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EDITORIAL

Compassion fatigue and doctors

The job of a care giver is difficult. In day to day life, a young doctor needs to stay in an artificial environment where he or she needs to respond to crisis constantly and face heart wrenching emotional challenges too frequently while his friends and folks enjoy their time in parties, movies and in many other ways.

Unfortunately, the society and the polity disregard the basic human demands and aspirations of a doctor. Painfully in our country in particular, in many occasions doctors are made to scapegoats of systemic faults and deficiencies. This adds stress to the life of the caregivers and results in development of casual or negative attitude in those who join the discipline to devote as a full time care giver. More unfortunately, nobody consider to look into this issue in a scientific and systematic way to understand why and how our best students often turn apathetic to ailing patients. For example, when doctors go for strikes everyone condemns the act and many smell political remote control in that but following any such unrest, hardly ever we come across the result of a systematic investigation been published in the press. When a doctor behaves bad or odd, everyone points finger at him but people hardly realize that this is likely to be just a symptom of a condition the doctor is suffering from : the compassion fatigue.

The deviation from the expected, the change displaying the lack of human behavior many have may reasons but one very important of them is definitely the **compassion fatigue**.

The Wikipedia defines compassion fatigue as "a condition characterized by a gradual lessening of compassion over time" It is commonly seen in trauma victims and in individuals who care the trauma victims.

For doctors as care givers, compassion fatigue is common. Listening to stories of sufferings and caring them gives a feeling of helplessness and reduces the human desire to help them. It is really taxing to show compassion continuously by any human being. Doctors often use a term "burnout" or "stressed" to express the state. It is found that those who have "enormous feeling and exposing empathy" tend to be more at risk of compassion stress.

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The stressed persons often behaves bad, show lack of concern though he or she performs the duty and appear not sympathetic enough as expected by the other side.

In long run, this secondary state or compassion stress can lead to personality problems or even physical sickness.

There are several ways to fight with and prevent compassion fatigue and rest is one very important remedy. Exercise, good food, social activities etc. are also helpful. The sufferer must learn to identify the state and should try his or her best to get well.

The society should also accept the fact. All blames of a hospital goes to the doctors and everyone act smart to give sermons – be him a journalist or a politician, a teacher or an actor. One must realize that care giving, especially is an adverse situations, as it prevails in our country in most of the circumstances, is extra difficult and stressful. Here, the hospitals are overtaxed with ailing patients – there is deficiency everywhere from administration to availability of even a sweeper in time and many a times the doctor feels him or herself helpless to do the best in the compromised situation when the healthcare cost is beyond the reach of the sufferer. So, it is not unexpected to be fatigued early. Today, more awareness is needed amongst the caregivers and the society at large to accept and respect the compassion fatigue. One should keep in mind that this can take place in our family environment as well if one has to suppress him or herself for a long time and carry on performing the duties. So, we must try to understand the stress of others in our family and the environment. Love, respect, compassion and tolerance can bring happiness.

LATERAL THINKING

What is science, anyway?

"It's supposed to be a secret, but I'll tell you anyway. We doctors do nothing. We only help and encourage the doctor within."

Albert Schweitzer, M.D.

Science is only a method. The method, making use of all the human faculties to understand the working of nature,

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called science, gives mankind greater insight into the working of this enigma called the universe. With better understanding and better technology, naturally newer things come to light in science. Therefore, science is, per force, a constant change. That which does not change does not qualify to be science. With the advent of the magnifying glass and the microscope we could see newer things like germs etc. With electron microscopic magnification, subtler things came to light. Science has gone to the nano and piko levels of understanding but the Giga problems of the world like poverty, illiteracy, ignorance and illness still stare us at the face in the 21st Century. That is a curse, indeed. We have no scope yet to fathom the human mind, at the bottom of which are the emotions of greed, anger, pride, jealousy and ego perpetuating suppression, oppression, denial, and power over the lives of others. The last four decide and maintain poverty all over the world. Even in the so called advanced west, the gap between the poor and the rich is widening by the day. The poor, unfortunately, pay for their poverty with their lives.

You must have known about the Corporate Greed that is eating into the belly of the whole human race. Interestingly, all that is done using the cover of science and technology! People like Isaac Newton did not patent their findings. Patenting for monopoly is at the root of the exorbitant drug prices these days. How did they get the scientific tag? One has to go into the origin and the working of two large commissions that have given scientific dignity to these greedy business corporates-the Abraham Flexner commission of 1905 and the Benedict Fitzgerald commission of 1953 in the USA. By then following the US model became fashionable and "scientific" for the rest of the world. Abraham Flexner, a retired school principal, directly and/or indirectly, made the present pharmaceutical industry based medicine alone as scientific and all the other systems, however, effective they were, as unscientific. It was the Flexner Commission that was responsible for making homeopathy, chiropractic, radio aesthesia, energy medicine, ayurveda, and many other effective healing outcomes declared as unscientific, thus forcing majority of medical schools in the US closed. Only 47 medical colleges working on and using pharmaceutical chemicals and surgical methods remained at the end of 1910. Many good and safe systems like homeopathy and chiropractic died a natural death there. Thanks to British Royal family homeopathy survived in that country. Lately I find a concerted effort to kill homeopathy from all those people who matter. However, the Fitzgerald commission in 1953 unearthed this huge conspiracy but was suppressed as a secret document of fifty years to be in the open now!

A young doctor in London writes a full page column in the Guardian condemning homeopathy. Naturally, he does not have enough experience with modern medical hazards to hapless patients and so he documents his theoretical arguments against homeopathy. In the US the newly born American Medical Association fought against homeopathy and destroyed it initially. One of the prominent members of the AMA, Dr. J.N. McCormack, AMA, 1903 said that "we must admit that we have never fought the homeopath on matters of principle. We fought them because they came into our community and got the business." Now one can realize how homeopathy became pseudo science to begin with. Rest is history. The story is still murkier in that arena. The American Homeopathy Association started about 40 years before the American Medical Association. Homeopathy association was started by some of the leading lights of mainline American medicine who were fed and shocked by the results of their medical therapeutics like blood letting and many other procedures that prematurely sent patients to meet their makers in heaven with added agony. Even the first American President, George Washington, was not spared. They let all his blood out for his Typhoid fever until he died of exsanguinations!

May be Samuel Heinemann started homeopathy as a Placebo science. He was a regular MD himself who got disillusioned after losing his young son to a simple septicaemia. Curiously, an elaborate study published in 2011 in four leading universities of Oxford, Cambridge, Hamburg and Munich did show modern medical therapeutics also to be predominantly a Placebo effect! To date no body seems to say that modern medicine is unscientific. Even the higher ups in medicine are now expressing their concern about the evidence base of modern medicine, their bench mark, the Randomised Controlled Trials, which seems to be built on loose sand foundation. Sir Michael Rawlins, the Chief of NICE (National Institute of Clinical Excellence) did say in his recent Harveian Oration at the London Royal College that the RCTs, the bench mark of scientific excellence in medicine, have been put on an undeservedly high pedestal! Who listens, but? This kind of occasional signals are lost in the cacophony of daily information overload in modern medicine most of which is pure "noise" in the scientific sense of the term.

The founding fathers of the American Constitution knew that this kind of monopoly will be bad for society. One of them, Benjamin Rush, MD., a signer of the Declaration of Independence and personal physician to George Washington wrote thus:

"Unless we put medical freedom into the Constitution, the time will come when medicine will organize into an undercover dictatorship to restrict the art of healing to one class of men and deny equal privileges to others; the Constitution of the Republic should make a special privilege for medical freedoms as well as religious freedoms."

It was, I think, Lord Churchill who once said that there are three questions in any saying. Who said it? How did he say that? And last, what did he say? Of the three, Churchill opined that the last question is the least important and does not warrant an answer. If a great man says something, that too with big authority behind him, it is usually accepted as gospel truth by society. Reading yesterday's national dailies made me very sad. It reported that this year's Nobel Laureate, an Indian born US scientist, is reported to have said in a lecture in Chennai that homeopathy has no science base at all. News papers are notorious for quoting people out of context as their sales go up if they give "man eating dog" news. I would still think that the great man did not condemn homeopathy in those terms. If I interpret Winston Churchill about this Nobel Laureate's opinion, as reported by the news papers, the last part need not be taken seriously by a serious student of human healing. In fact, homeopathy is a very important part of the healing armamentarium. There is enough and more scientific research base from very authentic scientists and institutions to back Homeopathy as a good holistic science.

Late Professor Rustum Roy, the man who invented the "Sol-Gel" technique, to extract nano particles way back in 1954 which is being used even today (paper has been cited 68,000 times to date!) was the leader in this field. His work on the structure of water and the energy signature of water gave birth to the new science of homeopathy, the system he swore by. He was nominated 21 times for Nobel. He had all the awards in the world a scientist could get and fellowship of all country's Science Academies. He was the Evan Pugh Professor of Material Sciences at Penn. State till his last breath last year. For his innovative and ground breaking work in the healing sciences, Prof Roy was made Professor of Medicine at the Arizona State University. Many of his colleagues in other parts of the world had joined him in his work. Details could be got from authentic scientific literature. This is not the place to give details. Recently one of the IITs in India did show that homeopathic pills had effective nano particles in them! A founding member of the IOM, an audit body of medicine started by the American Academy of science, Professor Roy got his pet definition of health and healing accepted by IOM during (his last) the meeting of IOM in February 2010, as Whole Person Healing (WPH), the future definition of healing. Reductionism has NO PLACE in healing sciences. Further, vivisectionist research which goes deeper still has to be useless in the long run. Even human genomics has run into slippery slopes with the discovery of human metagenome showing trillions of germ genes incorporated into the 25,000 human genes! Less said about reductionism the better. The future scientific medicine will have to be holistic, homeopathy as a part of it, taking the useful methods from many other systems Ayurveda and modern medicine. Most of us, including scientists who talk about healing methods, would do well to first read The New Biology, so beautifully explained by Nobel Laureate Albert-Szent Gyorgi in his classic, Sub Molecular Biology!

