung function testing. Variability (noise) is greater in pulmonary function tests than in other clinical tests, because of the inconsistency of efforts by patients. (Becklake M R, 1986)

The American Thoracic Society and the European Respiratory Society, and other organizations have published standards designed to minimize the variability in these tests. [ATS, 1987,European Respiratory Society,1993]

The elements that lead to high-quality test results are

- Accurate equipment

- Good test procedures
- An ongoing program of quality control
- Appropriate reference values
- Good algorithms for the interpretation of result

→ Some salient features regarding the mechanics of breathing, patho-physiology of respiratory disease and physiological basis of pulmonary function tests are discussed below:

**(1)** During inspiration, small airways get stretched, partly due to increase in the volume of lungs and partly due to negative pressure in the alveoli Hence, airway resistance is lower during inspiration Conversely, during expiration, smaller lung volume and the positive alveolar pressure compress the airways The diameter of small airway decrease and some might collapse and close completely during forceful expiration.

**(2)** Work of breathing During breathing work is performed by respiratory muscles Work of inspiration can be divided into three fractions, a) that required to expand the lungs against the lung and chest elastic forces, called compliance work or elastic work, b) that required to overcome the viscosity of lung and chest wall structures, called the tissue resistance work; and c) that required to overcome airway resistance during movement of air into the lungs, called airway resistance work (Mead and Milic-Emili, 1964) During expiration, work is done only to overcome viscous resistance. Elastic recoil of lung and thorax provides energy for viscous resistance and additional energy is dissipated as heat.

**(3)** On functional basis, respiratory diseases are mainly of two types, restrictive and obstructive In restrictive lung diseases i e. diseases in which distensibility of lungs may be reduced, e g fibrosis of lungs, the elastic component of the work of breathing is increased, the magnitude of which depends on the degree of expansion of the lungs Hence, the patients with restrictive lung disease tend to take shallow breaths and increase the frequency of breathing in order to achieve satisfactory alveolar ventilation On the other hand, in obstructive lung disease i.e. disease in which airway resistance may be increased, e.g bronchial asthma, the work required to overcome airway resistance is increased, the magnitude of which depends on the velocity of airflow Therefore, patients with obstructive lung disease tend to take slow breaths. Their frequency accordingly is slow They achieve satisfactory alveolar ventilation by increasing the tidal volume

**(4)** Patho-physiology of airway resistance· Airway resistance is increased as in bronchial asthma due to bronchospasm and due to mucosal edema and secretions as in chronic bronchitis It is also increased if any type of swelling obstructs the airways from within, or presses on the airways from outside

The characteristic diagnostic feature of airway resistance is slower expiration, - so $FEV_1$ is reduced. This has many potential consequences. First, since expiration needs more time, respiratory frequency may be reduced However, this cannot be done beyond a certain limit because it impairs alveolar ventilation Second, employing expiratory muscles quickens expiration Nevertheless, this also has limits; therefore, a) it makes the patient tired, and b) increased intrathoracic pressure compresses the airways, and increases the airway resistance further Third, the next inspiration begins before expiration is complete i.e Functional Residual Capacity (FRC) is increased. Since tidal volume remains same, person begins expiration at higher volume, and the elastic recoil of the lungs is stronger than before This assists expiration As disease progresses, the FRC increases further and lungs are stretched more and more, till the limit of tolerance of elastic tissue is reached. This contributes to breakdown of lung elastic tissue in chronic bronchitis leading to emphysema (Burrows et al, 1975)

The main methods of screening lung function status are assessments of ventilatory functions, ventilation/perfusion ratio, diffusion measurement for gas transfer, blood gas analysis functions Among the above function tests the widely used ventilatory function test are spirometery and forced spirometery

**Forced spirometery:** This consists of volume of air inhaled and exhaled, plotted against time during a series of ventilatory maneuvers. The curves obtained permit the determination as to whether subject has a normal pattern of ventilatory reserves or an abnormal pattern characteristic of obstructive, restrictive, or mixed ventilatory abnormalities None of these patterns is specific, although most diseases cause a predictive type of ventilatory defect Spirometery alone cannot make diagnosis of specific disease, but it is sufficiently reproducible to be useful in following the course of many different diseases.

