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THE INDIAN JOURNAL OF CHEST DISEASES AND ALLIED SCIENCES

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# CONTENTS

EDITORIAL

# Does Increased Dietary Salt Intake Worsen Asthma?

*[Indian J Chest Dis Allied Sci 2004; 46 : 247-249]*

In addition to raising the blood pressure, dietary salt is responsible for several other harmful effects[1]. The best known are the effects on the cardiovascular system including an increase in the mass of the left ventricle, thickening and stiffening of arteries, including the coronary and renal arteries, and an increased risk of stroke. In renal disease, a high salt intake accelerates the rate of renal functional deterioration. It also has an effect on calcium and bone metabolism, increasing the risk of osteoporosis. Dietary salt is also related to the occurrence of carcinoma of the stomach.

It is not often appreciated that there is some evidence suggesting that salt intake may be a determinant of the severity of asthma. One of the several explanations for the wide geographical variation in asthma prevalence as well as its increasing prevalence is increased dietary salt consumption. Although several investigations have shown a relationship between asthma (or airways responsiveness) and dietary salt intake or urinary sodium excretion, others have not, and the matter remains debatable.

As early as 1938, Stoesser and Cook[2] proposed a relationship between salt intake and the severity of asthma. They reported that a low sodium diet contributed to a decrease in symptoms in children with severe asthma. Subsequently, several investigators have presented ecological, observational and experimental evidence supporting a relationship between salt intake and bronchial responsiveness in men and children[3-7]. Sodium transport has been implicated in many aspects of the regulation of airway smooth muscle tone. One likely explanation is a mechanism that involves an increase in intracellular sodium content because this could lead to an increase in cell calcium through $Na^+/Ca^{2+}$ exchange[8]. Raised erythrocyte sodium has been documented in asthmatic subjects[9]. We have shown that the activities of two key enzymes regulating the movement of sodium and calcium ions across the cell membranes, $Na^+ K^+$ ATPase and $Ca^{2+}$ ATPase are decreased in lymphocytes of asthmatics and correlate well with the severity of asthma[10]. This would result in sodium loading of cells.

Sales of table salt in different regions of England and Wales are independently correlated with mortality from asthma for men and for children. In a study by Burney *et al*[3], it was suggested that a high sodium diet may potentiate bronchial reactivity. Medici *et al*[11] found that salt loading worsens the clinical and functional status in asthmatics. This effect was presumably mediated by sodium, not chloride, as it was also demonstrated by loading with sodium citrate. There is some evidence of a positive association between increased dietary salt consumption and both increased bronchial reactivity and mortality from asthma in men[6].

A cross-sectional study among 2593 children by Pistelli *et al*[12] found that personal table salt use was strongly related to cough and phlegm apart from colds, wheezing apart from colds, wheezing with dyspnoea and wheezing after exercise. Gotshall *et al*[13] reported that a high salt diet worsened postexercise pulmonary function values in subjects with exercise-induced bronchospasm. In a study to determine the influence of both elevated and restricted salt diets on pulmonary function during exercise in individuals with exercise-induced asthma, Mickleborough *et al*[14] concluded that low salt diet improved and the high salt diet exacerbated pulmonary function during exercise.

Although the above-mentioned studies suggest a positive relationship between asthma severity (or bronchial responsiveness) and dietary sodium intake, other workers have not been able to corroborate these observations.

In a case-control study conducted by

Demissie *et al*[15], after accounting for important confounding variables, there was no association between the severity of asthma and salt intake. However, the methacholine dose-response slope increased with increasing salt intake and bronchial responsiveness was greater in the highest quartile than in the lowest quartile of salt intake. In two recent epidemiological surveys of men in northern England, Devereux *et al*[16] reported a lack of relationship between airways responsiveness and the 24-hour urinary sodium excretion in one population and concluded that if at all airways responsiveness was related to dietary sodium, the strength of correlation was weak.

The effect of changing dietary salt intake (normal, low, and high) for two weeks on the severity of asthma as measured by PEFR was studied by Lieberman and Heimer. There were no significant differences in PEFR or an index of asthma lability, PEFR amplitude (highest-lowest PEFR), among the three dietary salt periods. A search of randomized controlled trials (RCTs) that involved dietary salt reduction or increased salt intake in patients with asthma, was conducted using the Cochrane Airways Group asthma register by Ardern and Ram[18]. Fifty-six abstracts were identified and 15 studies were reviewed in full text. Only five fulfilled the inclusion criteria. All the studies were small and of short duration. Data from only three could be pooled. Low sodium diet was associated with a significantly lower urine sodium excretion than normal or high salt diets. There were no significant differences in any asthma outcomes between low salt and normal or high salt diets, but $FEV_1$ was slightly higher with low salt diet as compared to normal, as was daily PEFR. In patients on low compared to high salt diet, $FEV_1$ was slightly higher as was daily PEFR. Bronchodilator use was also slightly lower in these patients. As the association between dietary salt intake and the severity of asthma came out as weak, the reviewers observed that based on currently available evidence, it was not possible to conclude whether dietary salt reduction has any place in the treatment or management of asthma.

From the above review of studies it is apparent that the association between salt intake and asthma remains to be established conclusively. A reasonable case cannot be built up on current evidence for restricting dietary salt intake yet. However, patients with asthma would be as prone to the increased risk of cardiovascular, renal, bone and other diseases as a non-asthmatic if the salt intake is high in their diets. Therefore, it would be prudent to restrict salt intake with the hope that while reducing the other risks associated with a high dietary intake of salt, there may be some reduction in the severity of asthma.

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ORIGINAL ARTICLE

# DOTS Centre at a Tertiary Care Teaching Hospital: Lessons Learned and Future Directions

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ABSTRACT

***Background.*** In 1993, Government of India started the Revised National Tuberculosis Control Programme (RNTCP). A model Directly Observed Therapy, Short-Course (DOTS) centre was established at the All India Institute of Medical Sciences (AIIMS) to *(i)* identify the challenges and opportunities in establishing DOTS centres at tertiary care facilities, (*ii)* to teach the strategies of RNTCP to medical and paramedical staff, and *(iii)* to undertake relevant operational research connected with tuberculosis (TB) treatment and control. In this communication, we describe the experience of establishing a DOTS centre at India's premier medical institute and discuss the lessons learned.

***Methods.*** Since September 2001 through November 2002 AIIMS employees and their dependants diagnosed with tuberculosis were enrolled for treatment at AIIMS DOTS centre. One hundred sixty–eight patients were diagnosed as suffering from tuberculosis. Of these 49 patients were referred out and remaining 119 patients were treated at AIIMS DOTS centre.

***Results.*** Treatment success was achieved in 80% (20/25) of new smear positive cases and the DOTS centre achieved other targets set up by the RNTCP. As the results of the pilot study at AIIMS DOTS centre were favourable, the facilities of AIIMS DOTS centre were extended to the general public from September 2002 onwards.

***Conclusion.*** Despite tremendous patient load at tertiary care facilities, it is possible to achieve targets established by the RNTCP. However, additional research needs to be conducted especially relating to drug resistance and surrogate markers of failure under RNTCP.

***Key words:*** *Tuberculosis, Directly observed therapy-short course, Revised National Tuberculosis Control Programme, India.*

***[Indian J Chest Dis Allied Sci 2004; 46 : 251-256]***

## INTRODUCTION

The Revised National Tuberculosis Programme (RNTCP) of India has adopted the World Health Organization (WHO) recommended Directly Observed Therapy, Short-Course (DOTS) strategy for the control of tuberculosis (TB). Since its inception the programme has extended its reach to cover approximately 600 million people, *i.e.* almost 60% of the India's

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entire population (*Dr L.S. Chauhan: personal communication*). Continued success of the programme, however, remains a daunting task as there has been very little co-ordination between the RNTCP, faculties of medical schools and health providers in the private sector. In medical schools, training on TB and HIV/AIDS does not focus on the public health aspects relating to prevention and control of these diseases. Staff at medical schools and practitioners in the private sector continue to treat a large number of TB patients with different drug regimens. Moreover, treatment outcomes are not systematically documented. Therefore, the impact of national disease control programmes is not fully realised. The emergence of the HIV/AIDS pandemic and the threat of multi-drug resistant tuberculosis (MDR-TB) further accentuate the need for greater co-ordination and co-operation between public health programmes, medical teaching faculty and the private sector.

The continuing success of the RNTCP will depend to a large extent on the involvement of all large-scale health care providers, especially medical schools, which play a crucial role. They are important not only in imparting knowledge and skills, in shaping the attitudes of medical students but also in updating the knowledge of medical practitioners. Improvements in teaching methodology and content will promote long-term sustainability of the programme.

The All India Institute of Medical Sciences (AIIMS) is a premier medical institute of India, and a role model for other medical schools. A model DOTS centre was established at AIIMS with the help of World Health Organization (South East Asia Regional Office-SEARO) in September 2001. This report describes the experience and results of RNTCP and also discusses prospects and challenges for the future.

## MATERIAL AND METHODS

### Study Population

In September 2001 the Revised national tuberculosis control programme (RNTCP) was implemented in a target population of approximately 80,000, which includes the staff working in the hospital and their family members or dependants residing in AIIMS campus.

### Diagnosis

*Pulmonary Tuberculosis*

The essential basis of diagnosis of pulmonary tuberculosis was three sputum smear examinations for *M. tuberculosis* (two spot and one early morning sample) according to the RNTCP guidelines.

A faculty member in the central microbiology laboratory provided quality control of sputum microscopy by cross checking all (100%) sputum smear positives and 25% of sputum smear negatives.

The physician confirmed the diagnosis of tuberculosis in patients with two positive sputum smear specimens for acid-fast bacilli (AFB). They were further categorised as new (category I or category III) or old cases (category II) based on their treatment history as per the RNTCP criteria. If all the three sputum smear samples were negative for AFB and there was no response to one to two weeks of antibiotics, chest radiograph was taken and if consistent with TB, the patient was treated for smear negative TB. If only one of these samples was positive, chest radiograph was taken and patient was evaluated for pulmonary tuberculosis.

*Extrapulmonary Tuberculosis (EPTB)*

Extrapulmonary TB (EPTB) was diagnosed by the following criteria: *(i)* constitutional and organ specific clinical features depending upon the site of TB; *(ii)* radiographic features suggestive of TB; *(iii)* microbiological and /or histopathological diagnosis depending on the site (not an essential criteria for mediastinal lymph nodes and pleural effusion) and *(iv) a* satisfactory response to anti-tuberculosis treatment.

### Categorisation of Patients

Patients were categorised into various

treatment categories as per the RNTCP guidelines. Briefly, new sputum smear positive and seriously ill sputum smear negative pulmonary TB and extrapulmonary TB patients (Category I) were treated during intensive phase with four drugs: isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) for two months followed by continuation phase of four months of two drugs, H and R. New sputum smear negative pulmonary TB and not seriously ill extrapulmonary TB patients (category III) were treated during the intensive phase with three drugs, H,R,Z for two months followed by continuation phase of four months of two drugs, H and R. Previously treated patients (category II) were treated during the intensive phase with five drugs H,R,Z,E and streptomycin (S) of initial two months and one month with four drugs as previously mentioned except S, followed by the continuation phase of five months with H, R and E. Smear positive patients whose smear was positive at the end of intensive phase received another month of intensive phase treatment. During the intensive phase every dose was given thrice weekly on alternate days under direct observation. Medications for continuation phase were packaged into weekly blister pack, the first dose of which was given under direct observation. The empty blister pack was returned the following weeks as evidence that the patient had taken the medicines.

### Monitoring, Reporting, Follow up

Senior treatment supervisor (STS) and senior treatment laboratory supervisor (STLS) supervised the activity of the DOTS centre. Regular reporting was carried out every month to the State TB officer by the senior treatment supervisor. Patients were followed up as per RNTCP guidelines during the treatment.

## RESULTS

The programme began in the month of September 2001 and was restricted to employee health scheme (EHS) beneficiaries. Since September 2002 patients reporting to the other out-patient departments (OPDs) at AIIMS were also registered. From September 2001 to November 2002, 800 chest symptomatics were evaluated. Of these, 311 patients underwent sputum microscopy. Seventy-five of these patients were sputum smear positive (24.1%) for *M. tuberculosis* [24 of these 75 patients (32%) were referred to other DOTS centres for treatment and follow up]. The number of referrals as expected was high since AIIMS is a tertiary care referral centre and patients also come from far away locations.

Among 119 patients, who received treatment at the AIIMS DOTS centre, there were 48 females and 71 males, with a mean age of 33.75 (range 15-90 years). Fifty-one patients had smear positive pulmonary TB, 43 had smear negative pulmonary TB, and 25 had extrapulmonary TB. Categorisation of these patient is shown in table 1.