Modern medical science uses statistics to survive-it is not pure science but, statistical science. Modern medicine uses the wrong mathematical base of Euclidean geometry in a dynamic holistic system where only Mandelbrot's Fractal Geometry works. In fact, another American Nobel Laureate Hungarian born scientist, John von Neumann, defined science as "making models, mostly mathematical constructs, which, with verbal jargon, are supposed to work." Modern medicine's mathematical base is faulty; naturally, the building built on that should be very shaky and dangerous. Recent audits show that the medical establishment, built on this kind of science, is proving to be the leading cause of human mortality and morbidity in the US where records are kept meticulously. Let us develop a humble respect for the true science, which is nothing but a method to unravel the mysteries of nature who keeps her secrets very close to her bosom.

"It is not... That some people do not know what to do with truth when it is offered to them, but the tragic fate is to reach, after patient search, a condition of mind-blindness, in which the truth is not recognized, though it stares you in the face."

Sir William Osler, 1849-1919

ARTICLES

Role of Small Airways in Asthma

Definition and description :

Small airways are usually defined as airways <2 mm in internal diameter; they are membranous and without cartilage. The total volume and the surface area of the small airways are much greater than those of the large airways due to extensive branching pattern of the tracheobronchial tree. The small airways are considered traditionally to be pathways of little resistance, contributing less than 10% of the total airflow resistance in the lung. Accordingly, extensive damage of small airways may occur before the appearance of any symptoms or the results of any of the conventional lung function tests become abnormal. For that reason, in the 1970s the small airways were described as the "quiet zone" of the lung[1].

Importance :

Small Airways in Patients With Asthma Differ From Those in Healthy Control Subjects :

Small airways are thickened in asthma by chronic inflammation in the epithelium, submucosa and muscle area. The outer wall is also more thickened, with higher numbers of lymphocytes, eosinophils, and neutrophils, accompanied by increased levels of IL-4, IL-5, and eotaxin.[1,2]

Patients with fatal asthma have more thickened small airways and higher numbers of eosinophils than those with nonfatal asthma. Patients with a short duration of fatal asthma have more goblet cells and neutrophils than those with a long duration. Patients with severe asthma have more neutrophils in lung parenchyma than patients with moderate asthma, and subjects with nocturnal asthma, as compared with non-nocturnal asthma and had more CD4 lymphocytes and eosinophils, particularly at night. Finally, more severe asthma is associated with more severe air trapping (as measured with quantitative CT scanning), indicating small airway disease.[2,3]

The Outer and Inner Walls are different in Small Airways

There are indications that the outer wall is more inflamed than the inner wall, and that peribronchiolar regions are also involved in the inflammatory process. The latter may contribute to an uncoupling of the small airways and the surrounding lung parenchyma and thus increase collapsibility of small airways.[4]

Small Airways Changing Over Time, Spontaneously or After Pharmacologic Intervention

Subjects with nocturnal asthma show significant increases of eosinophils at night in the alveoli collected by transbronchial biopsies, together with CD4 lymphocytes. Flunisolide reduces inflammation in the small airways together with smooth muscle actin in asthma[3].

Small Airway Changes Correlate with Lung Function

One study in nocturnal asthma demonstrated that higher numbers of eosinophils in the alveoli correlate with increased airway obstruction at night. Also, flunisolide-induced reduction in smooth muscle area in the small airway walls correlates with improved mid-expiratory flow rates. Together, these studies suggest that, at least in more severe asthma, the underlying inflammatory process is also present in the small airways. It may even be more intense and involve the complete airway wall and peribronchiolar region. Small airway disease appears also to be present in milder asthma, because several studies showed a higher degree of air trapping on HRCT scan even in mild disease. Definitive conclusions are hard to draw because asthma is a heterogeneous disease and different asthma populations have been investigated, the number of studies is small, and different techniques have been applied to characterize aspects of inflammation and remodelling.[2,3]

Assessment :

The necessity of assessment of small airway function in patients with asthma has not been fully elucidated. In general, when regular first-choice treatment, which currently is large-sized particle ICS, is insufficient in achieving optimal control of disease, investigation of involvement of small airways is indicated.

RV/TLC via body plethysmography and FEF 25%-75% via spirometry are easily accessible and are moderately sensitive to detect small airway involvement in asthma and COPD

The forced expiratory flow at 25-75 % of FVC is the spirometric value most commonly used to asses small airway obstruction, although the literature supporting its validity is not conclusive and conflicting data have been

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presented. It is widely recognized that forced expiratory volume in 1 s (FEV1) does not provide comprehensive evaluation of the whole bronchial tree. In particular, it does not properly reflect small airway abnormalities specifically, but does reflect the cross-sectional area of the lung. Lung volume measures, including forced vital capacity (FVC), residual volume (RV), total lung capacity and functional residual capacity, which have been used to characterize air trapping and, hence, small airway function, may provide more reliable information. Among them, RV has shown a closer relationship with changes in peripheral resistance, indicating that it could correlate with small airway functions.[2,5]

The regional heterogeneity of airflow resistance is best quantified by multiple nitrogen breath washouts (MBW). Nitrogen washout can distinguish between ventilation inhomogeneity originating in the peripheral conducting airways vs. the more proximal conducting airways : analysis of the wash-out curve generated in the single-breath or multiple-breath tests can actually provide information regarding distal lung abnormalities.

Exhaled nitric oxide (eNO) is the most widely used marker in exhaled breath. Alveolar nitric oxide, derived by measurements of eNO at multiple expiratory flows (MEFe-NO), has largely been investigated as a potential hallmark of distal lung inflammation. Recent studies suggest that MEFeNO measurements are reproducible, free of diurnal variation and can be applied in both asthma and COPD.[5]

High-resolution CT (HRCT) allows direct assessment of large and medium airways (diameter.2–2.5 mm), but also indirect assessment of small airways. HRCT can only estimate wall thickness of bronchi that are >2 mm in diameter. Although this does not allow direct assessment of the signs of small airway abnormalities, such as bronchial wall thickening, areas of mosaic lung attenuation (on inspiratory CT) and air trapping (on expiratory CT) have been studied as markers of small airways disease in both asthma and COPD.[6]

Magnetic resonance imaging following inhalation of hyperpolarized helium and xenon, which are inert, non-toxic, inhaled contrast agents that can be detected by MRI to provide a high-resolution image of ventilated lung air spaces. It has gained increasing interest as this could provide further insight into small airway involvement in asthma and COPD. Indeed, these gas-enhanced techniques allow higher resolution, and they could detect and quantify ventilation and perfusion heterogeneity, which is mainly because of regional and dynamic patterns of airway closure but also because of distal lung abnormalities without radiation exposure.[1,2] ^{129}Xe with recent advances in polarizer technology have improved the quality of images using and ^{129} Xe can moreover be used to evaluate gas exchange from the air spaces into the tissue/blood, which cannot be achieved with ^{3}He.[5,7,8]

MRI with ^{3}He as the contrast agent used in one of the study. In this study ^{3}He MRI assessments were made before and after respiratory challenge, and the results were provided an excellent appraisal of regional lung ventilation with good discriminatory power between healthy and asthmatic individuals.[4] However, this technique requires further validation in patients with severe asthma because large areas of severe ventilation defects impair correct processing of the imaging data.[7,8]

Therapeutics target :

Asthma has been recognised as an inflammatory disease affecting the whole respiratory system from central airways to lung parenchyma. By using sophisticated techniques of endobronchial catheterization it has been documented that the distal airways, is not a 'quiet zone' but actively contributes to enhanced airway hyper-responsiveness and airflow obstruction in asthmatic patients. [9] But most of the inhaled drugs used can only reach till large and medium airways >2 mm. Also in a subset of patients using non extra fine inhaled drugs, which cannot reach small airways, even with adequate doses of ICS or ICS/LABA combinations there is no adequate control of the disease. In this context whether specifically targeting small airways <2mm can lead to further clinical benefit is still an open question. Interestingly, in asthmatic patients, the dose of non-extrafine BDP required to achieve an improvement in lung function is 2.5 times higher than the dose of HFA extrafine formulation required to produce the same increase in FEV1.[9,10]

In this context, interest has been raised by hydrofluoroalkane (HFA) pressurized metered-dose inhalers, which can deliver compounds with a mass median aerodynamic diameter that is significantly smaller than other available devices. Thus, these data lead to the speculation that targeting the distal lung in asthmatic patients is a relevant issue, because comparable clinical effects can be obtained with a lower amount of delivered compound and with fewer unwanted effects. Also there was no increase in systemic side effects due to extrafine formulations with ICS or ICS LABA combination.[9, 10] Treatment with an extra fine ICS/LABA combination resulted in a reduced

suppression of the hypothalamic–pituitary–adrenal axis, as indicated by a significant increase in cortisol levels in those patients treated with extrafine combination compared with those treated with equipotent dose of non-extra fine BDP plus LABA.[11,12]

Future directions : These evidences of small airways although a major seat of airway obstruction and inflammation in asthmatics still continues to be less accessible for studies and pharmacotherapy. This provides us with a rationale for further research to target this part of the lung for better disease control and a more targeted approach.

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ALLERGY TEST – USE, MISUSE AND INTERPRETATION

The term **"allergy"** (allos-altered, ergos-action) was coined by Von Pirquet in 1906 to denote the phenomenon of sensitization of an individual to a foreign substance in a way that produces an accelerated or altered response on a second or subsequent exposure to the same substance[1,2]. The reaction is manifested within seconds or minutes after allergen exposure and is thus known as immediate type of hypersensitivity (HS). The mechanisms underlying allergic reactions are multiple and involve a number of regulatory cells and mediators. Presently "allergy" is defined as a hypersensitivity reaction initiated by specific immunologic mechanisms, such as production of IgE class of antibodies by B cells in genetically predisposed individuals on encountering some foreign substances[3]. Hypersensitivity diseases affect various systems of human body, including skin gastrointestinal tract and/or respiratory system. The treatment of allergic diseases is based on allergen avoidance, pharmacotherapy, allergen immunotherapy, and patient education[4].