Spirometry is used in the early detection and treatment of respiratory disorders It is an excellent screening test for detection of chronic airflow obstruction, but may also be useful in detecting restrictive disorders as well.

The principal tests included in included in spirometry are

**(A) Forced vital capacity:** Expiratory and inspiratory measurements of the Forced Vital Capacity (FVC) are standard in pulmonary function laboratories Unless otherwise specified, spirometry refers to the forced expiratory maneuver. The FVC maneuver entails a full inspiration to total lung capacity followed by a rapid, forceful, maximal expiration to Residual Volume (RV). The FVC is normally equal to the slow vital capacity (VC), which represents a more relaxed expiration to RV The FVC is displayed in one of two ways expired volume against time or air-flow plotted against lung volume- i e an expiratory 'flow-volume' curve Volumes determined from the volume- time plot of the forced vital capacity include.

**(a) $FEV_1$:**

The volume expired in the 1st second, expressed either as an absolute volume ($FEV_1$), or as a percentage of the forced vital capacity ($FEV_1$/FVC %)

**(b) $FEV_3$:**

The volume expired in 3 seconds, expressed either as an absolute volume ($FEV_3$) or as a percentage of the forced vital capacity ($FEV_3$ / FVC %)

**(c) The forced mid-expirtory flow rate ($FEF_{25-75\%}$):**

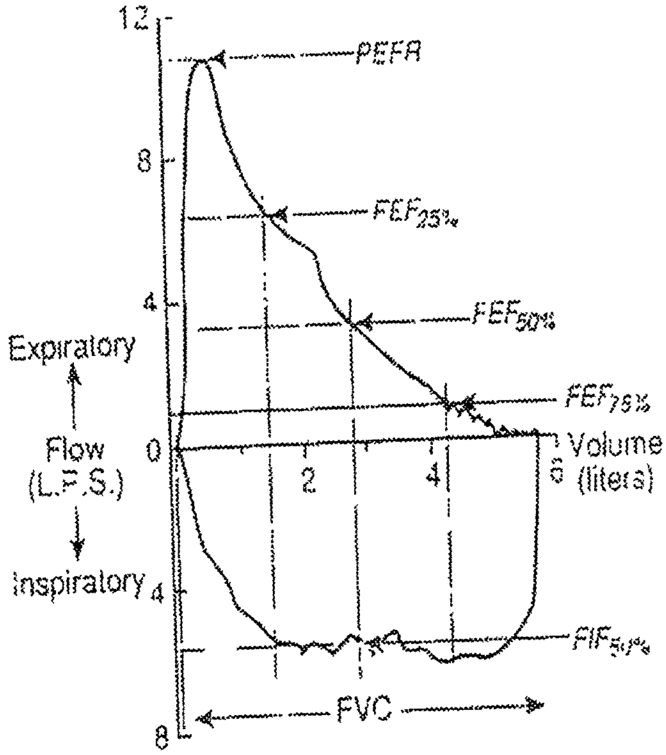
The $FEF_{25-75\%}$ is determined by locating the points on the volume-time curve corresponding to 25 and 75 percent of the FVC and then calculating the slope of a straight line passing through these points The slope of this line represents the average airflow over the midportion of the FVC

**(d) Forced Inspiratory Vital Capacity (FIVC):**

Measurement of the forced inspiratory vital capacity (FIVC) involves full expiration to residual volume, followed by a rapid maximal inspiratory effort

**(B) Maximum voluntary ventilation:** The Maximum Voluntary Ventilation (MVV) depends on the movement of air into and out of the lungs during continued maximal effort throughout a preset interval The MVV is a simple, informative test that provides an overall assessment of effort, co-ordination, and the elastic and the flow-resistive properties of the respiratory system In performing the test, the patient is urged to breathe as hard as possible The total volume that is expired during a 12-s interval, expressed in litres per minute (BTPS), is the maximal voluntary ventilation The difference between the MVV and the resting minute ventilation is the breathing reserve (Fishman et al, 2002)