Out of 25 patients with extrapulmonary TB, 13 had lymph node TB, two had osseous TB, two had gastrointestinal TB, three had tuberculous pleural effusion and another five had genital TB. Of the 51 patients with positive sputum smears, 28 were also sputum culture positive. Three of 43 patients with smear negative pulmonary TB had positive sputum

**Table 1.** *Details of 119 patients diagnosed at DOTS Centre**

| Categories | Smear positive pulmonary TB | Smear negative pulmonary TB | Extra-pulmonary TB | Total |
|---|---|---|---|---|
| Category I | 38 | 19 | 16 | 73 |
| Category II | 13 | 8 | 2 | 23 |
| Category III | - | 16 | 7 | 23 |
| **Total** | **51** | **43** | **25** | **119** |

*A total of 168 patients were diagnosed as suffering from tuberculosis. Forty-nine patents were referred to other DOTS centres as they belonged to far off areas.

cultures (Table 2). In addition, 12 patients who were culture negative at the time starting the treatment developed positive cultures during treatment, seven in category I, three in category II and two in category III. Therefore, out of 93 pulmonary TB patients; both sputum positive and negative; 43(46.23%) patients had at least one positive culture for *M. tuberculosis.*

## Evaluation, Treatment Completion and Success Rate

At the time of writing this communication, 52 patients were still receiving treatment at DOTS centre. Hence, the treatment outcome has been evaluated for 67 patients who have completed treatment. Cure in pulmonary tuberculosis patients was assessed by bacteriological evidence of sputum conversion. In extrapulmonary TB patients, clinical response along with imaging modalities including ultrasonography, contrast enhanced computed tomography (CECT) were used to determine the response to anti-tuberculosis treatment.

Treatment success was achieved in 20/25 (80%) of new smear positive patients 21/22 (95%) new smear negative and 15/15 (100%) in extrapulmonary TB patients (Table 3). In the treatment category II (others), success was achieved in 3/5 (60%) patients and two patients defaulted.

*Defaulters*

Three patients (4.4%) defaulted during treatment. One was a new smear positive case (category I) who changed residence. Two patients in the re-treatment category (category II) also defaulted, one due to change in residence and the second patient discontinued as he was not convinced with DOTS regimens.

*Patients "transferred out"*

One patient (category I) was transferred to another DOTS centre. This patient is following up at the same DOTS centre.

*Treatment failure*

**Table 2.** *Details of culture reports (at month 0) of smear positive and smear negative pulmonary TB cases*

| Categories | Smear positive pulmonary TB (a) | Culture positive and smear positive pulmonary TB (b) | Smear negative pulmonary TB (c) | Culture positive and smear negative pulmonary TB (d) | Extra-pulmonary TB (e) | Total (a+c+e) |
|---|---|---|---|---|---|---|
| Category I | 38 | 19 | 19 | 1 | 16 | 73 |
| Category II | 13 | 9 | 8 | 0 | 2 | 23 |
| Category III | - | - | 16 | 2 | 7 | 23 |
| **Total** | **51** | **28** | **43** | **3** | **25** | **119** |

**Table 3.** *Results of treatment in 67 patients at DOTS Centre*

| Patients' features | No. of patients evaluated | Treatment successful | Died | Treatment failed | Defaulted | Transfer out | Per-centage (%) |
|---|---|---|---|---|---|---|---|
| New positive sputum smear | 25 | 20 | Nil | 3 | 1 | 1 | 80 |
| New negative sputum smear | 22 | 21 | Nil | 1 | Nil | Nil | 95 |
| Extrapulmonary TB | 15 | 15 | Nil | Nil | Nil | Nil | 100 |
| Other retreatment | 5 | 3 | Nil | Nil | 2 | Nil | 60 |
| **Total** | **67** | **59** | **Nil** | **4** | **3** | **1** | **88** |

Three patients were declared as treatment failure cases in category I, and were registered for treatment in category II, which is ongoing at present. One patient who failed treatment in category III, was smear negative at the time of diagnosis and subsequently became smear positive after five months of DOTS regimen. This patient is presently under category II treatment regimen.

*Side effects and hospitalisation*

Two patients receiving antituberculosis treatment at AIIMS DOTS centre became seriously ill. Both were hospitalised at AIIMS. After recovery one patient was transferred to another DOTS centre for further in-patient management and the other is still continuing treatment at the AIIMS DOTS centre. A small proportion of patients developed minor side effects during anti-tuberculosis treatment. The most common side effects were: itching (7) and vomiting (7) followed by tinnitus and giddiness (1), which were relieved by symptomatic treatment. Only one patient developed drug-induced hepatitis. This patient was hospitalised and managed with modified antituberculosis drug regimen. There was no recurrence on resumption of treatment.

## DISCUSSION

Tuberculosis remains the leading infectious cause of death in India, killing close to 500,000 people a year. India has far more cases of tuberculosis than any other country in the world, approximately two million new cases are added each year[1] which accounts for nearly one third of prevalent cases globally.

The Tuberculosis Research Centre, Chennai first documented the efficacy and safety of ambulatory treatment of tuberculosis[2]. The necessity, feasibility and long- term benefit of treatment supervision in community now called DOTS and effectiveness of intermittent regimens for treatment of TB were established in India[3,4]. However, over the years the principals of tuberculosis management which were discovered and established in India were not widely and adequately applied within India.

DOTS was launched in India in 1993 as a pilot project of the WHO. It is a component of RNTCP in India and has covered substantial area by now. DOTS centre at AIIMS was set up as a model centre to overcome the short-comings between knowledge and practice of medical and para-medical personnel, also to conduct operational research in collaboration with the national TB control programme.

The first year concluded with cure rates in sputum positive patients comparable to targets of RNTCP. In sputum negative patients and extrapulmonary tuberculosis, monitoring for outcome was based on a combination of clinical response and radiological investigations, and the treatment outcome has been consistently good based on these criteria. However, some extrapulmonary tuberculosis patients required extended treatment especially cases with bone tuberculosis (on the recommendation of orthopaedic surgeons). Even though the follow up period is too short to make an authoritative statement, no relapses were reported. Only 4.4% (3/67) patients defaulted. Following RNTCP recommendations, out of 168 patients diagnosed with TB, 75 smear positive patients were picked up (smear positive to smear negative ratio of 1.2:1), which reflects good diagnosis and programme implementation.

Our results showed that a high proportion of sputum positive patients yielded negative cultures. The reasons for this are unclear. The authors have noted that many of these patients had received fluoroquinolones, especially levofloxacin, gatifloxacin or ciprofloxacin, during the work up and management of their symptoms at first presentation and before the diagnosis of TB was made. In addition, many of these patients were diagnosed in various out-patient departments as TB case based on chest radiographs and were started on antituber-culosis therapy before being referred to DOTS centre for further management. Initiating potent antibiotics that have antituberculosis activity before collecting sputum for cultures could have been a reason for poor isolation on

culture. The bacilli on smear examination could have been dead bacilli. Moreover, 12 patients developed positive cultures on treatment, seven patients belonged to category I, three to category II and two to category III. Reasons of developing positive cultures during treatment though unclear could have been manifold. They can be classified as patient related and patient unrelated. Patient unrelated reasons could be: *(i)* cross contamination of samples during processing, *(ii)* contamination during collection and transport, *(iii)* quality control issues related to quality of tap water, reagents and culture media etc., (iv) labelling errors, and *(v)* poor quality of drugs. Patient related reasons that could have been responsible are: *(i)* inadequate absorption of drugs due to malabsorption, *(ii)* drug-drug interactions as many patients were taking medications for other medical problems and including some non allopathic medications, and *(iii)* irregular drug intake during the continuation phase even though the patients regularly picked up their weekly medications and took first dose of continuation phase under direct observation. The authors recommend that in addition to the DOTS recommendations, culture and sensitivity should be routinely carried out at least at tertiary care centres and medical colleges. This will enable a better diagnosis (smear negative but culture positive patients), and helps in early identification of drug resistance in patients. Moreover, it could be an early indicator of failure or drug resistance and large-scale studies are needed to confirm our findings. It is anticipated that early diagnosis and effective treatment of patients with drug resistance or treatment failure will help in reducing the transmission from these patients to the community.

## CONCLUSION

RNTCP has made impressive progress since its inception in terms of providing treatment to patients suffering from TB. Even though medical colleges were co-opted only during later stages of expansion, our results indicate that they are in unique position to contribute towards the programme and by conducting operational research can help in clarifying controversial issues which will lead to better utilisation of national resources. In addition, culture and drug sensitivity should be carried out on samples at least at medical colleges so that true incidence of new culture positivity at follow up can be estimated as it might be a marker of drug resistance, surrogate market for failure and indirectly of programme performance. We believe that this model DOTS centre should be replicated in medical colleges across India so that graduates can have hands on experience and resources are available to conduct operational research as relevant to tuberculosis control programme.

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ORIGINAL ARTICLE

# Intrapleural Streptokinase in Complicated Parapneumonic Effusions and Empyema

**M.S. Barthwal, R.B. Deoskar, K.E. Rajan and R.S. Chatterjee[1]**

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ABSTRACT

***Background.*** The management of complicated parapneumonic effusions (CPE) and empyema by chest tube drainage usually fails because of thick viscous fluid and multiple pleural space loculations. The use of intrapleural fibrinolytic agents facilitates pleural drainage and can obviate the need for more invasive surgical interventions in these types of effusions.

***Objective.*** To evaluate the role of intrapleural fibrinolytic therapy with streptokinase (STK) as an adjunctive therapy in the management of CPE and empyema.

***Material and Methods.*** Thirty patients of CPE and empyema were considered for intrapleural fibrinolytic therapy when the chest tubes / catheter drainage became insignificant (*i.e.*, less than 50 ml a day) and the tube was adequately positioned and patent. Intrapleural STK was administered eight hourly in the dosage of 2,50,000 IU in 50 ml of saline. The end points were volume of fluid drained and radiological resolution.

***Results.*** There were 24 (80%) patients with CPE and six (20%) with empyema, with a mean age of 35 years. The median of STK doses used were three in 26 (87%) cases and two in four (13%) cases. There was significant drainage (mean ± SD) 1094 ml ± 116 and radiological resolution in 26 (87%) cases. The only complication observed was transient chest pain in one and fever in two patients.

***Conclusion.*** Intrapleural fibrinolytic therapy with STK is a safe and effective adjunctive therapy in the management of CPE and empyema.

***Key words:*** *Complicated paraneumonic effusions, Empyema, Intrapleural streptokinase.*

***[Indian J Chest Dis Allied Sci 2004; 46 : 257-261]***

## INTRODUCTION

Pneumonia is complicated by the development of parapneumonic effusions in about 36-57% of cases[1,2]. A parapneumonic effusion, if not treated timely with appropriate antibiotics, may ultimately lead to the development of complicated parapneumonic effusion (CPE) and empyema. The drainage of these types of effusion by standard chest tubes or small bore radiologically guided catheters usually fails because of thick viscous fluid and multiple pleural space loculations[3,4]. In case of failed drainage, the other modalities of treatment

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available are video assisted thoracoscopic surgery (VATS) or more invasive surgery in the form of empymectomy and decortication. Intrapleural fibrinolytic agents in the form of streptokinase (STK) or urokinase (UK) used as an adjunct in the management of CPE and empyema have shown encouraging results in various case series[5] and randomised controlled trials[6-8]. The early use of fibrinolytic agents decrease viscosity, breaks loculations and early pleural peel, thus resolving the pleural sepsis and avoiding more invasive surgical interventions. There are only a few case reports[9-11] and one controlled trial[8] from India on the use of this form of therapy. The present study was undertaken to evaluate the role of intrapleural fibrinolytic therapy as an adjunctive measure in the management of complicated parapneumonic effusions and empyema.

## MATERIAL AND METHODS

The study was conducted in two tertiary respiratory centres of service hospitals from June 2000 to May 2002. All cases of community acquired pneumonia with parapneumonic effusions were included in the study. All were subjected to a detailed history and clinical examination with special emphasis on the duration of symptoms and the presence of free or loculated effusion. The investigation included blood count, sputum microbiology, chest radiology, postereo-anterior, lateral and decubitus views, wherever indicated. Ultrasonography of chest was done in all the cases but computed tomography was performed in selected cases to look for the presence of septations/loculations, fibrin strands, pleural thickening and to quantify the size of the effusion.

Diagnostic aspiration was performed in all the cases. When the pleural fluid was clear or slightly turbid, examination consisted of cytology, biochemistry including sugar and lactate dehydrogenase (LDH), pH analysis and bacteriological examination. In case of frank pus, fluid was sent only for bacteriological examination. Complicated parapneumonic effusion (CPE) was defined by the presence of loculation/septations or fibrin strands on ultrasonography or computed tomography and one or more of the following criteria: (*i*) pH < 7.0, (*ii*) sugar < 40 mgm%, and *(iii)* LDH > 1000 IU/L. This was consistent with complex complicated parapneumonic effusion as defined by Light[12]. Empyema was defined by the presence of thick purulent appearing fluid as defined by Light[12]. All cases of CPE and empyema underwent pleural space drainage using either standard chest tubes (24-30F) or pigtail catheters (8-14F). The standard chest tube was preferred in all the cases of empyema, all cases of CPE with turbid fluid while pigtail catheters were used in cases of clear fluid and wherever the largest loculation was located posteriorly. Bed-side drainage was performed in cases of free flowing fluid and image guided in cases of multiloculated effusions. The patency of chest tube was checked twice daily and the pigtail catheter was flushed with saline three times daily to maintain its patency. The antibiotics were initially used empirically and later modified as per the culture sensitivity report, wherever available.

When the chest tube drainage became insignificant (less than 50 ml per day), the chest tube was patent, properly positioned and ultrasonography revealed still significant amount of pleural fluid, it was decided to initiate intrapleural fibrinolytic therapy with streptokinase (STK). The contraindications in the form of bleeding diathesis, stroke or significant haemorrhage in the preceding six months and the use of STK by any route in the previous two years were ruled out before starting the therapy. Baseline and 24 hours post-STK prothrombin time (PT) and partial thromboplastin time (PTT) were initially done in 10 cases but in view of no significant change in coagulation parameters the same was not done in rest of the cases. Premedication with injection hydrocortisone 200 mg intravenous and injection phenergan 25 mg intramuscular, was given in all the cases. The dosage schedule followed was 2,50,000 IU of STK dissolved in 50 ml of normal saline eight-hourly through chest tube or pigtail catheter. The tube was clamped

for two hours after each dose of STK.