Historical Prospective of Allergy test

First described by Dr. Charles Blackley in 1867, skin tests have evolved as reliable, cost effective techniques for the diagnosis of IgE mediated diseases. Although Blackley first documented the first potential of allergic skin testing by placement of an allergen on abraded skin, the introduction of skin test for tuberculosis by Von Pirquet became the chief method for quick allergy testing[5,6]. The first of these tests was the scratch test made by rubbing the allergen to a small, blood free scratched area of forearm and introduced by Schloss for diagnosis of food allergy in children[6].

Allergic diseases of respiratory system, such as bronchial asthma and allergic rhinitis, are increasingly becoming global health problems[7,8]. The increase in prevalence of these diseases, in Africa, Latin America and parts of Asia including India, indicates that they are no longer confined to developed countries. The prevalence differences in different parts of the world are rapidly becoming lesser and lesser with time. In Delhi, India the prevalence of bronchial asthma has been reported to be a 8-10% in children and 11% in adult population[9,10]. The prevalence of allergic rhinitis has been found to be 11.69% in adults.

There is considerable interest in the medical community and the general public regarding the diagnosis and

management of allergic disease. In vivo tests are viewed as the most relevant indicators of IgE antibody as they involve direct observation of a biological response in the subject. It is the primary method used by allergists to detect specific IgE antibody, because of its sensitivity, specificity, speed, cost effectiveness, and ease of performance.

Mechanism

Immediate type I HS reactions typically occur in people with atopy who had been sensitized to a certain allergen. During the sensitization phase, the allergen enters the body, usually through the respiratory or gastrointestinal tract, and induces production of specific IgE by activated B lymphocytes.

In respiratory allergy, during sensitization to allergen, priming of allergen specific (CD4+) T helper 2 (TH2) cells results in the production of TH2 cytokines (such as interleukin-4 (IL-4) and IL-13, which are responsible for class switching to the immunoglobulin heavy chain, allowing IgE production by B cells. These IgE molecules go in circulation and bind in large numbers to the target tissue (respiratory system) through high-affinity receptor for IgE (FcåRI), which is expressed at the surface of these cells. Re-exposure to the same allergens, results in cross linking of the IgE–FcåRI complexes by allergen, degranulation of mast cells and basophils, and release of vaso active amines (mainly histamine), lipid mediators (prostaglandins and cysteinyl leukotrienes), chemokines and other cytokines. All these mediators characterize the immediate phase of the allergic reaction. IgE also binds FcåRI at the surface of dendritic cells (DCs) and monocytes, as well as the low-affinity receptor for IgE, FcåRII (also known as CD23), at the surface of B cells. This process increases the uptake of allergen by the antigen presenting cells (APCs) and the subsequent presentation of allergen-derived peptides to specific CD4+ T cells, which results in the generation of late phase of the allergic reaction[11].

USE

The goal of allergy testing is to identify antigens to which patients are symptomatically reactive and to quantify the sensitivity if immunotherapy is planned. The purpose of an allergy test should be to help confirm a suspected allergy, not to look for an allergy in a person or child that doesn't show any symptoms. Allergy tests are simply one weapon used to find out if a suspected allergy exists. They should never be used as standalone evidence that a child has an allergy.

A positive test indicates sensitivity to the test substance, that the substance does cause a reaction of the immune system. But an allergy is a much stronger reaction and neither skin prick tests nor blood tests can reveal if a person has an allergy.

Indications:

- To help confirm a suspected allergy after observing possible symptoms of

1. Asthma
2. Allergic rhinitis
3. Atopic dermatitis
4. Allergic rhinoconjuctivitis
5. urticaria
6. Suspected food allergy or
7. Severe reaction to an insect sting

- To help determine if allergies suspected to have been caused by a vaccine were actually due to that vaccine.
- For providing justification for recommendation of specific avoidance measure in home and work place.
- For instituting immunotherapy, or anti allergic medicines.

Misuse:

- As general screens to look for allergies in symptom-free children.
- To test for allergens in patients of chronic obstructive pulmonary disease who are misdiagnosed as allergic bronchial asthma.
- Misdiagnosed food allergies appear to be on the rise, and countless families are needlessly avoiding certain foods and spending hundreds of dollars on costly non allergenic supplements. In extreme cases, misdiagnosed allergies have put children at risk for malnutrition. Also avoiding food in the mistaken fear of allergy may be making the overall problem worse — by making children more sensitive to certain foods when they finally do eat them.

TYPES OF ALLERGY TEST[12,13]

In-Vivo allergy testing

1. Skin Tests

- o Skin prick tests (SPT)
- o Intra-dermal skin testing
- o Skin patch and photo patch tests
- o Skin end point titration (SET)
- o Skin scratch testing

2. Others

o Provocation and challenge testing (Bronchial and Nasal challenge, Double blind placebo controlled food challenge)

o Prausnitz-Kustner (P K Testing)

In-vitro testing

- Antigen - Specific IgE estimation in serum RAST, ELISA

- **Other tests-**

- Leukocyte histamine release test
- Mediator release test
- Allergy cytokines assay
- Mast cell tryptase
- Blocking antibodies food immune complex assay

Interpretation of skin tests – Skin Prick test (SPT) and Intradermal test

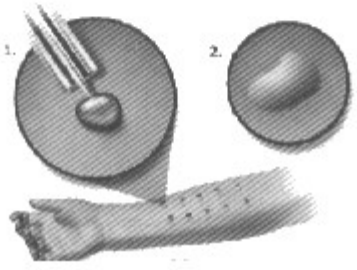
Positive and negative control-

A positive control test is used to determine if the patient reacts to histamine. If the patient does not immediately react to histamine, the results of allergy skin tests can be difficult to interpret. A negative control test involves applying a saline solution that does not include any allergens. Patients who react to this solution may have skin that is too sensitive to allow correct interpretation of allergy skin tests.

(A) Skin Prick Tests :

SPT is considered most convenient and least expensive test for allergy nowdays. SPT has been shown to be highly reproducible when carried out by trained individuals. This test is dependent upon the skill of the individual tester, the device, the potency and stability of the allergen extracts, the depth of the needle puncture and force, and the duration and angle of the application device. This can result in variability in results of tests done by different technicians.

Procedure -



SPT is usually performed on the upper back or more commonly on volar surface of the forearm. A sharp instrument (hypodermic needle, solid bore needle, blood lancet) is pushed downward thorough a drop of extract into the skin at a $45^0 - 60^0$ degree angle to the skin. The skin is then gently lifted, creating a small break in the epidermis through which the suspected allergen should penetrate. To ensure proper interpretation, positive (Histamine) and Negative (Saline) control should be performed at the same time. Skin prick testing is performed with at least 5 cm distance between adjacent sites. Antigens are tested in 1:10 or 1:20 w/v dilution.

Reading of result -

Grading for SPT[12]	
0 mm	Negative
<3 mm than control	1 +
3 – 5 mm than control	2 +
5 – 7 mm than control	3 +
7 – 9 mm than control	4 +

Results should be read at the peak of the reaction, which usually is 15 to 20 minutes after application.

Both erythema and wheal diameter should be measured and recorded using a millimeter ruler. A skin test wheal response of at least 3 mm greater than a saline control is considered positive and indicates presence of allergen specific IgE antibody. The larger the test reaction, the more likely it is to be clinically significant. Test results need to be interpreted in the context of the positive and negative controls.

Percutaneous skin tests are more specific but less sensitive than intradermal tests. Percutaneous tests appear to be safe and can easily be completed even on infants.

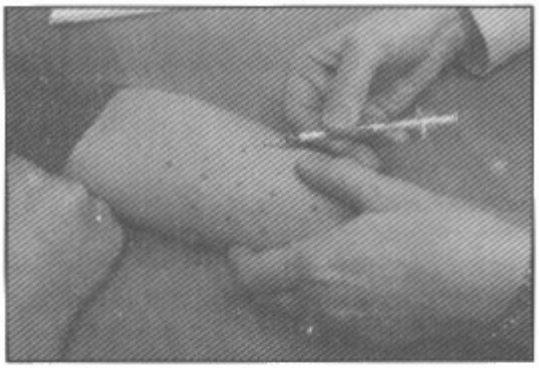
Common errors in prick testing include too close prick testing sites (< 2 cm), induction of bleeding which can induce a false positive reaction, insufficient penetration of skin by puncture instrument causing false negative results and spreading of allergen solutions after application causing mixing of test results.

(B) Intradermal Tests :

Intradermal tests are generally used when percutaneous tests are negative despite an adequate history of exposure and symptoms. They permit identification of a large number of clinically reactive patients, especially those with lower skin sensitivity, and they provide a

means to confirm a negative diagnosis for potentially important allergens.

Procedure -



Intradermal test is more difficult to perform and cause more discomfort. This test is performed on the forearm by the injection of 0.02 ml of extract with a 1 ml disposable syringe and 27-gauge hypodermic needle to raise a wheal of 3 to 4 mm and 3 cm distance between two tests. Antigens are injected in 1:500 w/v dilution.

Reading of results -

Reading is taken 15 minutes after the intradermal injections with a millimeter scale. The measurement of

Grading for intradermal tests	
<6 mm	Negative (control |C|)
2°C	1 +
3°C	2 +
4°C	3+, with 1-2 pseudopodia
>4°C	4+, >2 pseudopodia

the longest diameter is considered for the reading. If a permanent record is necessary, the wheal can be marked with a pen and tape transferred to the paper document.

Criteria for a positive intradermal skin test response is a wheal of 6 mm or more with definite erythema. Any reaction greater than the negative control may indicate the presence of specific IgE antibody. Common errors during the intradermal tests are too close injection sites, splash reaction when air is injected, large volume greater than 0.05 ml is injected when a false positive reaction can occur and when injection is given subcutaneously instead of intradermal a false negative reaction can occur. Histamine (equivalent to 0.01mg/ml of histamine base) is used as a positive control to assess skin reactivity and Saline is used as a negative control.

Precautions for skin testing

Skin testing should always be performed with a physician on site

1. Emergency medications should be at hand
2. Need to be careful with patients with current allergy symptoms
3. Perform tests on a normal skin
4. Assess for dermatographism
5. Determine and record of the medications taken by the patient and the time of the last dose
6. Record the reactions at the proper time.