Flow-volume curve: A flow - volume curve shows the relationship between lung volumes and maximal airflow as lung volume changes during a forced expiration While breathing into a spirometer, the subject makes several tidal breaths and then a maximal inspiratory effort to TLC (Total Lung capacity) Volume is displayed on the horizontal axis and airflow on the vertical axis




Flow–volume curve during forced exhalation shows a rapid ascent to peak flow, which depends on muscular effort rather than mechanical characters of lung. Therefore, this portion of the curve has limited diagnostic use Rest of the curve follows a remarkably reproducible effort-independent envelop as flow diminishes in proportion to volume until RV (Residual Volume) is reached It is altered when mechanical properties of lungs are changed by the effect of disease

Flow-volume curves during forced inhalation are entirely effort-dependent The shape of inspiratory portion is symmetric with flow, increasing to a peak midway through inspiration and then decreasing as inhalation proceeds to TLC Inspiratory part of flow-volume curve is more sensitive to a major central airway obstruction than is the expiratory part of flow-volume curve.

**Normal values:** The American Thoracic Society (ATS) has published a formal recommendation on selection of reference values and interpretative strategies for lung function tests including FVC, $FEV_1$, $FEV_1$ / FVC for adult white and black men and women (American Thoracic Society, 1991). Predicted values can be obtained on the basis of age and height mainly

The ATS suggests that individual laboratories use published reference equations that most closely describe the populations tested in their laboratories It is useful to compare the results observed in 20 to 40 local subjects with those provided by the intended reference equations. These local subjects should be lifetime nonsmokers selected by age, ethnic group, and sex to match the population usually studied in the laboratory

The range of normal for measurements derived from flow-volume curve has been even more difficult to define than those for spirometery This wide range of normal values limit the interpretation of spirometric and flow-volume curve (McCarthy et al, 1975).

For evaluation of respiratory impairment, except for FVC, lung volume shows poor correlation with exercise tolerance. Tests of so called small airway function are too variable to be useful in respiratory impairment evaluation for multiple reasons· it involves a larger learning effect, is more fatiguing and requires better instrumentation than simple spirometery The social security scheme in USA, however, mandates the use of MVV and $FEV_1$ in rating of impairment due to chronic airflow obstruction (Berend and Thurlback, 1982). With interstitial lung disease, the MVV may be normal even when there is a severe impairment of gas exchange

The prediction equations for $FEV_1$ and FVC recommended in 1986 ATS statement on respiratory impairment evaluation are those of Crapo and coworkers (Derenne et al 1978) Black lung benefits program mandates the use of Knudson equation (Petty et.al 1981)

All the predicted equations commonly used by pulmonary function laboratories in United States are derived from studies of Caucasian populations Although studies have repeatedly demonstrated racial ethnic difference in the predicted values for $FEV_1$ and FVC, there is no consensus on what correlation factor should be applied for persons of various racial and ethnic groups. The American Medical Association recommends a correlation factor of 10 % for persons of African or Asian descent (i e multiply Caucasian predicted values by 0 9) and many computerized spirometers automatically correct predicted values when a non-white racial category is selected It is important to know what predicted values the individual laboratory is using and whether any routine adjustment for race is being applied, as well as to indicate this information in the evaluation report

**(2) Pulmonary function testing in adolescent obese:** Though it is generally acknowledged that obesity is the leading cause of disease worldwide, its relation with changes in various lung function parameters, is still unclear Although adolescent obesity is a common problem, few studies have evaluated the pulmonary complications of obesity in this population. Investigators have come to different conclusions on this subject and proposed a number of hypotheses for the same. Hence, data on this subject are limited and conflicting.

To study the pulmonary physiological changes in adult obese, Zerah F et al (1993) studied forty-six healthy subjects. Lung volumes and expiratory flows were determined and significant negative co-relations with BMI were found. Expiratory flows diminished in proportion to lung volumes, and the ratio of forced expiratory volume in 1 second to forced vital capacity was within normal limits.