The total net pleural fluid drainage after intrapleural STK till the removal of chest tube was noted. Chest radiology was initially done 48 hours after STK therapy and subsequently depending upon the response to therapy. The criteria used for radiological improvement were as described by Sanchez *et al*[13]. These were: maximum (normal or near normal chest radiograph); moderate (a clearance of 50 to 80% of pleural effusion); minimal (<50% clearance); none (no change). Fibrinolytic therapy was discontinued if after two doses of STK there was no significant drainage and repeat ultrasonography or computed tomography of chest showed multiple loculations and significant pleural thickening. The patients were closely monitored for side effects. The criteria for successful outcome were the volume of pleural fluid drained and the radiological resolution. All values were expressed as mean ± SD.

## RESULTS

There were 30 patients (27 males and 3 females) with a mean age of 35 years (range 20 to 65 years). The youngest patient was a two-year-old child. Bed-side unguided pleural space drainage was performed using conventional chest tubes (24-30F) in 22 (65%) cases that included all six patients with empyema and 16 cases of CPE. Drainage with radiologically guided pigtail catheters was performed in rest of the cases.

The median of STK dose used was 3 in 26 cases (86%) and only two doses were required in four (14%) cases. There was a significant drainage of fluid in 26 cases (1094 ± 116 ml). Out of these 26 cases there was maximum radiological resolution of effusion in 22 cases and moderate resolution in four cases. The remaining four cases who had insignificant drainage (325 ± 111 ml) and minimum radiological resolution were subjected to decortication and empymectomy. The only side effects noticed were mild chest pain in one and transient low grade fever in two cases.

## DISCUSSION

Intrapleural fibrinolytic therapy using streptokinase (STK) and deoxyribonuclease (streptodornase) was first used by Tillett, Sherry and Co-workers[14-16], followed by others[17,18]. All these workers reported excellent results. However, the therapy was later almost abandoned because of systemic side effects, in the form of febrile reactions, general malaise and leukocytosis noted in high percentage of patients by all the authors[19]. These systemic side effects were attributed to contaminants in the relatively crude preparations of fibrinolytic agents. The therapy was revived in 1977 by Bergh and Co-workers[19], who used purified streptokinase in 12 patients with empyema, out of which 10 patients showed significant radiological improvement with minimum side effects. Since then, the use of STK in CPE and empyema with successful outcome has been shown in many uncontrolled case series[5], with most of these having small number of patients but at least three of them [13,20,21], having more than 20 patients. In all these studies, the indication for intrapleural STK was a failed chest tube drainage, dose of STK used was 2,50,000 IU in 50-100 ml of saline with a clamping time of 2-4 hours, number of doses used were two to ten and success criteria were volume of fluid drained and radiological resolution. The average success rate in these case series was 67 percent to 100 percent. Till date, there have been three randomised controlled trials of intrapleural STK. In the first trial by Davies *et al*[6], three daily doses of intrapleural STK were compared with saline flushes in 24 patients (13 with empyema and 11 with CPE). The STK group had significantly greater drainage of pleural fluid and radiological resolution. In the second study by Chin *et al*[7], intrapleural STK was compared with chest tube drainage in 52 patients (40 with empyema and 12 with CPE). A significantly larger volume of pleural fluid drained in the STK group. In a recently published study by Talib *et al*[8], there was significant drainage with intrapleural STK in 24 cases of chronic tubercular empyema as compared to controls treated with saline. The

success rate of 87% in the present study is similar to the one observed in the previous studies.

In the present study, the dosing schedule of STK was different from all other studies. We had to resort to an 8-hourly schedule instead of a 24-hourly schedule followed in previous studies, because of the following reason. The minimum strength of STK freely available in India is 7,50,000 IU and once the vial is reconstituted the solution can be stored only for eight hours at 2-8 °C. By adopting this regimen we could at least utilise two doses, thereby minimising the wastage of this costly drug and at the same time maintaining its potency. The same dosing regimen was used in cases reported earlier from this country[9-11]. However, Strange *et al*[22] in an experimental study demonstrated that increasing the dosing interval might in fact increase the efficacy of fibrinolytic therapy. The wide variation in the number of doses of STK required in the present study and other studies may be due to the initiation of therapy at different stages of evolution of the para-pneumonic effusion. The early initiation of fibrinolytic therapy, before the development of severe pleural adhesions may lead to a more effective pleural drainage as has been demonstrated in an experimental study[23] and in a study by Boures *et al*[24]. It is likely that the excellent success rate in our study was due to early initiation of therapy, as the four cases which had not shown significant response had an interval of more that eight weeks between the onset of symptoms and the initiation of fibrinolytic therapy. The fibrinolytic therapy has no systemic fibrinolytic effect[25]. We also observed no significant change in the coagulation parameter before and after STK therapy in the first 10 cases. Hence the same was not done in rest of the cases.

There were no significant side effects observed during fibrinolytic therapy. This has been observed in majority of the previous studies too. The alternative fibrinolytic agent, UK, has also been used successfully in the doses varying from 50,000 to 2,50,000 IU[5]. As compared to STK, it has the advantages of being non-antigenic and freely available in the required strength but it has the disadvantage of being more expensive.

To conclude, the present study supports the usefulness of intrapleural streptokinase as an adjunctive therapy in the management of CPE and empyema. It is safe, easily administered, and without any significant side effects. The early use of fibrinolytic therapy can avoid the use of more invasive surgical intervention in most of the cases.

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ORIGINAL ARTICLE

# Development of a Computer Software for Easy Storage and Analysis of Fibreoptic Bronchoscopy Data

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ABSTRACT

***Objective.*** To develop a simple software for management of fibreoptic bronchoscopy records. ***Methods.*** After identification of the specific needs at our hospital, a software was developed. A graphical interface with structured data entry related to patient information and diagnosis, bronchoscopic findings and specimens obtained, and their reports were envisaged. After initial construction, the software was tested over a four-week period. The software was put to routine use after necessary corrections, and validated over the next few months through actual data entry.

***Results.*** The software has various modules for input and modification of data, as well as for generation of reports, and can work both on stand-alone personal computers and on networks. With little practice, residents soon became adept at entering details correctly and quickly. The slightly increased time of data entry into the computer was more than made up by uniform and complete report generation. The database component was evaluated by analyzing 1000 consecutive records entered over a 14-month period, and no discrepancies were observed.

***Conclusion.*** A user-friendly software providing uniform and complete data entry regarding fibreoptic bronchoscopic procedures was developed.

***Key words:*** *Computer programme, Database, Data analysis, Fibreoptic bronchoscopy.*

***[Indian J Chest Dis Allied Sci 2004; 46 : 263-267]***

## INTRODUCTION

The role of computer based information systems has considerably increased in clinical practice in the last decade. However, the use of such systems in medical endoscopy is still not widespread. Several computerized endoscopic medical record systems are commercially available for gastrointestinal endoscopy[1]. In addition, comprehensive systems customised to specific needs have also been developed[2]. The use of such systems in bronchoscopy is, however, not widespread[3,4]. Even among the existing endoscopic databases, questions regarding the role of structured data *versus* free text input, standardisation of nomenclature, and compatibility with other systems, are hotly debated. We describe the development of a simple software for management of bronchoscopy records, which attempts to resolve some of these issues.

The software described herein was specifically designed to meet the requirements of the

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bronchoscopy programme of a tertiary referral and teaching hospital with a high volume of procedures. Only a few softwares tailored to suit requirements of bronchoscopy units have been described in the past. One of these was developed using dBASE language and provided reporting and auditing facilities[3]. Another software (Endotrace) was written in COBOL language and used different hierarchical modules with both structured data entry and free text options[4]. Although using entirely different programming techniques, this software is in principle quite similar to the one that we have developed.

## MATERIAL AND METHODS

### Requirements

The central objective of this project was to create a data model capable of accurately representing commonly encountered broncho-endoscopic observations in a computer-suitable format. Our main requirements included that the system should *(a)* be simple enough to be directly operated by the physician(s) in bronchoscopy room, *(b)* run on personal computers, *(c)* allow comprehensive data entry conforming to well recognised nomenclature and covering all bronchoscopic procedures which are currently carried out, *(d)* generate a printed report, *(e)* allow modification and update of data at a later date, and *(f)* permit subsequent statistical analysis of records in a tabular format. As medical data were to be handled by physicians with minimal previous computer experience, an emphasis was laid on a user-friendly interface.

### Software Construction

The software was written in Visual Basic 6.0 (Microsoft Corporation, USA) and generated a series of successive screens for data entry. Three screens, relating to *(a)* patient characteristics, indication for procedure and radiological data, *(b)* endobronchial abnormalities and *(c)* diagnostic specimens, were envisaged. Data flow was designed in two directions: *(a)* to a database, after appropriate coding, for storage and subsequent analysis at a later date, and *(b)* to the report generator. An additional module was included to allow modification and update of previously recorded data. Another module was designed for filling microbiological and pathological reports on specimens obtained during the procedure, as and when these results became available. A unique bronchoscopy number assigned to each patient was to be used as a primary identifier throughout the record.

### Data Entry

Modules were developed to allow easy user access and facilitate data entry. On completion of one module, automatic transfer to the subsequent module was envisaged. The basic module was structured as a large window, with smaller sub-windows appearing only on demand. The entire software was kept menu driven, with a simple and consistent hierarchical structure. As far as possible, all fields were structured, with the user allowed to choose one or more options from a previously prepared list of choices. These options included important and/or commonly observed conditions, and were chosen to cover majority of everyday findings after consulting experienced faculty members and reviewing previous bronchoscopy records. A standard terminology was developed for the structured items based on available literature and general consensus. The fixed choices were displayed either as searchable list boxes, check boxes, or as radio buttons. Free text was allowed in some fields, such as those recording the name of the patient, or the information beyond the fixed choices available to the user. To allow complete data acquisition in each patient, all data fields were marked mandatory, and the user was not allowed to proceed to a subsequent field without recording data in such fields.

### Debugging and Modification

After initial development, the software was tested over a four-week period by input of bronchoscopy data. An attempt was made to rectify problems faced initially by the users.

Opinion was sought from residents and faculty members regarding possible modifications and improvements. Inconsistencies in the programming script, which gave rise to error messages during operation of software, were corrected. Finally the software was put to routine use.

**Software Validation**

To evaluate the actual utility of the software, all consecutive bronchoscopy records were entered using this computer software. Physicians in the department and elsewhere in the hospital were asked to assess the overall quality of the reports and the content of information. After entry of data for 1000 consecutive bronchoscopic procedures, these details were subjected to statistical analysis to evaluate the robustness of the database component.

## RESULTS

The computer software currently used has five modules for data input: *(a)* patient information, *(b)* endobronchial abnormalities, *(c)* specimens obtained, *(d)* modifications to any of the previous modules, and *(e)* specimen report entry. The data is linked to a Microsoft Access project having a set of three databases related to *(a)* patient information, *(b)* bronchoscopic abnormalities, and (c) specimens obtained and their reports. The three databases are linked to each other using the unique bronchoscopy number. Another module deals with screen preview of reports and generation of printed reports.

In the patient information module, the bronchoscopy number identifies each case record uniquely. The date of procedure is automatically derived from the system date maintained by the computer clock, but can be changed manually. The user has to enter the patient's name, chest clinic and / or hospital registration numbers, age, gender, name of the referring consultant, and radiological abnormalities. Up to two disorders can be selected out of the list of indications of bronchoscopy. In case an indication is not listed as a choice, the user can select 'miscellaneous' from the list, and can enter the indication as free text. He then indicates whether the bronchoscopic examination was normal or abnormal, and also mentions complications of procedure, if any. In case the bronchoscopic examination was normal, the user is transferred directly to the 'specimen' module, otherwise to the 'abnormalities' module.

In the 'abnormalities' module, the user first selects vocal cord abnormalities, if any. He then records the endobronchial abnormalities. The possible locations in the bronchial tree are represented by a cascading hierarchy of tables. In the primary table, trachea, both main bronchi, and all the lobar bronchi are listed. On selection of any of these sites, an additional table listing the appropriate divisions / segments appears. After selection of the proper site, the user can select the abnormality seen from another list of options. These segments and abnormalities have been named as per the standard nomenclature. The user can select up to four sites and up to four abnormalities for each site. On completing this module, he is transferred to the specimen module, where he selects the specimens obtained, if any.

On completion of data entry, the user is transferred to the print module, where he can preview the report prior to printing. The printed report contains all the information entered in the database. It also contains a standard set post- procedure instructions for the patient, and also has space for signatures for the resident and consultant carrying out the procedure.

Problems initially faced by users were primarily related to data entry. Residents, not having any working knowledge of computers, encountered problems such as a slow speed of data entry and failure to enter data in mandatory fields (with a consequent error message that did not allow the user to proceed further without rectifying the mistake). With little practice, they became adept at entering details correctly and quickly. Almost all the physicians reported a slightly increased time of

data entry into the computer, in comparison to writing reports on a standard printed proforma. However, all agreed that the report and data generated through the software were uniformly complete, and more than made up for the extra time spent. The new report has a uniform and easily understood structure, and is free of any inadvertent omissions.