Advantages of skin tests

- Painless.
- Rapid test with immediate results.
- Easy for any physician to perform in his chamber or by a nurse, trained in the technique of this test and the interpretation of results.
- Most cost effective test for specific IgE.
- High degree of sensitivity towards potentially life threatening allergens like stinging insects, penicillin and macromolecular agents.
- True representation of the allergic reaction at the affected site.
- Visual illustration by positive result can reinforce the need for allergen avoidance measures and removing unnecessary fears for other allergens.
- Informative to the patients and relatives.
- Patient's compliance is high.

Factors affecting the test results

❑ Decreased reactivity in patients of

➢ Eczema

➢ Diabetes

➢ Neuropathies

➢ Cancer and

➢ Anaphylaxis within last one week.

❑ Drugs and medications

➢ H1 histamine antagonist - Inhibits the wheal and flare reaction for a duration depending upon half life of the drug. Varies from 3 to 10 days for cetrizine, levocetrizine, loratidine, Terfenadine, Fexofenedine, Rupatidine etc. and 60 days for astemizole. In practice, 72 hours off anti

histamine is adequate when positive histamine control is used.

➢ Corticosteroids - Less than 1 week in therapeutic doses does not affect. Long term steroid affects the skin mast cells and modifies skin texture so that interpretation is difficult. Inhaled steroids do not modify the results. Less than 15 mg should not be discontinued. Topical corticosteroids more than 1 week reduces both immediate and Late phase reaction.

➢ Other drugs affecting wheal and flare

- Phenothiazines
- Ranitidine
- Anti depressants, (imipramine)
- Clonidine
- Immunotherapy
- Chronic heamo-dialysis

❑ **Age** - Infants (after 3 months) react with large erythrematous flare. skin test wheal size increases from infancy to adulthood and then decline after age of 50 years. Histamine is parallel to allergen.

❑ **Sex** - women have weakest histamine wheal during the first day of menstrual cycle.

❑ **Race** - bigger wheal in blacks.

❑ **Circadian rhythm** - reactivity peaks in late evening and decreases in morning.

❑ **Seasonal variations** – reactivity increases after the pollen season and then declines till next reactivity.

❑ **Allergen extracts** - quality, source and storage of allergen extracts.

❑ **Area of body** –

➢ mid and lower back more reactive than fore arm.

➢ antecubital fossa is most reactive and wrist is least reactive.

➢ ulner side of arm is more reactive than radial.

Conclusion

Skin tests often are used to diagnose allergies. These tests take about 30 minutes to perform. An allergist interprets the results of the test in conjunction with the patient's history and uses these results to determine the best course of treatment. Treatment may include medications and immunotherapy.

There are two types of skin tests, prick tests and intradermal tests. Prick tests involve placing small drops of common allergens on the skin usually on the forearms and then lightly pricking the skin through the drop with a small needle. Intradermal tests involve injecting a small amount of allergen into the outer layer of skin. When a patient is allergic to a substance, redness, itching and swelling develop at the site of the test within 20 minutes.

Certain medications (e.g. antihistamines, antidepressants) and skin conditions (e.g., eczema) can interfere with allergy skin tests.

In addition to allergy skin tests and allergy blood tests, patients with a suspected food allergy may undergo food allergy tests. Food allergy testing often begins with keeping a food diary, which is a detailed list of all foods, the date and time they were eaten, and any symptoms that occurred. When a single food allergy is suspected, the patient may be advised to eliminate the food from the diet and then, if symptoms are relieved, add the food back to the diet to determine if an allergic reaction occurs. This allergy test is not used in patients with a history of severe allergic reaction (anaphylaxis).

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ADVANCES IN LUNG CANCER TREATMENT – FROM TRADITIONAL CHEMOTHERAPY TO BIOLOGICAL THERAPY

Globally, 12.4% and 17.6% of total cancer deaths is attributed to lung cancer[1]. Lung cancer is by far the leading cause of cancer worldwide both in terms of incidence and mortality[2]. Even today consumption of tobacco products is strongly associated with lung cancer. In fact, 87% of all lung cancers are detected in individuals who are active or former smokers, with an additional 6–7% associated with second hand smoke also referred to as ETS composed of partners of smokers or their offspring or any other nonsmoker exposed to smoke.

Initially considered curable only in its earliest stages, the last two decades have seen tremendous advances in the treatment of lung cancer. The development of a multimodality approach has rendered 15–20% of patients with locally advanced disease curable, and has produced substantial progress even in the most advanced stages of disease.[2] Once approached with the attitude of therapeutic nihilism among physicians, can now be treated with therapies that prolong survival for all stages of the disease[3].

MOLECULAR BIOLOGY OF LUNG CANCER

Decades of research have contributed to our understanding that lung carcinoma is a multistep process involving genetic and epigenetic alterations, through which resulting DNA damage transforms normal lung epithelial cells into lung cancer[4]. In addition, while the tumor initiating cell may have only a handful of mutations, as the tumor cell expands, cells may acquire additional mutations[5]. Two main types of lung cancer –Non small cell lung cancer (NSCLC) (representing 80-85%) and small cell lung cancer (SCLC) (representing 15-20%) are identified based on histologic, clinical and neuroendocrine characteristics. They differ molecularly, with many genetic alterations exhibiting subtype specificity[6]. There are various changes occuring in different classes of epithelial cells or different molecular changes occuring in same target lung epithelial cells, different genes are involved in different pathway and this determines the biological behavior of lung cancer, which can be used as diagnostic and therapeutic targets.

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The key new concept is that with genetic and epigenetic changes that occur during carcinogenesis, the cancer becomes both dependent to the continued presence/function of these changes and also must make other cellular adaptations, including mutations to minimize the "oncogene stress" induced by these changes. While mutated oncogenic proteins themselves are therapeutic targets like EGFR (Epidermal growth factor receptor) mutation, the other cellular adaptations that are present in tumor but not in normal cells also become cancer- specific therapeutic targets. Ultimately these oncogenic changes are translated by using molecular alterations as biomarkers for early detection and risk assessment, targets for prevention, signatures for personalizing prognosis and therapy selection for each patient, and therapeutic targets to selectively kill or inhibit the growth of lung cancer. Till now, three molecular targets have been validated in the treatment of advanced NSCLC: Epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), and Vascular endothelial growth factor(VEGF)[7].

CURRENT ASPECTS ON CHEMOTHERAPY FOR LUNG CANCER

The role of adjuvant and neoadjuvant chemotherapy has been now established with significant improvement in survival rates based on new randomized trials and metaanalysis.. The aim of adjuvant chemotherapy that is post surgery is to eradicate the occult metastasis. The rationale of neoadjuvant chemotherapy is to regress the primary cancer in order to facilitate and simplify subsequent surgery, treat occult micrometastatic disease at the time of presentation and also inhibit the growth of tumor growth factors at the time of surgery. In routine clinical practice it is likely that the standard of care will be towards adjuvant chemotherapy in the post-operative setting. Patients treated post-operatively have the advantage of an accurate pathological stage whereas, even with modern staging techniques such as positron emission tomography/computed tomography and endoscopic mediastinal staging (endobronchial and endoscopic ultrasound), tumors can be over staged and inappropriate treatment given. There may be some circumstances, however, where neoadjuvant chemotherapy is preferred[8]. Staging is central to the therapeutic approach to NSCLC. In early stage disease, surgery remains the best option for patients with localized disease who do not have overwhelming medical contraindications to a lobectomy or pneumonectomy. Surgical therapy is predominantly for

patients presenting with stages I to III A. For advanced/metastatic disease i.e. stage IIIB and stage IV, the current standard of treatment is chemotherapy alone[9]. Most of the patients reporting to the physicians are in the advanced stage of the disease i.e. either stage III B or stage IV. Here chemotherapy plays an important role in improving the overall survival of these patients as well as quality and life. Hence every patient should be offered the option of chemotherapy to improve the survival.

Platinum based chemotherapy remains an important component of the management protocol for almost all patients with NSCLC -early, locally advanced, and metastatic. The greatest evidence is for the use of a platinum based double regimen. Earlier, agents like vincristine, vinblastine, cyclophosphamide, ifosfamide, methotrexate, adriamycin and mitomycin – C, were being used for treatment of NSCLC. However, currently because of a more favourable toxicity profile, third generation agents like taxanes, gemcitabine, premetrexed and vinorelbine are the preferred drugs that are used in combination with a platinum agent[10].

CHOICE OF PLATINUM AGENT :

Most of the trials reported have used cisplatin-based regimes and there is no direct comparison between cisplatin and carboplatin in the adjuvant or neoadjuvant setting. Carboplatin-based regimes are easy to administer in the outpatient setting and have a favourable nonhaematological toxicity profile compared with cisplatin-based regimes. Extrapolation of the data from advanced NSCLC, the meta-analysis is suggestive of a slight benefit of cisplatin over carboplatin, especially in combination with new agents[11]. In the adjuvant setting, where the aim is cure, cisplatin-based regimes may be preferred over carboplatin-based regimes. Acute nausea and vomiting are very common after cisplatin which range from 10% to 20% with the availability of newer second generation . longer-acting, 5-hydroxytryptamine 3 antagonists and newer anti-emetics such as aprepitant, the major toxicity of nausea and vomiting has become less of an issue[12].Thus superior overall survival and response rates makes cisplatin a better agent in the standard regimen , while carboplatin is preferred when cisplatin is relatively contraindicated.

Choice of third generation agents: Phase III trials were performed to compare outcomes of different platin-based doublets i.e. platinum salt with a third generation agent. In the Eastern Cooperative Oncology Group study[13], four regimens were compared: cipslatin + paclitaxel; cisplatin + docetaxel; cisplatin + gemcitabine; and carboplatin + paclitaxel. The survival rates were similar in all the four arms of therapy.In another study[14] there was no difference in outcome of the patients treated with cisplatin+gemcitabine, or caroplatin+paclitaxel as compared to cisplatin+vinorelbine. In a recent meta-analysis by Douillard et al[15], docetaxel-based doublets showed a longer survival while another meta-analysis by Le Chevalier suggested that gemcitabine + platin-salt might be the best regimen[16]. It can be thus concluded that chemotherapy has reached a plateau and the preference/ choice between different doublets are mainly related to toxicity profiles and costs of the regimens.