Similarly, forty-three massively obese but otherwise normal, non- smoking, young adults underwent spirometry in a study carried out by Ray C S et al (1983) They observed two types of changes in respiratory function . changes that occurred in proportion to the degree of obesity, Expiratory Reserve Volume (ERV) and DLco and those that changed only in extreme obesity . vital capacity, total lung capacity and maximum voluntary ventilation

Biring MS et al (1999), studied pulmonary physiologic changes in the morbidly obese (defined as those, with a ratio of weight in kilograms to height in centimeters of greater than 0.9) The patient underwent standard pulmonary function testing in the Cedars - Sinai Hospital on an in-patient or out-patient basis during the period of 1979 to 1997 Forced Vital Capacity (FVC), Forced Expiratory Volume ($FEV_1$), Expiratory Reserve Volume (ERV), Functional Residual Capacity (FRC), Maximum Voluntary Ventilation (MVV) and Forced Expiratory Flow during the mid expiratory phase ($FEF_{25-75\%}$) were significantly reduced. They concluded that extreme obesity is associated with a reduction ERV, FVC, $FEV_1$, FRC, $FEF_{25-75\%}$ and MVV.

A M Li et al (2003) carried out a study on 64 obese children (16 girls and 48 boys) with median age and body mass index (BMI) of 12 years and 30 1 kg/m2 respectively None of the patients had clinical evidence of cardiopulmonary disease. Obstructive ventilatory impairment was detected in three patients, though no negative co-relation was found between the reduction of FRC and BMI.

The effect of obesity on pulmonary function in 13 children, aged 15 years, with 147-300% ideal body weight (IBW) was studied by Inselman et al (1993) Measurements included lung volumes, airflow rates and Maximum Voluntary Ventilation (MVV). When compared with predicted normal values for sex, height, and Body Surface Area (BSA), decreases were observed in Expiratory Reserve Volume (ERV), Forced Expiratory Volume in 1 second ($FEV_1$, 73 +/-5) and Maximum Voluntary Ventilation (MVV). On the other hand, residual Volume (RV) and RV/TLC (Total lung capacity) were elevated Based on this study, they concluded that obese children have altered pulmonary function, which is characterized by reductions in DLco and ventilatory muscle endurance and airway narrowing These alterations may reflect extrinsic mechanical compression on the lung and thorax, and/or intrinsic changes within the lung.

Ho T F et al (1989) evaluated the lung function of 65 Singapore obese children with a mean age of 12 1 years They observed substantial changes in Forced Expiratory Flow Rates, and Maximum Voluntary Ventilation (MVV), with reductions to between 60% and 70% of predicted normal values The results were suggestive of narrowing of small airways, increased respiratory inertance possibly due to excessive accumulation of adipose tissue in the chest wall and abdomen leading to respiratory limitation

Mallory G B Jr et al (1989) studied seventeen adolescents with greater than 159% ideal body weight (IBW) Mallory observed that 18% (3/17) had a restrictive defect and 47% (8/17) showed obstructive changes In a study of nineteen children with moderate obesity,

Bossisio E et al (1984) observed that the pulmonary volumes of children were within the normal range. They proposed that in obesity, the main factor is a decrease of the distensibility of the chest wall, which worsens with age. This change probably does not occur in children and adolescents.

Thirty-nine obese children, (20 girls and 19 boys, aged from 7 to 15 years) whose weight excess for their height ranged from 25 to 105 percent, were investigated by Chaussain M et al (1977) They observed that in these obese children in contrast to obese adults, the vital capacity and residual volume were normal

A study of the pulmonary function changes with exercise in obese children was carried out by Tang RB et al (2001) Forced Expiratory Volume ($FEV_1$) in first second, Forced Vital Capacity (FVC) and Peak Expiratory Flow Rate (PEFR) were studied in 42 obese and 10 normal students, aged 11, in a school in Taipei The above parameters were similar in both the groups Thereby, they concluded that physiologic responses to exercise were not sufficiently different between the obese and non-obese and suggested that we should pay more attention to fostering confidence in obese child exercise.