The database component was evaluated by analysing 1000 consecutive records entered over a 14-month period. Statistics were generated on the demographic variables, indications for bronchoscopy, proportion of abnormal records, sites of broncho-endoscopic abnormalities, nature of endobronchial lesions, and complications. Data access and analysis were easily and quickly performed. Data were found to have been completely transferred from data entry screens to the database and no missing values were encountered.

## DISCUSSION

Structured input and free-text input represent two fundamentally different ways of entering data into a computer. Initial reports of endoscopic databases relied heavily on text based tools. Such input facilitates personalised style and flexibility in description of abnormalities, and generates a well readable report. However, free-text input weakens the utility of the database, as it is not suited to subsequent analysis. Structured input and the resulting categorical data offer an important advantage in this regard. Data thus entered is more likely to be complete and is well suited for research and analysis, as well as for the generation of administrative reports and for quality control. It has been estimated that use of computerised endoscopic records improves completeness of data entry by more than 50 per cent[5]. However, a major trade-off for structure is flexibility. We therefore used a basic structured data entry protocol, supplemented by use of free text only under special situations.

Experience with previously designed bronchoscopy software has shown that the reporting procedure is slightly lengthened using computerised data entry[3]. This increase in time is variable. Besides operator related factors, it is related to the amount of free text entered and the number of tables accessed during structured data entry[4]. However, the additional effort is rewarded by a more comprehensive and accurately documented report, and constant availability and better management of clinical and bronchoendoscopic data[3,4].

A major feature of the software is the powerful database component. We had laid particular stress on this aspect in view of the stress on academic and research activities at our hospital. This portion of the software has been built as a set of three interrelated databases in Microsoft Access, which can easily handle large databases (and is thus suited to the volume of bronchoscopic procedures performed at our department) and also offers a wide range of analytical tools through a versatile query system. We have evaluated the robustness of this module of the software through an analysis of 1000 consecutive bronchoscopy records. Although such analysis requires some working knowledge of the database system, it is easy of learn. No data was lost and statistical analysis could be easily performed.

Both user-friendliness of the software and completeness of data entry are critical to the success and acceptance of such a software. We allowed easy integration of buttons, text boxes, check boxes and fields for free text to achieve this end. The format for data input was optimised through continuous interaction between clinicians and the programmer. Residents and other physicians were involved early and frequently during the development of the software, so that they were able to contribute ideas and advice. The software has now been under routine use for over a year, and has performed well in areas of data entry, report generation and data analysis. Successful development and routine application of the database is, however, only a short-term achievement. More importantly, continuous improvements need to be made as and when new areas emerge. The system is adaptable and capable of keeping pace with new technological advances.

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# National College of Chest Physicians (India) — NAPCON 2004

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|---|---|---|
| *Postgraduate Courses-cum-Workshop* | : | *November 16-17, 2004* |
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REVIEW ARTICLE

# Lung Cancer in India

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ABSTRACT

***Background.*** Lung cancer is one of the commonest malignant neoplasms all over the world. It accounts for more cancer deaths than any other cancer. It is increasingly being recognized in India.

***Methods.*** We did a systematic review of the published studies on epidemiology, diagnosis and treatment of lung cancer in India. Literature from other countries was also reviewed.

***Results.*** With increasing prevalence of smoking, lung cancer has reached epidemic proportions in India. It has surpassed the earlier commonest form of cancer, that of oropharynx, and now is the commonest malignancy in males in many hospitals. In addition to smoking, occupational exposure to carcinogens, indoor air pollution and dietary factors have recently been implicated in the causation of lung cancer. Squamous cell carcinoma is still the commonest histological type in India in contrast to the Western countries, although adenocarcinoma is becoming more common. Molecular genetics of lung cancer has opened up new vistas of research in carcinogenesis. Various modalities for early detection through screening are being investigated. Majority of the patients have locally advanced or disseminated disease at presentation and are not candidates for surgery. Chemotherapy applied as an adjunct with radiation improves survival and the quality of life. New anticancer drugs, which have emerged during the last decade, have shown an improved efficacy- toxicity ratio.

***Conclusions.*** In view of our large population, the burden of lung cancer will be quite enormous in India. Drastic measures aimed at discouraging people from smoking must be taken to reduce the morbidity and mortality due to lung cancer.

***Key words :*** *Lung Cancer, Epidemiology, Smoking, Air pollution, Chemotherapy.*

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## INTRODUCTION

Lung cancer was considered to be rare in the beginning of the century[1] but has now reached almost epidemic proportions. It is the leading cause of cancer deaths in developed countries and is also rising at alarming rates in developing countries[2]. Deaths due to lung cancer are more than those due to colorectal, breast and prostate cancers put together. Incidence and mortality from lung cancer in females is rising while it is declining in males in developed countries. This is the single most devastating cause of cancer-related deaths[2] with

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approximately 1.5 million cases world-wide and more than 1.3 million cancer-related deaths in 2001. The five-year survival rate for lung cancer has improved only marginally from 5% in the late 1950s to 14% by 1994. This is in contrast to the five years survival rate of 52% for some other cancers. Lung cancer is responsible for about one million deaths per year at present and it will rise to three millions per year by the year 2010.

## WORLD SCENARIO

There is a great variation in the prevalence of lung cancer in different geographical areas. Nearly 70% of all the new cases of lung cancer in the world occur in the developed countries[3]. USA, Canada, New Zealand (Maori population) and Europe have the highest incidence (>50 per $10^5$ population) followed by China, Ireland, Malta, Spain, Australia, and New Zeland (non - Maori population) with a moderate incidence (35-50 per $10^5$ population) and low incidence (<35 per $10^5$ population) countries include Utah (USA), Latin America, most Asian countries, lceland, Norway and Sweden[4]. This is the most frequent tumour in males, and 2nd or 3rd most common in females. In the US alone, there were about 1,64,100 new cases in 2000, of which 70, 000 were in the metastatic stage (stage IV) and another 70,000 were locally advanced (stage IIIA and IIIB disease)[2]. In the European Union, the crude incidence of lung cancer is 52.2 cases per $10^5$ per year and the death rate is 48.7 per $10^5$ per year. For men, the rates are 79.3 and 78.3 and for women, 21.6 and 20.5 respectively per $10^5$ per year. Non-small cell lung cancer accounts for about 80% of all lung cancer cases[5,6].

The incidence rates in France are close to the average rates observed in Europe. Between 1985 and 1995, as a result of changes in tobacco consumption, the incidence rates increased by 56% in women and by 5% in men under the age of 65. In 1995, lung cancer led to 23,900 deaths in France (mortality rate standardised to Europe: $36.6/10^5$). Eighty-five percent of deaths due to lung cancer occurred among men. Prognosis of lung cancer remains poor and has not improved appreciably over the last few decades. Fifty-eight per cent of all patients died during the first year and 82% during the three years following the diagnosis[7].

During 1977-86, the incidence and mortality of lung cancer ranked first among cancers at all sites in Beijing and has been on the increase from year to year[8]. The annual average crude incidence rate of cancer was $31.3/10^5$ in males during 1982-84 compared to a world standard rate of $33.0/10^5$. Incidence due to lung cancer accounted for 20.3% of all male cancer cases. The crude incidence rate was $22.8/10^5$. Incidence due to lung cancer accounted for 16.1% among all female cancer cases. Female mortality rate due to lung cancer in Beijing is the highest compared to other countries of the world.

Janssen-Heijinen *et al*[9] did a survival analysis of 173,448 lung cancer cases diagnosed between 1985 and 1989 in 44 population-based cancer registries, participating in the EUROCARE study in Europe. Relative one-year survival rates for patients with lung cancer varied from 24% to 40%, being the highest in Finland, France, the Netherlands and Switzerland and lowest in Denmark, England, Poland and Scotland. Half of all the patients under the age of 45 years died within one year of the diagnosis, increasing to almost 80% for those aged 75 years or older. Whilst the prognosis for patients with non-small cell carcinoma remained more or less constant between 1978 and 1989 (25% in Denmark and 44% in Finland), that for patients with small cell carcinoma improved slightly, especially in the Netherlands and Switzerland. A fairly large variation in lung cancer related survival rates existed between European countries. The most likely explanation for the differences is the variation in access to specialised care. Except for a slight improvement in short-term survival for patients with small cell lung cancer, survival has remained poor since 1978.

Retrospective analysis of data from the New South Wales Cancer Registry and Australian Bureau of Statistics population data for NSW for 1985-1995 revealed that increased smoking

cessation has halved lung cancer rates in men. The distribution of histological subtypes of lung cancer in women was different from that in men[10]. In a large series of autopsy cases of lung cancer in 41,988 males and 13,818 females consecutively registered between 1958 and 1987 in Japan, the percentage was found to be 9% for males and 5% for females. The percentage of lung cancer cases among all malignant tumours was about 17% for males and 9% for females. Among fatal malignant tumours, gastric cancer and lung cancer showed the highest frequency. The relative incidence of gastric cancer was seen to decrease, whereas that of lung cancer was observed to increase. Of the histological types of lung cancer in both sexes, adenocarcinoma was the most frequent, followed by squamous cell carcinoma. During the period studied the peak age of patients with lung cancer shifted from the seventh to eighth decade, and a significant elevation of mean age was demonstrated for all of the major histological types in both the sexes. The male to female ratio for all lung cancer cases was 3.0, which was much lower than those for the United States and Europe, but very similar to the ratios of mortality statistics in Japan and other Asian countries[11].

Some of the increases compared to that prior to 1950, may be due to improved diagnosis but changes more recently reflect an actual increase. In 1980, it was estimated to cause 15.8% of all new cancer cases in males varying between 4.5% in Africa to 23.3% in Europe. In females lung cancer is rare. However, the increase between 1975 and 1980 was 10.1% in males, but 16% in females. The situation was different in 1985. Ignoring the non-melanoma skin cancers, lung cancer was estimated to be the most common cancer in men in the world around 1985. It comprised 17.6% of all new cancers in men and 5.8% in women. In men there were about 667,000 new cases in 1985, and 219,000 in women[12-15]. The age adjusted mortality trends in 14 countries show that the increase is universal, at rates between one to five percent a year. Although the overall mortalities are less in females, marked increases have been seen in some countries, such as Canada, Denmark, and USA.

## INDIAN SCENARIO

Lung cancer was initially thought to be infrequent in India[16]. Lung cancer constituted 14.4% of all cancers in a review of 9210 consecutive autopsies by Banker[17]. Sirsat[18] reported that lung cancer formed one per cent of all cancers in Tata Cancer Hospital. Viswanathan *et al*[19] collected information from different hospitals of the country and found that the incidence of lung cancer in hospital population was 27.4 per million in 1950 and in 78.6 per million in 1959. They also found an increase in the incidence of bronchogenic carcinoma (16.1 in 1950 to 26.9 in 1961 per 1000 malignancies), following analysis of the records of 15 teaching institutions in India over a period of 10 years. According to Wig *et al*[20], lung carcinoma was a frequent diagnosis amongst all types of chest diseases. The survey conducted in Uttar Pradesh in 1966 by Misra and others showed that the incidence was 4.2 per 10,000 hospital admissions and 2.1 per cent of all malignancies[21].

The National Cancer Registry Programme of the Indian Council of Medical Research, which collected data from six different parts of the country, both rural and urban areas, showed varying figures in different areas[22]. While cancer of the trachea, bronchus and lungs was the most common form of malignancy in males in 1989 from Bombay, Delhi, and Bhopal, it was the second most common in Madras and third in Bangalore, and was most unusual in Barshi, a rural area. The disease was uncommon in females and only in Bombay it was the sixth common malignancy while in Bhopal, it was the seventh in rank. International comparison of incidence rates of lung cancer with that seen in India showed a low figure (age adjusted rates of 66.5-100.4 in Europe and USA *versus* 2.0 to 14.6 per $10^5$ in India males; the same is 16.1 to 33.3 *vs* 0 to 3.7 in females). However because of the overall population size, the absolute number should be large.

Hospital data from different parts of the country has also shown different patterns. Behera and Kashyap[23] analyzed the pattern of malignancy in patients admitted to PGIMER,

Chandigarh from 1973 to 1982 and found that of the 223,930 hospital admissions, there were 863 lung cancer cases (0.38%). Lung cancer was the fifth common cancer after lympho-reticular malignancy carcinoma cervix, oropharyngeal cancer and carcinoma of breast. The total number of lung cancer admissions steadily rose from 1973.

As of 1st July 2002 a total of 41,000 cases of lung cancer would have been diagnosed for that year in India as per the ICMR data from its Cancer Registry[22]. Table 1 summarizes the published data on lung cancer from different parts of India[19-21, 24-46]. Jindal and Behera have reported the largest series of 1009 lung cancer cases[38]. They reported that both the mean and peak ages of lung cancer were lower compared to the West (54.3 years). The smoker to non-smoker ratio was 2.7:1. However, the smoker to non-smoker ratio is high, up to 20:1 in some other studies. Up to 40 years of age small cell type predominates and has a weaker association with smoking. After the age of 40 years squamous cell type is the commonest type in smokers and adenocarcinoma, in non-smokers[47-51]. When the cases reported from India before 1985 are compared with those reported after 1985, a marginal increase was seen in frequency of adenocarcinoma (Figures 1 and 2).