Duration of treatment : Current recommendation for optimal duration of treatment is that the chemotherapy regimen should be administered for a maximum of four to six cycles. In the absence of obvious disease progression, assessment of response to therapy is done by contrast enhanced CT scans after four cycles and an addition of two more cycles can e considered in those who show partial or complete response. There is little benefit in giving the same regimen in the presence of stable disease after four cycles, while second line therapy is warranted if there is evidence of disease progression at any point during the initial treatment[17].

TARGETED CHEMOTHERAPY

As mentioned earlier, epidermal growth factor receptor , anaplastic lymphoma kinase , and vascular endothelial growth factor are the molecular targets in the treatment of NSCLC. New IASLC/ATS/ERS lung adenocarcinoma classification, recommends that EGFR mutation testing be performed for all patients with a pathological diagnosis of : i)Adenocarcinoma , ii) NSCLC, favor adenocarcinoma, and iii) NSCLC-NOS (Non small cell lung cancer – not otherwise specified) because of the predictive benefit of EGFR mutation with treatment by EGFR TKIs (Tyrosine kinase inhibitors)[18].

1. EGFR Tyrosine Kinase inhibitors : EGFR is aberrantly expressed in 40% to 90% of NSCLCs and thus has become an attractive target for drug therapy[19]. The EGFR is a transmembrane protein composed of an extracellular ligand binding domain and an intracellular tyrosine kinase. Activation of this receptor by ligand binding leads to receptor dimerization and autophosphorylation of the intracellular tyrosine kinase domain. This activated receptor complex intum initiates a cascade of intracellular signaling resulting in cellular proliferation, inhibition of apoptosis, angiogenesis, and

metastasis[20].Two oral, small molecule EGFR tyrosine kinase inhibitors , geftinib and erlotinib, have been developed in parallel over the last decade. Geftinib received FDA approval first, based on two phase 2 trials reporting encouraging response rates, symptom control, and survival in previously treated patients with advanced NSCLC[21]. Wheras erlotinib showed good response in phase 3 trial randomizing patients with advanced NSCLC.The median survival improved by 2 months with better quality of life, and it can be used as a second line or third line of drug[22].

2. EGFR monoclonal antibody :Cetuximab is a monoclonal antibody to EGFR, has also been evaluated in a phase 3 trial in patients with advanced NSCLC. The FLEX trial[23] has found a modest improvement in median survival of 1.2 months with cetuximab added to chemotherapy.

3. Anaplastic Lymphoma Kinase inhibitor (crizotinib): Activating mutations or translocations of the anaplastic lymphoma kinase gene have been identified in several types of cancer, including anaplastic large-cell lymphoma, neuroblastoma, inflammatory myofibroblastic tumor, and non–small-cell lung cancer. EML4ALK is uncommon, occurring in 2 to 7% of all non–small-cell lung cancers, and is more prevalent in patients who have never smoked or who have a history of light smoking and in patients with adenocarcinomas. Crizotinib is an oral ATP competitive selective inhibitor of the ALK and MET tyrosine kinases that inhibits tyrosine phosphorylation of activated ALK. Phase 1 and phase 2 trials have shown promising results, and phase 3 trial for this drug both as an agent in standard chemotherapy and as a part of salvage therapy are under progress[24].

4. Vascular endothelial growth factor monoclonal antibody : Angiogenesis stimulates tumour growth, invasion and metastasis, and this process is regulated by vascular endothelial growth factor (VEGF). Bevacizumab is an anti-VEGF recombinant humanised monoclonal antibody that blocks the binding of all VEGF to the receptors, hence inhibiting all the biological activities of VEGF. The Eastern Cooperative Oncology Group (ECOG) 4599 trial evaluated carboplatin plus paclitaxel with or without bevacizumab in advanced stage NSCLC[25]. The median survival was 10.3 months versus 12.3 months favouring the Bevacizumab-containing arm. As angiogenesis is a key process in tumour growth and progression of microscopic disease, bevacizumab may have a role in the adjuvant setting. Another study in the bevacizumab reported a significant improvement in median survival to 12.2 months. The 1 year survival rate was 51%, with 20% of patients surviving for 2 years[26].

CURRENT ASPECTS IN MANAGEMENT OF SCLC

SCLC is a high grade neuroendocrine carcinoma of the lung, consisting of small cells with sparse cytoplasm, fine chromatin, nuclear molding, and the presence of markers such as synaptophysin and chromogranin A. Even patients with an ECOG performance status of 3 or 4 as a result of disease should be considered for treatment with chemotherapy, because response rates of chemotherapy exceed 75% and clinical improvement can be observed within a few days.

The treatment of limited stage-SCLC involves multimodality therapy with concurrent thoracic radiotherapy and chemotherapy with cisplatin and etoposide.The standard treatment of extensive stage - SCLC consists of chemotherapy alone, generally cisplatin or carboplatin plus etoposide for up to 6 cycles, followed by watchful waiting. Irinotecan and topotecan are active agents both in combination with platinum agents and in the second line setting, but pemetrexed and picoplatin seem to be relatively ineffective. It is believed that further understanding of the tumor biology of SCLC will help in the development of better targeted therapies[27].

CONCLUSION :

Time for nihilism towards the chemotherapy for advanced lung cancer is over. There is no dispute that it is the standard treatment for advanced stage IIIB and IV NSCLC. Platinum based doublets is the best accepted regimen for advanced NSCLC with PS 0-1 and results in a response rate of 25%-30%, with median survival 8-11 months. Also gene expression might become of primary importance for customized chemotherapy. Targeted therapies can be used as second line therapy or third line therapy.

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Metabolomic biomarkers in obstructive respiratory diseases : a special view on NMR metabolomics

Chronic obstructive pulmonary disease (COPD) and asthma, both are common respiratory diseases in India with fairly high prevalence and morbidity, which require major medical attention. Both the disease conditions arise from airways in?ammation and currently the treatment of both conditions is predominantly with inhaled glucocorticosteroids and bronchodilator drugs. However, there is a desire to find better and safer alternatives to existing drugs which is undoubtedly reflected in the considerable effort put into such endeavours by the researchers and pharmaceutical industries. There is a major effort going on to investigate and propose substitute(s) for glucocorticosteroids as potential new treatments for asthma and COPD [1,2] . However, one of the obstracles for such drug development is the inability to accurately predict the course of in? ammation in patients with asthma or COPD using noninvasive techniques and the lack of validated biomarkers to use to assess the effect of novel anti-

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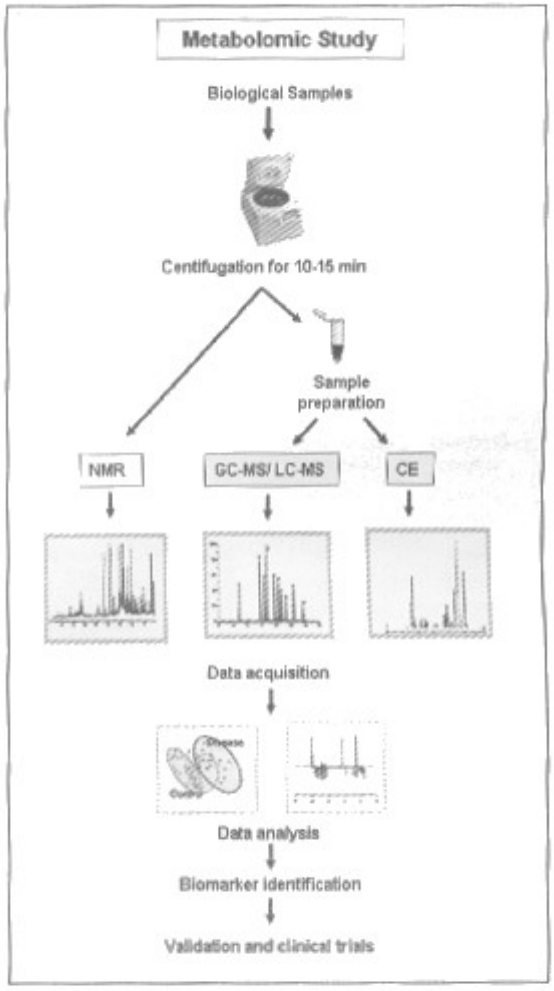
in?ammatory drugs. A considerable number of studies have approached to identify potential metabolomic biomarkers in (i) exhaled breath [3], (ii) sputum [4] (iii) blood [5] and (iv) urine [6] samples obtained from patients with obstructive respiratory diseases. Such biomarkers have served to some extent as markers disease diagnosis to assist and improve our basic understanding of the underlying mechanisms of asthma and COPD, as well as to serve clinical decisions and to assess the therapeutic effect on disease progression.

Whilst metabolomic biomarkers have been successfully used in other therapeutic areas, still most of the biomarkers investigated till date in respiratory diseases are to be validated. Until such validation is established the use of biomarkers in this field will not introduced in clinical practice. In this context, couple of areas have observed considerable progress, such as in the detection of volatile organic compounds in exhaled breath using sophisticated and sensitive techniques including chromatography based mass spectrometry (GC-MS, LC-MS, etc.), and proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy of serum and urine. The identification of several metabolites in different body fluids from several patient populations appears to be a promising and highly sensitive improved detection system that heralds the beginning of the era of "Metabolomics" which may find its application in the early detection and diagnosis of pulmonary diseases. This may also find its value in monitoring the disease progression and the impact of some therapeutic interventions.