Table 2 shows the demographic data of lung cancer patients from all the Indian studies divided broadly into two groups, *i.e.* studies before and after 1985. Lung cancer has remained predominantly a disease of males with a male-

**Table 1.** *Comparative clinical features and cell type patterns in different Indian studies*

| Authors | Total | M:F | Age (yrs) | Sm:NS | Squam | Anapla | Adeno | Uncla |
|---|---|---|---|---|---|---|---|---|
| 1. Viswanathan *et al*[19] 1962 | 95 | - | - | - | 50.5 | - | 28.4 | 21.1 |
| 2. Wig *et al*[20] 1961 | 65 | 4.9 | 55.8 | - | - | - | - | - |
| 3. Basu *et al*[21] 1971 | 24 | 7 | 48.3 | 5 | 62.5 | 8.3 | 25 | 4.2 |
| 4. Sinha[24] 1961 | 33 | 4.5 | 57.1 | - | - | - | - | - |
| 5. Karai *et al*[25] 1967 | 100 | 24 | 52.1 | - | 41 | - | 20 | 39 |
| 6. Shankar[26] 1967 | 20 | All M | 54 | 5.7 | 73.3 | 6.7 | 20 | - |
| 7. Nagrath *et al*[27] 1970 | 35 | 4 | 47.7 | 1.9 | 25.7 | - | 34.3 | 40 |
| 8. Reddy *et al*[28] 1970 | 46 | 6.4 | 50 | 0.1 | 50 | 25 | 25 | - |
| 9. Guleria *et al*[29] 1971 | 120 | 7.6 | 57.2 | 2 | 46.2 | 36.5 | 17.3 | - |
| 10. Jha *et al*[30] 1972 | 25 | 2.9 | 46.6 | 5.3 | 44 | 20 | 20 | 20 |
| 11. Nafae *et al*[31] 1973 | 25 | All M | 51 | 7.3 | 56 | 20 | 12 | 12 |
| 12. Malik *et al*[32] 1976 | 136 | 5.2 | 48.5 | 3.5 | 40.4 | 21.3 | 16.9 | 7.3 |
| 13. Narang *et al*[33] 1977 | 58 | 8.7 | 51.3 | 4.8 | 37.9 | 51.8 | 10.4 | - |
| 14. Jindal *et al*[34] 1979 | 150 | 5.5 | 51.7 | 2.4 | 32.5 | 19.3 | 15.8 | 21.9 |
| 15. Notani *et al*[35] 1974 | 520 | - | - | 3.9 | 27.5 | 11.3 | 7.3 | 53.4 |
| 16. Garg *et al*[36] 1973 | 82 | - | - | - | 46.3 | 28 | 20.7 | - |
| 17. Malhotra *et al*[37] 1986 | 70 | 7.8 | 49.6 | 4.8 | 50 | 17 | 14.3 | 17.1 |
| 18. Jindal and Behera[38] 1990 | 1009 | 4.5 | 54.3 | 2.7 | 34.3 | 27.6 | 25.9 | 12.2 |
| 19. Arora *et al*[39] 1990 | 100 | 4.05 | 40-60 | 1.2 | 27 | 1 | 21 | 41 |
| 20. Rao *et al*[40] 1992 | 539* | - | - | - | - | - | - | - |
| 21. Rajasekaran *et al*[41] 1993 | 232 | 7.9 | 53 | 2.7 | 72 | 4.3 | 3.9 | 15.1 |
| 22. Gupta *et al*[42] 1998 | 279 | 7.41 | 56.7 | 4.5 | 42.3 | 32.2 | 19.9 | 5.6 |
| 23. Thippanna *et al*[43] 1998 | 160 | 8.4 | 40-60 | 4 | 67.5 | 8.8 | 18.7 | 5.1 |
| 24. Arora *et al*[44] 1998 | 200* | - | - | - | - | - | - | - |
| 25. Gupta *et al*[45] 2001 | 265 | 7.8 | 50-70 | 3.6 | 60 | 21.5 | 16.2 | 2.3 |
| 26. Kashyap *et al*[46] 2001 | 638** | 6.17 | 54.6 | 2.4 | 58.3 | - | 10.81 | - |

*Data described only for those below 40 years of age; **:Personal communication. Data reported for 281 cases of *bidi* smokers, quoted in Ref No. 46; M:F=Male: Female; Sm: NS=Smoker: non-smoker; squam=Squamous cell carcinoma; Adeno=Adenocarcinoma; Anapla=Anaplaste carcinoma; Uncla=Unclassified.

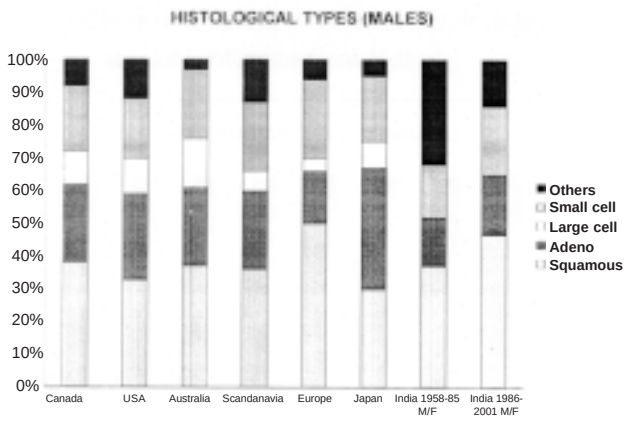


**Figure 1.** Distribution of histological types of lung cancer in males in various countries[1,16,18-51].
***Sex-wise data on histological types in Indian patients is not available. Therefore, it is shown as combined data for males and females***

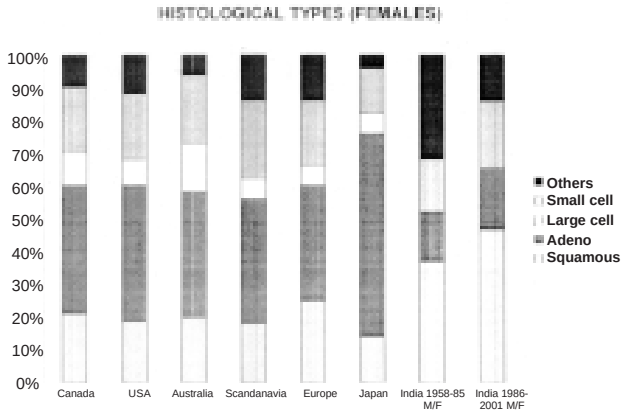


**Figure 2.** Distribution of histological types of lung cancer in females in various countries[1,16,18-51].
***Sex-wise data on histological types in Indian patients is not available. Therefore, it is shown as combined data for males and females***

to-female ratio ranging from 5.76:1 to 6.67:1. The mean age was 54.6 years in males and 52.8 years in females which has remained more or less the same over the years[38]. Around 80% of lung cancer patients come from the rural areas. The demographic pattern of lung cancer in India is similar to that observed in Western countries 40 years ago. Forty per cent of patients of lung cancer are less than 50 years of age and 11% are less than 40 years.

## SMOKING AND LUNG CANCER IN INDIA

Smoking is the most important contributory factor in the causation of lung cancer[52]. In patients with lung cancer a history of active tobacco smoking is present in 87% of males and in 85% of females. History of passive tobacco exposure is found in only three per cent.

**Table 2.** *Summary of demographic data of lung cancer reported from Indian studies[18-51]*

| Details | 1958-1985 | 1986-2001 |
|---|---|---|
| Total cases | 1735 | 2973 |
| M:F | 6.67:1 | 5.76:1 |
| Mean age (yrs) | 52.16 | 54.6 |
| SM:NS | 2.5:1 | 2.7:1 |
| Urban:Rural | 19.6–81.6 | 18.4–80.4 |
| Occupation | Farmers | 13.9-48% |
| | Labourers | 21.0–27.3% |
| | Clerks / teachers | 16.7% |
| | Businessmen | 21.3% |
| | Housewives | 8.0–14.7% |
| | Others | 23% |
| Religion | | |
| | Hindus | 75.1% |
| | Muslims | 18.9% |
| | Christians | 5.9% |

SM: small cell carcinoma; NS: non-small cell carcinoma.

The relative risk of developing lung cancer is 2.64 for *bidi* smokers and 2.23 for cigarette smokers with 2.45 as the overall relative risk[35]. *Bidi* is more carcinogenic as has been shown in studies by Jussawalla and Jain[49] and Pakhale *et al*[51]. *Hooka* smoking has also been associated with lung cancer as reported by Nafae *et al*[31].

In a recent study by Gupta *et al*[45], 80% of men and 33% of women among the patients were ever-smokers as compared to 60% of men and 20% of women among controls. The odds ratio (OR) for ever-smoking was 5.0 (95% CI=3.11-8.04) among men and 2.47 (95% CI=0.79-7.75) among women. Smoking of *bidi* and *hooka* as well as cigarettes had similar ORs for cumulative consumption. The risk increased with both the duration and quantity of all smoking products[45].

## PASSIVE SMOKING AND LUNG CANCER

Environmental tobacco smoke is a known

lung carcinogen. A meta-analysis of 41 studies showed that environmental tobacco exposure carries a relative risk of development of lung cancer of 1.48 (1.13-1.92) in males and 1.2 (1.12-1.29) in females[53]. Risk increases with increase in exposure. Exposure at work place results in a relative risk of 1.16. In a study on non-smoking lung cancer patients, environmental tobacco exposure during childhood carried an OR of 3.9 (95% CI-1.9-8.2). There was an increasing risk with increase in number of smokers in the household and the duration of exposure. Women had a higher OR of 5.1. Work place, and vehicular pollutant exposure have shown a weak association. Another study by Rapiti *et al*[54] has shown that environmental tobacco smoke exposure during childhood is strongly associated with the risk of later development of lung cancer (OR 3.9, 95% CI=1.9-8.2).

## OCCUPATIONAL RISK FOR LUNG CANCER

Certain occupations carry a higher risk of lung cancer[55,56]. The following occupational exposures are known to be associated with an increased risk: *(a) Asbestos:* insulation workers and shipyard workers are exposed to asbestos. There is some increase in the risk of lung cancer after 10 years of exposure and a substantial risk after 20 years of exposure. Concurrent smoking increases the risk to 90 fold; *(b) Arsenic :* smelter workers and vineyard workers are exposed to arsenic. The risk is dose related. Lung cancers have an upper lobe predominance and there may be multiple primaries; *(c) Nickel refinery workers :* squamous cell carcinoma is more common; *(d) Radiation (Uranium mining):* oat cell carcinoma is more common; *(e) Haematite mining:* due to radon exposure; *(f) Hard rock mining; (g) Chromium exposure in ore mining and pigment manufacturing*: squamous cell variety is most common; *(h) Chloromethyl exposure in workers in industries:* oat cell carcinoma is most common; *(i) Ethers and mustard gas:* squamous and undifferentiated carcinomas are most common; *(j) Soot, tars exposure in coke oven workers* and *(k) Oils and coke exposure in Gas house workers, roofers and rubber workers*.

Other occupational exposures that are suspected include those to acrylonitrite, berrylium, and dimethyl sulphate. No systematic information on occupational risk for lung cancer patients is available in India.

## GENETICS OF LUNG CANCER

Cytogenetic studies have identified many chromosomal changes in lung cancer with numerical abnormalities, and structural aberrations including deletions and translocations. These mutations include activation of the dominant cellular protooncogenes (which promote oncogenesis) of the *ras* and *myc* family and inactivation of the recessive or tumour suppressor genes ( these genes help suppression of tumour development). Small cell lung cancer is associated with oncogenes, like *c-myc*, L-*myc*, N-*myc*, c-*raf* and tumour suppressor genes, like p53 and Rb. Non-small cell lung cancer is associated with K-*ras*, N-*ras*, H-*ras*, c-*myc*, c-*raf* and tumour suppressor genes like p16 and Rb genes[57-58].

FHIT is a tumour-suppressor gene and is frequently altered in lung cancer[59]. Apoptosis or programmed cell death is altered in lung cancers due to changes in the anti-(BCL-3, Bel-xl) and proapoptotic members (Bax, Bad)[60]. The protein level expression of bCl-2, bax and bel-xl shows a variable expression ranging from negative to moderate positivity. Singh *et al*[61] reported that presence of arginine homozygous genotype of p53 codon 72 contributes to susceptibility for lung cancer and patients with proline homozygous genotype present early and may have a better prognosis. To elucidate that molecular mechanisms of chemotherapeutic effects, Sen *et al*[62] in an *in vitro* study concluded that while Bax was unaffected, there was downregulation of anti-apoptotic BCl-Xl during treatment.

## DIET AND LUNG CANCER

There is some evidence that certain dietary factors may be protective for lung cancer, and others may increase the risk. There are

conflicting reports about the role of beta-carotene and lung cancer, although most reports suggest a protective effect. Case control studies from China have shown that vegetable intake is a protective factor for lung cancer[63]. Sankaranarayanan[64] found that green vegetables and bananas have a protective effect on the development of lung cancer. Pumpkins and onions had the most consistent protective effect. On the other hand, animal food products and diary products have a predisposing effect on lung cancer. Dietary cholesterol and animal fat increases the risk of lung cancer. Behera *et al*[65], however, reported that β-carotene and vitamin A levels and vitamin C levels in patients with lung cancer compared to healthy controls were not significantly different.

## AIR POLLUTION AND LUNG CANCER

Urban air contains many known carcinogens and exposure to this has been shown to predispose to lung cancer in UK and US. Lung cancer is more frequent in subjects residing in neighbourhoods where outdoor air is smoky. Studies from China[66] have shown that coal burning at home is a significant risk factor for the development of lung cancer in non-smoking females. Coal smoke contains many potential carcinogens like radon and thoron.

Gupta *et al*[45] reported that among risk factors for lung cancer, cumulative exposure of > 45 years to indoor air pollution in women from use of coal or wood for cooking or heating showed an OR of 1.43 (95% CI=0.33-6.30)[45]. Residence in urban areas, however, did not entail an increased risk for developing lung cancer.