The concept of analyzing unknown samples of interest using NMR is quite well known for few decades. But in this "post-genomic era" analysis of human metabolome is increasingly becoming popular after being able to correlate the findings with disease outcome or assessing improvements following a therapeutic management study. Genomics and transcriptomics provide general idea at the level of genetic regulation, but this regulation is not always translated to proteomics level. Proteomics give further important information of the functional regulation, although is incomplete without knowledge of its involvement in cellular responses in terms of metabolite utilization and expression. While, metabolomics is used to investigate metabolic regulation and fluxes, and is a systemic approach towards determination of biochemical profiles and regulation at the end point of functional control. In view of the fact, metabolomic analysis, in a systems biology approach, opens a new window of opportunity to understand the connection of small metabolic compounds, which are usually the end products of different pathways involved in diseases. Availability of newly developed highly sensitive technologies and improvement of existing facilities are widening the scope of delve deep into the metabolite level of diseases and explore the possibilities.



Schematic workflow for NMR, GC-MS/LC-MS and CE metabolomic study

Several studies have successfully identified multiple metabolites that differ from patient groups when compared to their respective healthy subjects. Such studies were conducted on patients suffering from multiple sclerosis, ischemia myocardial infarction, cancer, Alzheimer's, etc. A recent review of some of the metabolomics studies in different diseases is provided in table below.

Metabolomic studies to identify biomarker for human diseases

Disease	Sample	Methods used	Reference
Multiple sclerosis	CSF	^{1}H-NMR	Simone et al.; 1996
Alzheimer and Multiple sclerosis	CSF	^{1}H-NMR	Nicoli et al ; 1996
Coronary heart disease	Serum	^{1}H-NMR	Brindle et al.; 2002
Motor neuron disease	Plasma	LC-EC	Rozen et al.; 2005
Myocardial schemia	Plasma	LC-MS	Sabatine et al.; 2005
Huntington's disease	Serum	GC-MS	Underwood et al.; 2006
HIV	Serum	^{1}H-NMR	Hewer et al.; 2006
Influenza associated encephalopathy	CSF	ICR-MS	Kawashima et al.; 2006
Multiple sclerosis	CSF	^{1}H-NMR	Lutz et al.; 2007
Hepatitis B	Serum	GC-MS	Yu et al.; 2007
MMA/PA	Plasma	LC-MS	Wikoff et al.; 2007
Childhood asthama	**Exhaled Breath Condensate**	**^{1}H-NMR**	**Carraro et al.; 2007**
Parkinson's disease	Plasma	LC-EC	Bogdanov et al.; 2008
Renal	Urine	MALDI-ICR-MS	Wang et al.; 2008
Echinococcosis	Tapeworm cysts	^{1}H-NMR	Hosch et al.; 2008
Ischemia	Serum	^{1}H-NMR	Barba et al.; 2008
Phenotype diversity' blood pressure	Urine	^{1}H-NMR	Holmes et al.; 2008
Myocardial injury	Plasma	LC-MS	Lewis et al.; 2008
COPD	**Exhaled Breath Condensate**	**^{1}H-NMR**	**Laurentiis et al.; 2008**
Celiac	Serum/urine	^{1}H-NMR	Bertini et al.; 2009
Silent myocardial ischemia	Plasma	LC-MS	Lin et al.; 2009
Lung function (COPD)	**Urine**	**^{1}H-NMR**	**McClay et al.; 2010**

Certain possibilities of future advancements in available technologies and associated analytical methodologies in metabolomics are building much hope for detailed insight into the effective use of metabolomics especially in the field of pulmonary diseases, throughout biomarker discovery, preclinical development and clinical trials. The increasing trend of using metabolomics can maximize and sustain revenues in post-marketing and in the development of clinical diagnostics of obstructive respiratory diseases. Metabolomic case studies can further improve current understanding and indicate future directions in early detection and noninvasive diagnosis as an objective indicator of treatment of asthma and COPD.

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NEWS:

● 1st gene therapy may get approval in Europe

1st gene therapy has been recommended in Europe for lipoprotein lipase deficiency. This condition, develops from a defect in the gene for synthesis of the enzyme lipoprotein lipase that breaks down fat. As a result excessive fat particles cumulate in blood causing pancreatitis.

The drug or the gene is named Glybera (Uni Qure) and adeno-associated viral vector (AAVI) has been modified to carry the gene for LPL without replicating.

The drug is injected to a muscle following which it enables the muscle cells to synthesize LPL and combat the deficiency.

This is a good news although the recommendation is made for marketing authorization under exceptional circumstances by the European medicine agencies.

Medscape 23/07/12; Posted by Froy Brown.

● FDA approves quick test to identify sepsis and drug resistance.

Sepsis is serious physiological event in response to infection. Early identification of sepsis is important to save life. Of late, resistant bacterial infection adds to mortality related to sepsis.

Identification of sepsis is often easy but determination of the causative infection is usually difficult as the conventional staining of the sample collected from the infected issue or culture of blood or material from the

infected site is time taking. Hence, the choice of antibiotics in sepsis is mostly guided by educated guess. Thus, a risk of use of inappropriate antibiotics remains and this influences the outcome of management adversely. Often two, three or more antibiotics are prescribed from panic reaction.

Nanosphere Inc. has prepared nucleic acid test from the blood culture growth of Gram positive bacteria: this test can defect 12 gram positive bacteria in blood samples including MRSA (methicillin resistant staphylococcus aureus), VRF (vancomycin resistant enterococci) and listeria in less than 2.5 hours.

The test is capable of simultaneously identifying crucial markers of anti microbial resistance from detection several genes that confer resistance to methicillin / oxacillin and vancomycin.

Interestingly, the accuracy of the test found to range between 93% to 100%

The USA FDA has shown its green signal to the test.

This is a welcome move. We have to wait for similar tests for Gram negative and other microbes.

Source : Medscape Medical News 27.6.12

JOURNAL SCAN

● Neutrophilic airway inflammation in asthma with infection and steroid unresponsive.

Some patients of asthma have chronic bacterial colonization of airways commonly with H influenzae and other bacteria. They have neutrophilic airway inflammation and poor response to corticosteroid therapy.

In a mouse mode, researchers have found that the combination of infection and allergic airway diseases promote bacterial persistence leading to development of a phenotype of steroid neutrophilic resistant asthma.

This indicates that targeting bacterial infection in steroid resistant asthma may be therapeutically worthwhile.

Thorax 2012; 67:588-599

● Bronchoscopic lung volume reduction : a new development

Bronchoscopic lung volume reduction has been an area of interest for treatment of emphysema – where lung volume reduction at the diseased area can lead to symptomatic improvement. Several methods are tried including bronchoscopic thermal vapor ablation (BTVA).

In a recent study, 44 patients with upper lobe predominant emphysema were treated unilaterally with BTVA. The results were measured in FEV1, SGRQ, 6MWT and lung volume. All the parameters have shown important.

BTVA appears to produce clinically relevant improvement in lung function and other parameters in upper lobe predominant emphysema. However lower respiratory tract events were the most common adverse sequel in 1st 30 days after the procedure.

Goegory Smell et all, ERJ. 2012: 39:1326 – 1333

● Do we need to anticoagulate our cirrhosis patients with raised INR for preventing venous thromboembolism?

It is thought that cirrhosis with raised INR is a state of "auto anti-coagulation". A recent literature search reveals facts contrary to this concept. If finds that (a) no significant co-relation of INR values and VTE (venous thromboembolism) risk, (b) serum albumin is a better reliable marker of coagulation status and VTE risk in context of cirrhosis, (c) malnutrition and significant co-morbidities as chronic kidney disease, CCF are the independent risk factors of VTE in cirrhosis.

Therefore, the "auto anti-anticoagulation" theory is no longer tenable as the conclusion writes "in hospitalized patients of cirrhosis who have elevated INR values, pharmacologic VTE prophylaxis should be strongly considered if there is no active or recent bleeding and if more than one risk factor for VTE is present.

Am J Health Syst Pharm 2012; 69 (8): 658-663.

Tantu talking about COPD :

Tantu is a friend of ours who always teaches us

Tantu talking about COPD :

Editor : Dear Tantu, you look happy but quiet. What is the issue for your unusual silence?

Tantu : Yes, I am really happy. Your bulletin is getting popular and a lot of articles have reached your desk. But I am little bothered since I feel that my interactive session may add bulk and cost to your publication.

Editor : No worry! You are our great friend – please continue to teach us.

Tantu : Okay – then don't ask me many questions now as you always do. Today I will give a briefing on COPD. Just jot it down and publish if you wish.

Editor : That's fine.

Tantu started talking : -

Understanding of COPD got momentum after the publication of the 1st Gold guideline – that wanted to streamline the definition criteria, and outline and classification in COPD according to lung function change. In last one decade or so – there have been a plethora if information about COPD and the world has learned perhaps a lot more about the disease than what they had learnt over a preceding century.

a) Definition and classification according to severity has given an uniformity in diagnosis and staging across the world.

b) COPD has been recognized as a systemic inflammatory disease with possible spillover of inflammation from the lungs to the system.

c) Many systemic manifestations have been identified and their importance in the management of the disease have been recognized.

d) The role of co-morbidities in the well being of COPD have been extensively studied and elaborated.

e) The associations of the COPD with the left heart function, COPD and coronary artery diseases, COPD and ischemic heart disease has got new dimensions and understanding.

f) Understanding a patient of COPD in terms of pathogenesis, lung function, functional capacity and quality of life have been emphasized in practice. A new instrument is developed to easily measure the quality of life: CAT (COPD assessment test) scoring

g) The role of exacerbation influencing the well being and possibility the life expectancy is far better understood than before.

h) Different clinical phenotypes are been studied and endotype understanding is in the process to understand COPD better.

I) New management strategies have been laid out and new drugs are under research and development.

j) Prevention of infection and exacerbation, rehabilitation etc. are far seriously stressed and have yielded a better quality life and life expectrery in COPD patients. There are many more evolving areas. Over all, a negative out look to this disabilitating illness has been changed to great extent.

Yet COPD remains one of the major case of mortality and morbidity for the humanity with a globally increasing frequency.

k) There are lot more things to say

NEWS FROM THE INSTITUTE :

The institute has been as active as before in last few couple of months.

In the academic field we have at least two good publications.

1. Left Ventricular Diastolic Dysfunction in COPD May Manifest Myocardial Ischemia (COPD, 9:1–5, 2012)

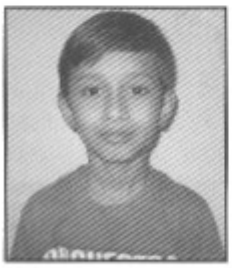
2. Long-term use of doxycycline can improve chronic asthma and possibly remodeling : the result of a pilot observation. (Journal of Asthma & allergy, 5: 33-7, 2012)

And few of our manuscripts are under consideration for publications. An abstract has been accepted for CHEST 2012.

The rural training and education programme for COPD patients is going well. We are in the process of looking at the improvements on the quality of life from our efforts.

The construction of our campus is likely to re-start after the monsoon.

Shubhankar Mondal, (8 years), and Shibham Mondal, (10 years), the two sons of our member Swapan Mondal are now upcoming dancing stars. Shubhankar has already charmed the audience at the Dance Dreamz 2012 at Jamshedpur with winning the runner's up trophy. He had lead the group in that national dance show.



Shubhankar Mondal

Shibham Mondal

Abstracts at Pulmocon – '12 :

A study of Sputum culture and sensitivity in cases of community acquired pneumonia in Barpeta and formulation of a simple working sensitivity scoring system

Dr. Anupam Dutta

Background : As community acquired pneumonia can be caused by various microbes and no single antimicrobial agent can cover all possible etiological agents, a study was conducted in Fakharuddin Ali Ahmed Medical College and Hospital to find out the most common etiological agents and their antibiotic sensitivity .

Methods : Any case that presented to the outpatients department of Medicine in FAAMCH from March 2011 to April 2012 with a clinical history and findings of CAP were included and their fresh sputum was sent for culture and sensitivity. After isolation of the pathogen antibiotic sensitivity was done according to the standard guidelines. For comparison of antibiotic sensitivity of various microorganisms to various antibiotics a novel method was used. Those cases which showed high sensitivity to a particular antibiotic were given a score of 2 (two) and those which were intermediately sensitive were given a score of 1 (one).Those which showed resistance toward the same antibiotic were given a score of -1 (minus one). The total score of all the cases infected with the same microorganism and tested against a specific antibiotic was added and a final score was given. Percentiles were calculated for each antibiotic used against a specific microorganism and compared together to come to a rough conclusion.

Results : A total of 134 cases were included initially, but after exclusion and a few cases lost to follow up, 90 cases were included in the study. Of them 66 (73%) cases were males and 24 (27%) were females. 49 (54%) cases had shown growth of a specific microorganism in culture media. Of them 26 (53%) cases showed growth of Staphylococcus sp, 15 (31%) cases showed growth of Klebsiella sp, 4 (8%) cases showed growth of Pseudomonas sp and 4 (8%) cases showed growth of Streptococcus pneumoniae. Staphylococcus sp was most sensitive to cephalosporins (99) and aminoglycosides (100), Klebsiallasp was most sensitive to aminoglycosides (100) and quinolones (97.45), Streptococcus pneumonia to carbapenems (100), aminoglycosides (87) and Pseudomonas was more responsive to carbapenems (87.5) and aminoglycosides (93.75).

Conclusion : A regular study of antibiotic sensitivity of the common organisms causing CAP and a simple sensitivity scoring system can be useful in judicious antibiotic use in any region.

Demographic, Clinical, Biochemical, Radiological and Etiological Characteristics of malignant Pleural Effusions from Eastern India.

Dr. Moumita Chatterjee, Dr. Malay Maikap & Dr. Supriyo Sarkar Dept. of Respiratory Medicine, NRS Medical College, Kolkata

Background : There are very limited data regarding clinical, radiological and etiological aspects of malignant pleural effusion from eastern India.

Aims : To review natural history, clinical features, radiological features and etiology of malignant pleural effusions.

Setting and Design : Hospital based cross sectional descriptive study.

Methods and Material : We had reviewed 166 diagnosed cases of malignant pleural effusions regarding demography; clinical, radiological and biochemical characteristics, diagnostic modalities and etiologies.

Results : Out of 166 patients, 72.89% were males and 27.11% were females. Mean age of presentation among males was 64.3 ± 12.7 and among females was 52.5 ± 14.8. Most common presenting symptom was dry cough (87.9%) and most common presenting sign was clubbing (54.5%). Massive effusion was found in 45.78% of cases. Pleural fluid macroscopic appearance was haemorrhagic in 54.82% of cases. Mean ADA activity in malignant pleural effusion was 24.05 U/L. Mean pleural fluid / serum protein ratio was 0.65, mean pleural fluid / serum LDH ratio was 1.01. Most of the cases (84.94%) were diagnosed by pleural fluid cytology for malignant cells. Primary cancer was diagnosed in 136 (81.93%) cases; among which 121 (88.97%) cases were lung cancers, among which adenocarcinoma (52.89%) was the most common histology.

Conclusions : Pleural fluid cytology for malignant cells usually sufficient to diagnose malignant pleural effusion in nearly 85% of cases and in remaining cases if thoracoscopy not available blind pleural biopsy can be helpful. Most common primary in cases of malignant pleural effusion is lung cancer with adenocarcinoma being the commonest culprit.

Key words : Malignant pleural effusion, pleural fluid cytology, pleural biopsy, lung cancer.

Usefulness of induced sputum eosinophil count to assess severity and treatment outcome in asthma patients

Dr. L. Mistry*, Dr. A. Banerjee*, Dr. P. P. Roy#& Dr. S. Sarkar *

*Pulmonary Medicine Department, N. R. S. Medical College, Kolkata. #Midnapore Medical college

Context : Currently treatment decisions of asthma are governed by clinical assessment and spirometry. Sputum eosinophil being a marker of airway inflammation can serve as a tool for assessing severity and response to treatment in asthma patients.

Aims : To establish correlation between change in sputum eosinophil count and forced expiratory volume in one second (FEV_1) % predicted value of asthma patients in response to treatment. In this study, we also predicted prognosis and treatment outcome of asthma patients from baseline sputum eosinophil count.

Settings and Design : A longitudinal study was conducted to determine the treatment outcome among newly diagnosed asthma patients who were classified into A (n=80) and B (n=80) groups on the basis of initial sputum eosinophil count (A = 3%, B < 3%).

Methods and Material :

After starting treatment according to Global initiative for asthma (GINA) guideline, both A and B groups were evaluated every 15 days interval for the 1st month and monthly thereafter for a total duration of 12 months. In each follow up visit detailed history, induced sputum eosinophil count and spirometry were done to evaluate severity and treatment outcome.

Results : FEV_1% predicted of group A asthma patients gradually increased and sputum eosinophil count gradually decreased on treatment. Longer time was required to achieve satisfactory improvement (FEV_1% predicted) in asthma patients with sputum eosinophil count = 3%. There was statistically significant negative correlation between FEV1 % predicted and sputum eosinophil count (%) in of group A patients in each follow up visit with most significant negative correlation found in 8th visit ($r = -0.9237$ & p value = <0.001). Change in mean FEV_1% (predicted) from baseline showed strong positive correlation ($r = 0.976$) with change in reduction of mean sputum eosinophil count at each follow up visits in group A patients.

Conclusions : Sputum eosinophil count being an excellent biomarker of airway inflammation can serve as a useful marker to assess disease severity, treatment outcome and prognosis in asthma patients.

Does the change in clubbing marks the course of DPLD : The result of a pilot observation

Dipanjan Saha, Partha Bhattacharjee, Bodhisattwa Chakraborty, Ratna Dey, Malabika Ghosh, Madan Sharma, Rana Dey, and Parthasarathi Bhattacharyya. Institute of Pulmocare and Research , Kolkata

Background : Clubbing is a common association of DPLD from different causes. There could be a relationship of the activity of DPLD with that of the degree of clubbing. Thus, it may be worthwhile to see the change in clubbing with the course of DPLD.

Objective : to see whether there is any change in clubbing in DPLD patients with therapy and whether such changes correlate with the course of the illness.

Methods : Patients of DPLD being diagnosed on clinic-radiological (HRCT) basis were evaluated with spirometry and six minutes walk test (6MWT). The measurement of clubbing clubbing was accomplished in all with the help of a modified shadow-gram at the beginning and at least once on follow up after treatment in a real world protocol. The change in FVC and 6MWT were calculated with that of the measurement of the different variables of clubbing as profile angle, hyponychial angle, and the ratio between the distal and proximal interphalangeal diameters over the follow up period.

Result : Out of 17 patients of DPLD observed in such fashion, 11 had improvement and 6 had deterioration in both the FVC (Forced Vital Capacity) and the 6MWT. This changes was noted significant in both the parameters for improvement ($p = 0.04$ and 0.01 respectively) and for FVC alone ($p = 0.001$) for deterioration. Though not statistically significant, there has been a parallel change in all the parameters of clubbing both in the improvement and the worsening group.

Inference : The change in clubbing appears to mark the course of a DPLD patient. The observation needs further validation.

Formation of an assessment tool to measure the Quality of Life (QoL) of patients of DPLD (diffuse parenchymal Lung diseases) on a newly develop questionnaire.

Dipanjan Saha , Partha Bhattacharjee, Bodhisattwa Chakraborty, Ratna Dey, Malabika Ghosh, Madan Sharma, Rana Dey, and Parthasarathi Bhattacharyya. Institute of Pulmocare and Research , Kolkata

Background : The measurement of the QoL (Quality of life) is important to understand the status, behavior, and the effects of interventions for a particular disease. Incidentally there has been no good QoL assessment tool for the DPLD patients.

Objective : to try to make a questionnaire based instrument to enable a physician note the QoL of DPLD patients in day to day practice

Methods : A 18 point questionnaire has been formed on 10 patients' perceived domains based on the existing knowledge to assess the QoL of DPLD patients in a consensus through series of group meetings among the members of a dedicated team of doctors treating DPLD. The instrument was tested on 10 DPLD patients randomly and modified accordingly without any change / addition of domains. The instrument thus formed was named as PILD (Pulmocare Interstitial Lung Disease) questionnaire and was applied along with other parameters of QoL assessment as SGRQ, Borg's scale, visual analogue scale CAT (COPD Assessment Test) score and the MRC (Medical Research Council) stages to a cohort of DPLD patients. The response collected through the application of the new instrument were correlated to the result available through use of the other known instruments .