## REACTIVE OXYGEN SPECIES AND ANTIOXIDANT DEFENSE SYSTEM IN LUNG CANCER

Studies by Sharma *et al*[67] have shown that there is a significant increase in *in vitro* superoxide anion and hydrogen peroxide formation in alveolar macrophages from malignant lobe and neutrophils of lung cancer patients. The activities of catalase and glutathione peroxidase were decreased. The assays of antioxidant vitamins such as retinal and α-tocopherol revealed that their levels in alveolar macrophages from malignant lobe were significantly decreased. This oxidant/antioxidant imbalance in the malignant lobe of lung cancer patients could potentially enhance the neoplastic behaviour by augmenting both the genetic instability of a tumour and its capacity to injure and penetrate the host tissues. Further, Sohi *et al*[68] and Bhardwaj and Khanduja[69] have also emphasized the role of oxidant and antioxidant balance in the pathogenesis of lung cancer.

## CLINICAL SPECTRUM OF PRIMARY LUNG CANCER IN INDIA

There are important differences in the clinical spectrum of lung cancer patients in India compared to those in the West[38]. Both the mean and peak ages of lung cancer are lower. The smoker: non-smoker ratios have been lower in most of the Indian studies as compared to those in the West. Most of the patients have advanced disease at diagnosis and 51.8% have evidence of metastases. The commonest presentation has been a mass lesion with or without collapse in 68% while 25% had a pleural effusion and 16.7% had superior vena cava compression syndrome[38, 70]. Squamous cell carcinoma has been found in 34.3%, anaplastic in 27.6%, adenocarcinoma in 25.9% and unclassified in 12.2 per cent.

## DIAGNOSIS OF LUNG CANCER

### Clinical Presentation (Table 3)[18-51]

Symptoms such as fever, cough, expectoration, hemoptysis, weight loss and anorexia are common to both tuberculosis and lung cancer. In India, where tuberculosis is rampant it is not uncommon to find a lung cancer patient being treated for tuberculosis initially. However, age of the patient, smoking history, mediastinal symptoms such as hoarseness of voice, SVC

obstruction and dysphagia favour the diagnosis of lung cancer. On examination, there may be signs of collapse or mass, clubbing and metastatic and non-metastatic complications of lung cancer. The duration of symptoms before lung cancer is diagnosed is reported to be < 3 months in 32.6 – 44% cases, 3-6 months in 16.0-34.3% and > 6 months in 21.0 - 24.0 per cent.

**Table 3.** *Presenting features of Indian lung cancer patients (%)*[18-51]

| Symptoms | Jindal and Behera (1990) | Other-Indian studies (range) |
|---|---|---|
| Cough with expectoration | 88 | 40-94.3 |
| Chest pain | 52.2 | 16-66.7 |
| Loss of weight | 90 | 11.4-77 |
| Breathlessness | Not reported | 24-59 |
| Weakness | 90 | 4-60 |
| Haemoptysis | 69.2 | 8-60 |
| Fever | 19.6 | 22-68.6 |
| Anorexia | 90 | 20.5-70 |
| Hoarseness of voice | 29.9 | 9-33 |
| Nausea and vomiting | 6 | 25.0 |
| Puffiness of face | 19.8 | 2.9-8.3 |
| Dysphagia | 20.8 | 2.9-6 |
| Others | 30.5 | - |

### Radiological Findings

Mass with or without collapse is the commonest radiological finding in lung cancer[70]. Other findings include pleural effusion in 25.1%, rib erosion in 4.8% and lymphangitis in 2.8 per cent. A normal chest x-ray is found in 0.4% of cases of lung cancer. Upper zone is involved in most cases followed by mid zone (32.7%), lower zone (16%) and the entire lung (8.8%). Adenocarcinoma presents as a peripheral mass in 61% cases and in 38.3% as a central lesion. Presentation as a central mass (72.2% cases) is more common among squamous cell carcinoma than as a peripheral lesion (27.8%). Small cell cancer also presents more commonly as a central lesion (83.6%) than as a peripheral lesion (16.4%). Isolated pleural effusion has been reported in 3.8% in squamous cell lung cancer, 22% in adenocarcinoma and only 4% in small cell lung cancer[70].

### Other Investigations

Tissue diagnosis and categorisation of the cell type is required before treatment can be planned in a case of lung cancer. With experienced personnel and using multiple, diagnostic techniques, 70-90% of all lung cancers can be diagnosed by cytopathological examination. Any mass lesion demonstrable on radiology can be subjected to bronchoscopy or transthoracic fine-needle aspiration cytology biopsy. The procedural yield is 93% and a firm diagnosis can be established in 78 per cent[71]. For peripheral lesions fluoroscopic guidance is required and an adequate yield is obtained in 75 per cent. The overall diagnostic yield of transbronchial needle aspiration is 75% and exact categorisation is possible in 82% of cases[72]. The diagnostic yield of bronchial biopsy specimens varies from 70 to 90 per cent depending on the site and type of the tumour, number of specimens examined, and experience of the pathologist and the endoscopist. Central lesions, with visible tumours and multiple samples give a better diagnostic yield.

Malignant cells especially small cell cancer type produce and release several hormones, enzymes and tissue antigens. Among the commoner hormones are ACTH, beta-hCG, FSH and LH. These are, however, not diagnostic.

## SCAR CARCINOMA

Some authors define a scar carcinoma as a peripherally located tumour with no evidence of bronchial origin, occurring around a true hyalinized scar tissue. Others include tumours superimposed on chronic regional or diffuse interstitial fibrosis. Scar cancers are almost always of the non-small cell type, with a preponderance of adenocarcinomas. Some of the conditions that are described to be associated with a scar carcinoma are tuberculosis, pulmonary infarction, emphysema, systemic sclerosis, bronchiectasis, idiopathic pulmonary fibrosis and asbestosis[75].

There are conflicting reports about the association of tuberculosis and lung cancer. In

an analysis of 1009 patients with lung cancer from Chandigarh only 1.2% had clinical evidence of tuberculosis and 3.8% had radiological evidence of tuberculosis[38]. In a prospective study from same centre only two out of 280 patients with past tuberculosis and two out of 272 controls were found to have lung cancer[76]. The authors concluded that subjects with a past history of tuberculosis are not at are increased risk of lung cancer. In a study from Bangalore sputum was positive for acid-fast bacilli (AFB) in 290 patients with malignancy, out of which 13.8% had lung cancer[77]. Unlike sear carcinomas lung cancer in a patient with old tuberculosis is predominantly of the squamous cell variety[78].

## MANAGEMENT OF LUNG CANCER

Surgery, radiotherapy and chemotherapy are the various options available for the management of lung cancer. In the early stages of NSCLC (Stage I to IIIA), surgery if feasible is the treatment of choice. The five-year survival rate after surgery are as follows: Stage I: 60-70%, State IA: (T1N0), 80%, Stage II: 35-40%, Stage IIIA (N2): 10-15%.

As most cases of lung cancer present in an advanced and inoperable stage, and radiotherapy is only a local form of therapy, chemotherapy has an important role in the management of lung cancer. Several regimens of chemotherapeutic agents have been studied in lung cancer. In a recent meta-analysis of randomized trials that compared chemotherapy with good supportive care, chemotherapy showed a modest benefit[5]. There is an improvement in the quality of life, prolongation of median survival by 1.5-3 months, increased survival at one year by 10% and a reduction in the risk of death by 27 percent. In our experience, chemotherapy results in a modest but significant improvement in survival in patients with inoperable lung cancer compared to good supportive care alone[79].

Newer chemotherapeutic agents that have increased one-year survival up to 40% and median survival of about 8-9 months are being increasingly used now a days . These include Gemeitabine, Docetaxel, Paclitaxel, Vinorelbine, Topotecan, Irinotecan, and Newer Platinum agents (carboplatin, Oxaloplatin, etc)[5]. Combinations of a platinum agent with a new generation cytotoxic agent have become the standard of care for first-line chemotherapy of advanced non-small cell lung cancer. In the presence of contraindications for platinum-based chemotherapy, platinum-free chemotherapy might be a reasonable option. There is not enough evidence to support the use of triple-drug chemotherapy. Administration of single-agent gemcitabine or vinorelbine can be considered in patients with poor performance status and in elderly patients. In case of non-progression and lack of severe toxicity, the administration of four to six cycles of chemotherapy is recommended. There is no evidence that prolongation of treatment has an impact upon survival. Second line chemotherapy using docetaxel should be considered for chemotherapeutically pre-treated patients with good performance status in order to relieve

**Table 4.** *Chemotherapy with median survival in weeks in lung cancer at a tertiary care centre (PGIMER-Chandigarh)[79-87]*

| Regimen | No. | SCLC | NSCLC | Total survival | 1-year survival |
|---|---|---|---|---|---|
| SFRT | 28 | - | - | 5 | - |
| CTX | 24 | - | - | 7.5 | - |
| *Combination* | 38 | 26 | 9.5 | 16 | 8.3-12% |
| V+C+B | 26 | - | 18 | - | 26.5% |
| V+C+M | 20 | 23.5 | 31 | - | 33% |
| V+C+A | 27 | 23.5 | 23 | - | 25-36% |
| VB+MIT+C | 27 | - | 16-28 | 24 | 12% |
| E+V+C+CC | 22 | 22.5-39 | - | 24 | 12.5% |
| IFO+V | 16 | 35.5 | - | - | 26.5% |

SFRT: Single fraction radiotherapy of 1000 rads; CTX: Cyclophosphamide; V: vincristine; C: Cisplatin; B:bleomycin; M: methotrexate; A: adriamycin; VB: vinblastin; MIT: mitomycin; CC: CCNU; IFO: Ifosfamide, E: etoposide.

**Table 5.** *Median survival (in weeks) in lung cancer with newer chemotherapeutic agents*[84-87].

| Regimen | NSCLC | SCLC | 6 M | 1 Yr |
|---|---|---|---|---|
| MIC (n=299) | 22 (24-36) | - | 30% | 15.5% |
| VIE (n=98) | - | 31 | 44.4% | 12.7% |
| DOC + CISP (n=50) | 38+ | (30-32) | 93.3% | 23.3% |
| GCB + CISP (n=16) | 36 | - | Response Rate-69% | |

MIC: Mitomycin, Ifosfamide, Cisplatin; VIE: VP-16, Ifosfamide, Etoposide; DOC: Docetaxel; CISP: Cisplatin, GCB: Gemcitabine.

symptoms, prolong survival and improve quality of life.

Studies from India have shown that without chemotherpay the median survival of unresectable NSCLC is five weeks, with a single agent it is 7.5 weeks (Tables 4 and 5), with less effective chemotherapy it is 9.5 weeks and with modern chemotherapy it is 23 weeks to more than 40 weeks[80-87]. The problems with chemotherapy in India include a large number of dropouts, because of the costs and the side effects.

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CASE REPORT

# Scimitar Syndrome: Imaging by Magnetic Resonance Angiography and Doppler Echocardiography

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ABSTRACT

We report magnetic resonance angiographic demonstration of both an anomalous pulmonary venous drainage and an anomalous systemic arterial supply in a patient with scimitar syndrome. Contrast-enhanced magnetic resonance angiography provides an excellent non-invasive diagnostic tool for demonstrating this complex congenital lesion in detail. A two-dimensional and colour Doppler echocardiography was also performed to show the anomalous venous drainage and to analyse the anomalous flow velocity pattern.

***Key words:*** *Congenital pulmonary venolobar syndrome, Doppler echocardiography, Magnetic resonance angiography; Scimitar syndrome.*

***[Indian J Chest Dis Allied Sci 2004; 46 : 283-286]***

## INTRODUCTION

The most consistent feature of the scimitar syndrome, also called congenital pulmonary venolobar syndrome, is drainage of a part of the right lung by an anomalous scimitar-shaped pulmonary vein that joins the inferior vena cava below the diaphragm[1]. This syndrome may be associated with other anomalies, *viz.*, anomalous systemic arteries arising from the descending aorta supplying the territory drained by the scimitar vein, absent or small right main pulmonary artery, hypoplasia of the right lung with fewer airways and bronchial isomerism, cardiac dextroposition, and diaphragmatic abnormalities. The morphological diagnosis is based on plain radiographs, ultrasound, computed tomography, and magnetic resonance imaging[2-4]. However, an evaluation of hemodynamic significance requires cardiac catheterisation[5] although non-invasive hemodynamic assessment has been reported by velocity-encoded cine magnetic resonance imaging[6,7]. The clinical significance and prognosis depend to a large extent on the amount of the resulting left-to-right shunt as well as on the associated malformations[5].

## CASE REPORT

A-30-year-old man presented to our hospital with complaints of productive cough of three months duration. His medical history was remarkable for an episode of hemoptysis lasting one week about five years ago for which he was prescribed anti-tubercular therapy (streptomycin, isoniazid, ethambutol) by a

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private practitioner which he took for three months. Physical examination of the patient was unremarkable.

Chest radiograph (Figure 1) revealed small right hemithorax, hyperlucent right lung with reduced and disorganised vasculature, a small right hilum and dextroposition of the heart. A large anomalous curvilinear vessel coursing down from mid lung zone towards the diaphragm was also seen through the cardiac shadow. The left lung was normal.

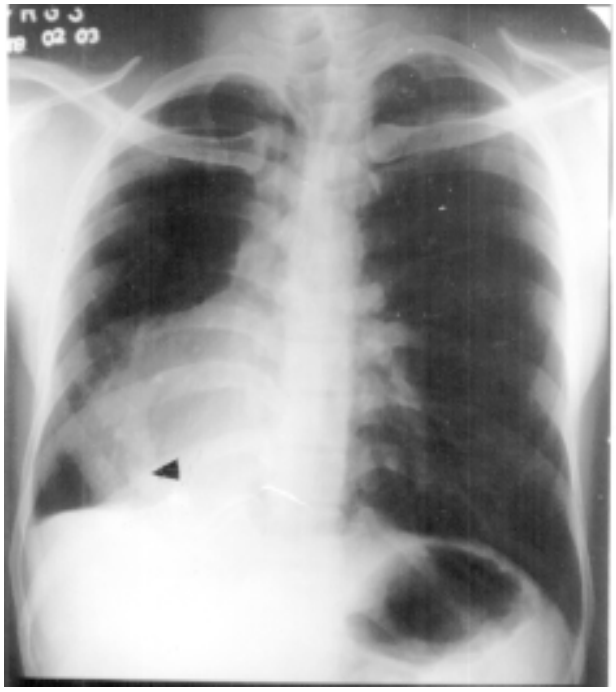

**Figure 1.** Chest radiograph (postereo-anterior view) showing hypoplastic right lung, dextrocardia and scimitar vein (arrowhead).

Fiberoptic bronchoscopy showed all the three right upper lobe segmental bronchi originating directly from the right main bronchus. The rest of the tracheobronchial tree was normal. Contrast-enhanced magnetic resonance angiography (Figure 2) demonstrated a large anomalous pulmonary vein draining a significant portion of the right lung coursing vertically to enter the terminal inferior vena cava. The right pulmonary artery was hypoplastic and an aberrant vessel, arising from the abdominal aorta, was seen supplying the lower segments of the right lung.

Two-dimensional and colour Doppler

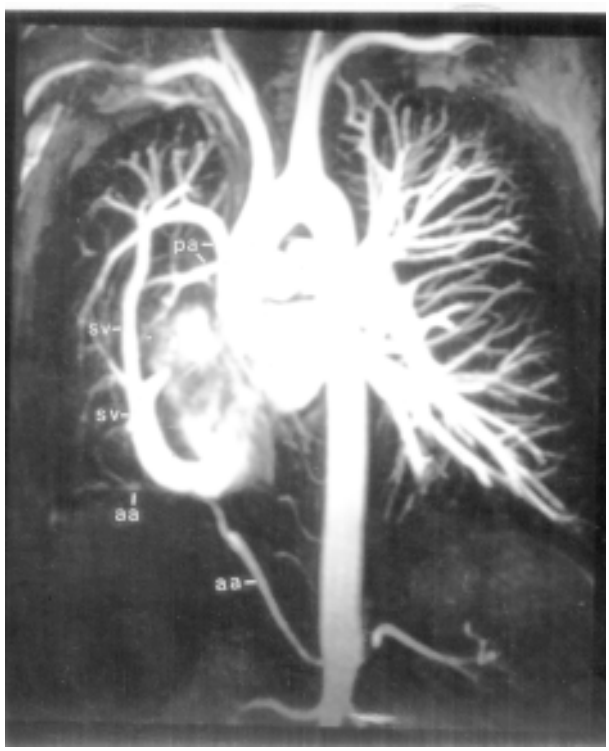


**Figure 2.** Contrast-enhanced magnetic resonance angiography showing a large scimitar vein (sv) that drains most of the right lung into the terminal inferior vena cava and an aberrant artery (aa) arising from abdominal aorta that supplies lower segments of the right lung. Note that the right pulmonary artery is hypoplastic (pa).

echocardiography (Figure 3) demonstrated the anomalous pulmonary vein entering the inferior vena cava just below the diaphragm. The

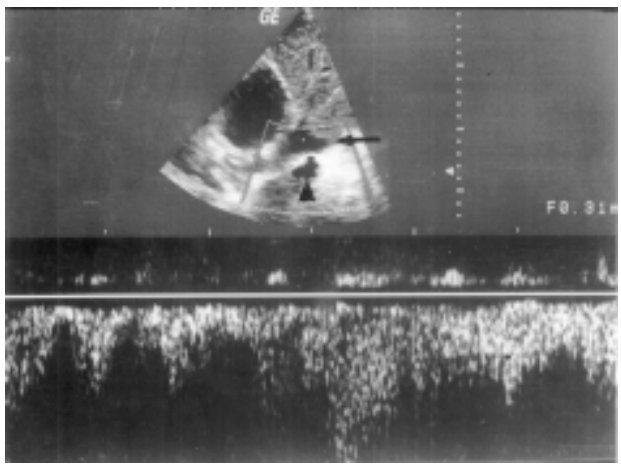

**Figure 3.** Two-dimensional and colour Doppler echocardiography showing scimitar vein (arrowhead) entering the inferior vena cava (solid arrow) just below the diaphragm. The flow is monophasic with peak velocity of 0.89 m/s.

anomalous flow velocity pattern was monophasic, without reverse flow at atrial contraction. The peak velocity was 0.89 meter per second. There were no signs of left-to-right intracardiac shunt but the right ventricle was slightly enlarged.

## DISCUSSION

Our case under discussion had a hypoplastic right lung, dextrocardia, anomalous origin of the right upper lobe segmental bronchi, hypoplastic right pulmonary artery, aberrant right lung systemic arterial supply arising from abdominal aorta and scimitar vein draining into inferior vena cava with abnormal flow pattern.

The abnormal venous return is the main component of scimitar syndrome, and gives a characteristic abnormal radiographic shadow descending along the right cardiac border, which resembles a curved Turkish sword (*i.e.*, scimitar)[8] or a women's leg[9]. However this radiologic sign may be obscured because of the associated dextrocardia[5], as happened in our case. The abnormal scimitar vein may drain the entire lung or only a lobe. In the case presented here the magnetic resonance angiography clearly delineated the scimitar vein, which was seen draining a significant portion of the right lung. Sometimes a "meandering" but normally draining pulmonary vein may be confused for a scimitar vein, as the former may resemble the latter on a plain radiograph[10].

The usual drainage of the anomalous vein is into the inferior vena cava below or just above the diaphragm but drainage can also be to the right atrium. In our patient, colour Doppler echocardiography clearly visualised the anomalous vein entering the inferior vena cava just below the diaphragm. The flow velocity pattern in the scimitar vein is different from the normal pulmonary venous flow[11]. The normal flow is biphasic or triphasic, with one or two peaks in systole and one peak in diastole (peak velocity of about 0.5 m/s), and reverse flow at atrial contraction (peak velocity of about 0.2 m/s). The flow pattern in scimitar vein is monophasic extending throughout the cardiac cycle with no reverse flow at atrial contraction, as was seen in our case. The peak velocity (0.89 m/s) recorded in our case was abnormally high and was similar to the earlier reported cases[11].

The right pulmonary artery is often reduced in size, as was seen in the chest radiograph and confirmed by magnetic resonance angiography. The incidence of aberrant systemic arterial supply arising from the aorta varies. Traditionally, evaluation of aberrant systemic arteries has been performed with conventional angiography, but computed tomographic scanning has demonstrated these aberrant vessels better[3]. Moreover, computed tomographic scanning may have the added advantage of demonstrating any associated pulmonary parenchymal anomaly although it was not done in the present case. Contrast-enhanced magnetic resonance angiography has also been used previously to evaluate scimitar syndrome[4,6] and the close similarity to the conventional angiography suggests that magnetic resonance angiography can be used as a non-invasive diagnostic tool to provide a comprehensive evaluation of the pulmonary vascular anatomy in this syndrome. In our case, the presence of an aberrant artery arising from the aorta was demonstrated only on magnetic resonance angiography and was seen supplying the lower segments of the right lung.

The clinical presentation of the patients can vary widely[12]. Infants who present with scimitar syndrome are almost always very ill, with evidence of congestive heart failure and severe pulmonary hypertension. Their symptoms are secondary to the associated congenital cardiac lesions, the presence of systemic collateral arterial supply and the obligatory left-to-right shunt from the anomalous pulmonary venous drainage. Adults on the other hand generally present with minor symptoms, or none at all and the condition is often discovered accidentally. Symptoms may be due to an associated cardiac malformation or to problems in the abnormal lung. Surgery may be needed for patients having associated tracheobronchial anomalies (such as bronchiectasis or pulmonary sequestration), associated cardiac anomalies or left-to-right shunts greater than 2:1. In these

cases, identification of a systemic arterial supply is important in order to avoid inadvertent transection during surgery.

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CASE REPORT

# Adenoid Cystic Carcinoma of Trachea

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ABSTRACT

A 20-year-old male presented with cough, haemoptysis, breathlessness and wheezing for the past one month. Contrast enhanced computerised tomographic (CECT) scan of chest and fibreoptic bronchoscopy revealed an endotracheal mass that on histopathological examination showed adenoid cystic carcinoma of trachea. Magnetic resonance imaging (MRI) scan of chest confirmed involvement of adjacent prevertebral, para-oesophageal and subcarinal lymph nodes rendering the tumour inoperable.

***Key words:*** *Adenoid cystic carcinoma, Trachea.*

***[Indian J Chest Dis Allied Sci 2004; 46 : 287-289]***

## INTRODUCTION

Adenoid cystic carcinoma referred to in older textbooks as cylindroma is a rare type of lung cancer arising from mixed seromucinous glands seen in tracheobronchial submucosa. It accounts for 20-25% of all tracheal tumours and 80% of all tracheobronchial gland tumours[1]. Thorough medline search has been done but failed to reveal any Indian report.

## CASE REPORT

A 20-year-old young male, occasional smoker with no significant past history presented with a history of cough, hemoptysis, breathlessness associated with wheezing for the last one month. He complained of difficulty in swallowing mainly for solid food for the last one week. There was no history of chest pain. He had similar complaints four months ago and was treated with antibiotics and bronchodilators by a general practitioner.

General examination was unremarkable. On examination of the respiratory system, the upper airways were normal. On auscultation he had bilateral wheezing. Auscultation over cervical trachea was normal; specifically there was no evidence of stridor. The hematological and biochemical profile was essentially normal. The chest radiograph was normal. Contrast enhanced computerised tomographic (CECT) scan of chest was performed followed by a contrast enhanced MRI scan of the chest that showed a space occupying lesion measuring 3.0 cm × 2.3 cm in the lower 1/3 of trachea just above the carina with involvement of subcarinal lymph nodes (Figure 1). There was as intrabronchial extension into the left main stem bronchus with minimal extension of the mass into prevertebral and paraoesohageal areas.

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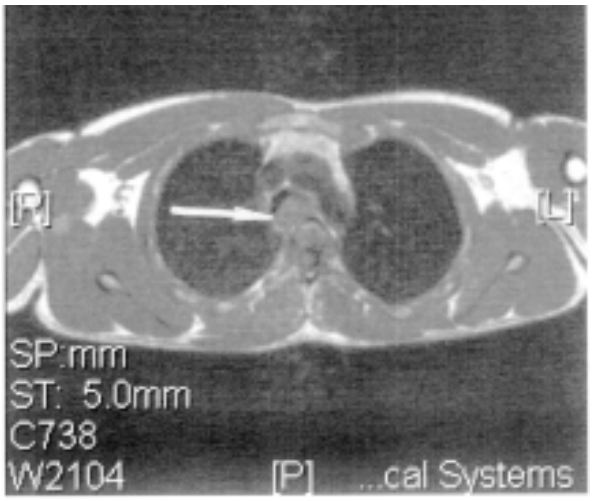


**Figure 1A**

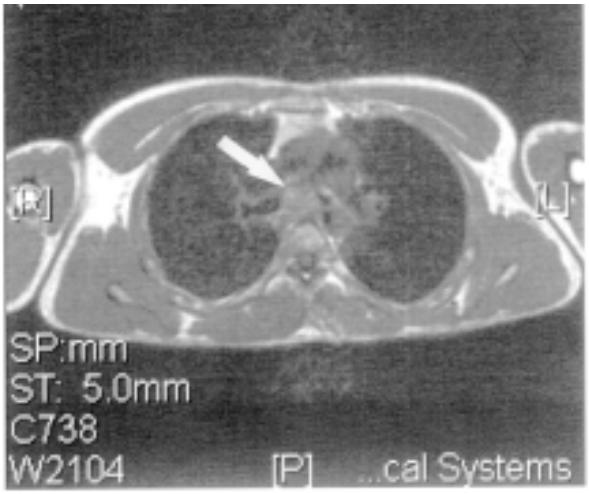


**Figure 1B**

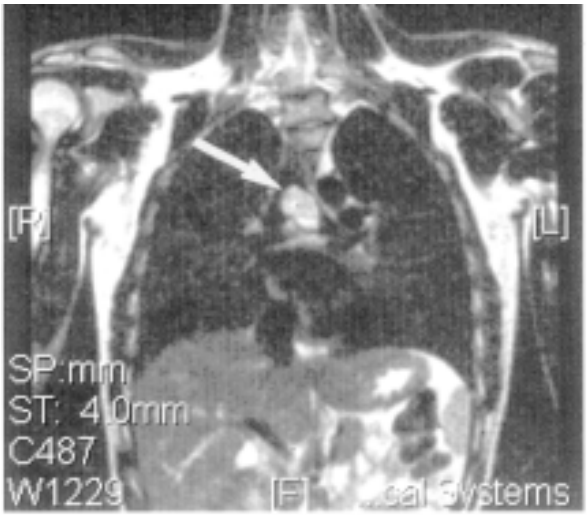


**Figure 1C**

**Figure 1.** T2-weighted images of MRI scan of chest in axial section (A, B) and coronal section (C) showing endotracheal tumour.