Results : 65 patients (35 males and 32 females; mean age 56.46±10.94 years) responded. The PILD score has shown to have significant ($p<0.01$) positive correlation to SGRQ total score, Borg's scale, VAS and the CAT score with the correlation co-efficient being 0.854, 0.8, and 0.846, 0.857, respectively. However the co-relationship with the MRC scale is relatively poor (r^2 linear = 0.677)

Inference : The newly developed QoL questionnaire with 18 questions covering on several domains of the life of DPLD patients has been found to correlate well with the other existing and widely used QoL assessment instruments. But such association is poor for standard dysponoea measurement scale as MRC staging.

Categorization of COPD patients according to the latest GOLD guidelines

Bodhisattwa Chakraborty, Partha Bhattacharjee, Dipanjan Saha, Ratna Dey, Malabika Ghosh, Madan Sharma, Rana Dey, and Parthasarathi Bhattacharyya. Institute of Pulmocare and Research, Kolkata.

Background : COPD subjects are recently (GOLD recommendation, 2011) categorized in a different way incorporating variables other than FEV1, as MRC staging, CAT Scoring and history of exacerbations.

Objectives : To look for the frequency distribution of COPD patients according to the latest GOLD categories presenting to a tertiary out-door services.

Methods : Clinically suspected COPD patients presenting to the OPD of the Institute of Pulmocare and Research, Kolkata were confirmed with spirometry observing the ATS guidelines. Their dyspnoea status was assessed in MRC scale and their quality of life was looked for with the help of COPD Assessment Test (CAT) scoring, along with the number of exacerbation being noted for last one year. They were further categorized according to the GOLD 2011 guided format of composite scoring of MRC grading, value of CAT scoring and the FEV1.

Results : The total number of patients incorporated has been 131; the distribution according to the GOLD 2011 format goes as follows: 25 (19.08 %), 66 (50.38 %), 18 (13.74 %) and 22 (16.79%) patients respectively in category A, B, C, and D. The mean CAT Score of the categories were 6.64±2.08, 16.29±5.02, 12.17±6.26, 19.95±4.96 and difference between these scoring have been found statistically significant between A and B, B and C, and C and D (p-values as 0.00004, 0.01, and 0.0001 in unpaired 't test') respectively. This quality of life assessment goes parallel to the post bronchodilator percentage of FEV1 values.

Discussion : It is interesting to note that GOLD categorization (2011) shows patients of progressively poor lung function and quality of life are being distributed from A to D; it reflects that the categorization is successful to mark the severity and the functional status of COPD effectively.

Inference : The distribution of our patients according to the GOLD 2011 system shows progressive worsening of quality of life and FEV1 values in patients responding to the questionnaire.

Difference between Smoker and Non smoker COPDs an observation at Kolkata

Bodhisattwa Chakraborty, Dipanjan Saha, Partha Bhattacharjee, Ratna Dey, Malabika Ghosh, Madan Sharma, Rana Dey and Parthasarathi Bhattacharyya. Institute of Pulmocare and Research, Kolkata

Background : Smoking, though the most common cause of COPD, is not contributory in a good segment of COPD populations. It is important to know separately the frequency, characteristics and the etiological associations of nonsmoking COPD patients.

Objective : To see the prevalence of COPD without history of smoking and to see how those patients differ from COPD subjects with history of smoking.

Methods : Suspected Chronic Obstructive Pulmonary Disease patients presenting to our OPD were evaluated for confirmation with Spirometry according to ATS guideline. Confirmed patients of COPD were interviewed randomly on a questionnaire after signing written informed consent form. Available responses were charted under two groups- COPD with history of smoking and COPD without history of smoking and were compared as per different variables taken into consideration

Results and Discussions : Out of 166 COPD patients included 33(20%) turned out as non smokers. They have better lung function parameters (FEV1 0.98±0.38 vs 1.23±0.59 p=0.03) and quality of life (CAT Score15.28±5.94 vs 11.79±6.48 p=0.007) compared to COPD patients with history of smoking. The male female ratio is 1:1 for nonsmoker patients, while all the smoker COPD subjects were all males. 9 out of 11 females (81.81%) of the nonsmoker COPD patients had history of significant exposure to biomass fuel.

Inference : 20% of urban COPD population develops the disease rive from some other cause but smoking. Though history of biomass fuel exposure is present in majority of females (9 out of 33), there is no etiological clue for the rest. The issue needs further investigations.

Matrix metalloproteinases mediated angiogenesis via P38 kinases signalling in idiopathic pulmonary fibrosis

[1]**Ardhendu Kumar Mandal,**[2]**Rantu Paul,** [3]**Parthasarathi Bhattacharya,** [1]**Sibani Sarkar,** [1]**Nilanjan Ganguly and** [1*]**Snehasikta Swarnakar**

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Background : Idiopathic pulmonary fibrosis (IPF), a disease of chronic relentless fibrosis of lungs has been characterized by over expression of pro-fibrotic cytokines, dysregulated fibrogenesis, admixed with angiogenesis. Recently, the up-regulation of the extra cellular matrix (ECM) remodelling enzymes, the matrix metalloproteinases (MMPs) with an imbalance of protease/ anti-protease activities in the tissue, has been implicated in the pathogenesis of IPF through the release of growth factors. In our previous study, we investigated MMP-9 activity and vascular endothelial growth factor (VEGF) expression in broncho alveolar lavage fluids (BALF) of normal (non-IPF) and IPF patients (n=6 for each group).

Methods : In this study, the BALF samples from IPF and normal patients (n= 4 for each case) were subjected for investigations of MMP-9 and 3, NADPH oxidase-3 (NOX-3), nitric oxide synthases (NOS-2 and 3), tumor necrosis factor-á (TNF-á), VEGF, pAkt,

Diagnosis of Lungs Status Using Morphological Homogeneity of the Thoracic Sound

Ashok Mondal*, P. S. Bhattacharya# , Goutam Saha**

**Department of Electronics and Electrical Communication Engineering

*Indian Institute of Technology, Kharagpur, India, Kharagpur-721 302, #Institute of Pulmocare and Research, Kolkata, India, Kolkata-700 064

BACKGROUND : Medical practitioners listen to pulmonary sounds using stethoscope and make interpretation. Its performance depends on the physicians experience and knowledge. There is a probability of misinterpretation due to human factor involved and presence of different interfering signals. The objective of our work is to develop an algorithm that can diagnose lungs condition in an automated environment.

METHODS : The recorded lung sound signals are contaminated with noises produced from different sources namely environment, data recording and processing instruments, man made disturbances and unavoidable heart sound interference. These noise sources lead a misinterpretation of the lungs status. In this study, the environmental noise and man made artifacts are reduced by acquiring the sounds in a proper recording condition, and properly placing the stethoscope on the body surface of the subjects. The instrumental hazards and heart sound noise are removed by using a first order differentiation algorithm and an empirical mode decomposition technique respectively. The analysis of enhanced lung sound signal is performed in two stages: respiratory cycle extraction process and evaluation of lungs status.

RESULTS : The performance of the proposed method is evaluated through quantitative and qualitative analysis. These results are validated through three types of medical tests: pulmonary function test, chest X-ray, and high resolution computed tomographic scan.

CONCLUSION : The derived algorithm can be used as a diagnostic tool that will assist the physicians in prognosis the lung status: normal vs abnormal.

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BREEZE CORNER :

স্বপ্ন দ্যাখো - একটু এগোও

একটা ছোট স্বপ্ন দ্যাখো
একটু সবুজ ভোর বেলা
একটা পাখী যায় উড়ে আর
একটু আলোর জল-খেলা।
একটা উদাস দুপুর হারাও
একটু কাজের ঘাম দিয়ে
একটা বিকেল একটু হাঁটো
এগিয়ে যাবার নাম নিয়ে।
ছোট্ট একটা শালুক ফুলে
থাকুক ফোঁটা তোমার সুর
একটু সবুজ বাড়াও অবুঝ
শোনাও বাঁশী অনেক দূর।
স্বপ্ন তোমার মেলুক ডানা
চলুক শরীর ছন্দেতে
গুণগুনানি মনের মাঝে
কিছু করার গন্ধেতে।
এমনি করেই কখন যেন
এগিয়ে যাবার উল্লাসে
তোমার আমার সবার বাঁচা
সুখের সুরে যাক ভেসে।

পার্থসারথি ভট্টাচার্যের লেখা -
"আরো মনের মলম" ছড়ার বই থেকে নেওয়া।

ABOUT THE INSTITUTE

The Institute of Pulmocare & Research (IPCR) was born in 2000 as a nonprofit organization with the motto of Research, Education and Patient Care. For the last eleven years the institute has been trying hard to achieve its motto to the best of its capacity despite a lot of logistic constraints.

We have already marked our existence with worthwhile activities. In the research front, we have innovated at least three new therapeutic procedures and have opened up a new horizon in treating a difficult to treat disease IPF (Idiopathic Pulmonary Fibrosis) and two of our manuscript are awaiting to unveil a new chapter in the treatment of obstructive airway diseases. We have published the maiden observation that left ventricular diastolic dysfunction in COPD may manifest in myocardial ischemia. There are other areas too where we are trying to bring forth tangible outcome from innovative and operational researches.

We are also active in educational and welfare front. Despite our limitations we arrange significant concession to our patients from our consultation fees and from investigations outside as well. We arrange different training programmes for different categories of health care workers. "Pulmocon" is an annual update of the institute meant to foster education and training on important aspects of pulmonary medicine.

We are recognized by the Govt. of India as a SIRO (Scientific Industrial Research Organization) and have been granted a special provision of IT act through which a corporate or a professional can earn 175% tax exemption on donating to our institute. We are trying to build up our own campus soon – which is under construction at the New Town, Kolkata.

All these have been possible through the constant involvement and zeal of our working members along with the love and affection of all concerned. We solicit your blessings so that we can continue to move on our path.