Fibreoptic bronchoscopic examination showed a large growth in trachea 0.5 cm from carina occluding 70% of the tracheal lumen. Multiple biopsies of the tumour on histopathological examination showed an infiltrative cribriform type of adenoid cystic carcinoma of the trachea (Figure 2). The patient also underwent tests to rule out extrathoracic metastasis such as CT abdomen, radionuclide bone scan and serum alkaline phosphatase estimation. In view of infiltrative nature of the lesion into the

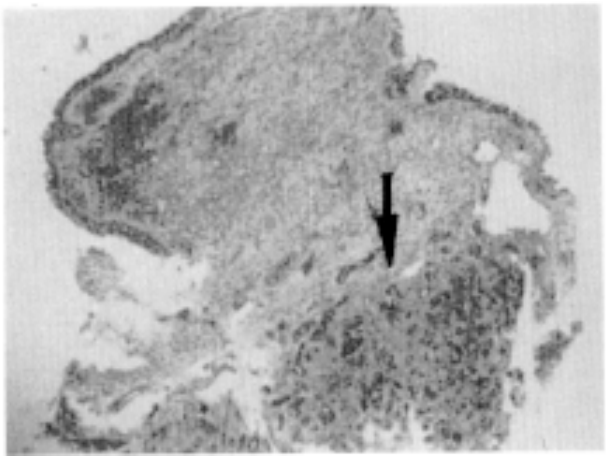

**Figure 2a**

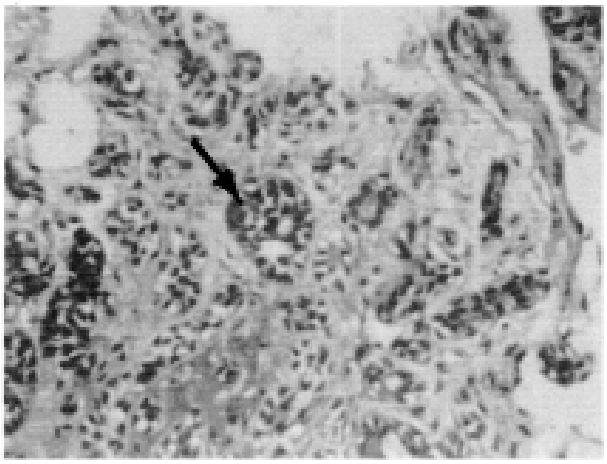

**Figure 2b**

**Figure 2.** Histopathological section of endotracheal tumour showing features of adenoid cystic carcinoma under: *(a)* scanner view showing very overlying normal mucosa and tumour cells infiltrating underlying stroma (H&E×40); *(b)* high power view of the tumour showing cells infiltrating the stroma in a trabecular and cribriform pattern typical of adenoid cystic carcinoma (H&E × 200).

adjacent structures, he was diagnosed to have an inoperable tumour and was advised palliative external beam radiotherapy.

A repeat contrast enhanced computerised tomographic scan on follow-up at three months after external beam radiation revealed significant regression of the tumour.

## DISCUSSION

Adenoid cystic carcinoma is the most common salivary gland neoplasm found in the lung[2]. These tumours most frequently occur in the trachea or mainstem bronchi and cause symptoms of obstruction. Men and women are equally affected. Earlier studies have reported it as a tumour of the middle age (mean age 50 years); being extremely rare under the age of 30[3-4]. Our patient presented at a relatively younger age of 20 years. Most tumours occur in main or lobar bronchi and often extend into trachea, but peripheral tumours, presumed to arise form glands in small bronchi are occasionally encountered[5]. The typical presenting symptoms are wheezing, progressive dyspnoea, stridor, cough and hemoptysis.

Adenoid cystic carcinoma are infiltrative tumours that cause irregular narrowing of the airways. The form poorly defined sessile, nodular growths or cause concentric thickening of the bronchial wall. The histological subtypes described are cribriform, tubular and solid tumours[2].

The level of invasion seen microscopically is nearly always greater than what is grossly apparent and hence complete resection may be quite difficult to achieve. They usually spread to adjacent structures with perineural spread being common. Rarely, metastases occur to lymph nodes, bone, kidney, liver, lung, and brain. The mainstay or treatment is complete resection of the tumour, which can lead to good long term survival[6]. Radiotherapy may be helpful for inoperable cases[4]. Recent study by Muller *et al*[7] has reported good survival rates for primary radiation therapy of adenoid cystic carcinoma[7].

## ACKNOWLEDGEMENT

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CASE REPORT

# Unusual Cause for Miliary Lung Mottling in a Child

**Julius Xavier Scott and J. Ebor Jacob Gnananayagam, E. Kala Ranjini Sundaravalli, Gordon Thomas[1], Nylla Shanthly[2] and Chellam Kirubakaran**

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ABSTRACT

A 12-year-old boy presented to us with a diagnosis of disseminated tuberculosis which was made based on a history of prolonged fever, multiple neck swellings and radiological findings of bilateral multiple micronodular opacities. Examination showed a diffuse thyroid gland swelling. He was diagnosed to have papillary thyroid carcinoma with distant metastases to cervical lymphnode on histopathology and to lungs.

***Key words:*** *Papillary carcinoma of thyroid, Lung metastases, Miliary mottling.*

***[Indian J Chest Dis Allied Sci 2004; 46 : 291-293]***

## INTRODUCTION

Miliary lung mottling is a radiological finding. Most common cause of miliary mottling in a chest radiograph in a developing country is miliary tuberculosis. Tropical pulmonary eosinophilia, varicella pneumonia, pulmonary alveolar lithiasis are other causes which are seen infrequently. Conditions such as metastases, histiocytosis, Gauchers disease are very rare[1,2]. We report an unusual case of miliary lung mottling.

## CASE REPORT

A 12-year-old boy with the complaints of multiple neck swellings and fever for three years had been diagnosed as tuberculosis elsewhere. He was given nine months of antituberculous treatment. Since his condition worsened in spite of therapy he was referred to us. On examination he was plethoric and cyanosed. His weight corresponded to the 3rd centile for age. He had significant bilateral cervical, inguinal and axillary lymphadenopathy. He also had a thyroid swelling that was firm and fixed to deeper and superficial structures. It measured 6 cm×5 cm on the right side and 7 cm×5 cm on the left side. Respiratory system examination revealed crepitations and decreased air entry in both the lower zones. Other systemic examination did not reveal any abnormality.

Laboratory investigations revealed an erythrocyte sedimentation rate of 50 mm at 1st hour, packed cell volume of 49% and lactate dehydrogenase of 598U/L. Arterial blood gas analysis showed a pH 7.42, $PaCO_2$ 45, $PaO_2$ 46, $SaO_2$ 78 percent. Tuberculin test was negative. Three consecutive samples of gastric juices for acid-fast bacilli were negative. Plain radiograph of the chest showed multiple micro-nodular opacities involving the left upper and mid zone of the left side and lower zones of both lung

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fields, which was suggestive of lympangitis carcionomatosa (Figure). Bone marrow

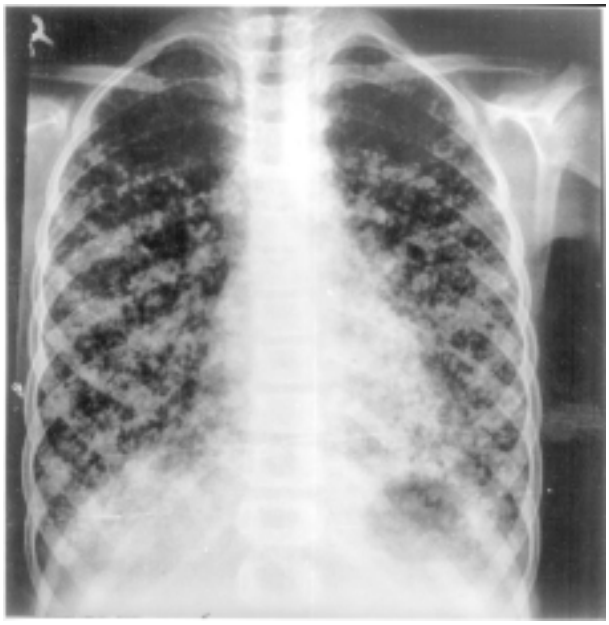

**Figure.** Plain chest radiograph showing micro-nodular opacities or the typical 'snow storm'; appearance of metastases involving both the lung fields.

aspiration showed a cellular marrow with moderate lymphocytosis with an infiltrate of atypical lymphoid cells. Histopathological examination of cervical lymph node showed metastatic thyroid carcinoma suggestive of papillary carcinoma. Thyroid scintigraphy revealed a warm nodule in the left lobe. Serum thyroglobulin level at presentation was 307ng/ml. Total thyroidectomy and bilateral functional neck dissection was done.

Post-operatively he developed bilateral recurrent laryngeal nerve palsy and hence tracheostomy was done. Post-operative $^{131}$Iodine whole body survey showed residual thyroid and extensive lung metastases. In view of the extensive pulmonary metastases $^{131}$I ablation therapy was carried out under dexamethasone cover. He has been started on hormone replacement therapy and followed up for two years post-operatively and is doing well. Pulmonary metastases are being monitored by clinical symptoms, chest radiographs, and $^{131}$I tracer uptake study. Serum thyroglobulin level is also being monitored and during recent follow up it was found to be 147 ng / ml.

## DISCUSSION

Carcinoma of thyroid is rare in childhood. comprising only one percent of all cancers diagnosed before the age of 18 years. A painless nodule in the thyroid or in the neck is the usual first evidence of disease[1,3]. A very common finding is metastases to the regional lymph node. These lymph node metastases are not indicative of metastases as in most other malignant diseases[4]. Our case also presented with enlarged cervical lymph nodes. He also had thyroid swelling, which was masked by the lymph node enlargement. This led to the misdiagnosis of tuberculosis elsewhere.

The lungs are the most common site of metastases beyond the neck, followed by bone, mediastinum and the axilla. Pulmonary infiltration may be hematogeneous or may possibly occur *via* regional, mediastinal lymphnodes. Lung metastases may develop in 5% to 9% of patients during the course of the disease[5]. In this child, lung metastases appeared during the course of the disease but he did not have involvement of any other site, such as bone. Pulmonary metastases carry a very poor prognosis in older patients, but children appear to have much better survival[6,7].

The diagnosis of pulmonary metastases can be made either by a chest radiograph, or by total body scan (TBS) or by both. Abnormal chest radiograph shows diffuse miliary or 'snow storm' pattern or micro-nodular infiltration principally in the basal regions due to the lymphatic spread of the tumour[3,6]. The lung metastases may be associated with a normal chest radiograph. These may be overlooked unless a TBS is performed in all children who have regional lymphadenopathy of neck[6]. Our child also had miliary mottling in the chest radiograph at presentation which was later confirmed to be metastases by the body scan.

Small (<2 cm) papillary carcinoma is effectively treated by sub total thyroidectomy and suppressive doses of thyroid hormones. For

larger papillary carcinoma, near total thyroidectomy with excision of the regional lymph nodes appears to be the treatment of choice. It is usually followed by a $^{131}$I ablative dose and hormone replacement[1]. In the child being reported, a near total thyroidectomy with bilateral functional neck dissection was done followed $^{131}$I ablative therapy and hormone replacement. Thyroglobulin i (Tg) is the marker for tumour recurrence and hence periodic monitoring of thyroglobulin level is being performed in our child as recommended in the literature[1]. A step-wise treatment approach allows long-term survival and frequent cure for younger patients with papillary thyroid carcinoma and concomitant pulmonary metastases[3]. Even with distant metastases, children often survive many years without therapy. The 10 year survival rate is 95% for patients younger than 40 years of age and 75% for those who are older than 40 years of age[8]. Our case is doing well now after two years of surgery and ablative therapy.

We report this case as an unusual cause for miliary lung mottling. This case illustrates the need for adequate clinical examination of the thyroid, when an unexplained cervical lymphadenopathy or miliary mottling is noted in children.

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CASE REPORT

# Disseminated Spina Ventosa

**Paras R. Kothari, Gowri Shankar, Arun Gupta, Ashish Jiwane and Bharati Kulkarni**

*Department of Pediatric Surgery, L.T.M. Medical College and General Hospital, Bombay, India*

ABSTRACT

Spina Ventosa is a rare condition. A rare case of disseminated tuberculosis of bones and skin without primary foci is presented. Gross sclerosis of the short bones of hand and leg were noted.

***Key words:*** *Spina Ventosa, Tuberculosis, Dactylitis*

***[Indian J Chest Dis Allied Sci 2004; 46 : 295-296]***

## INTRODUCTION

Spina Ventosa is a rare condition. Disseminated bone tuberculosis occurs mostly in infants and children. It is a result of massive infection. The long bones are more frequently involved in the destruction. Although skeletal tuberculosis is common, disseminated presentation without a primary focus is very rare.

## CASE REPORT

A 5-year-old female was admitted with complaints of a discharging and ulcerated lesion over the right lateral canthus (Figure 1), a painless swelling of the right second metacarpal, and a discharging sinus of right toe (Figure 2) and fever. There was no family or past history of tuberculosis. She was immunized till date. General examination revealed her to be emaciated. Vital parameters were normal. Pallor was present. No lymphadenopathy was detected. All other systemic examination was within normal limits.

Investigations revealed hemoglobin: 7.5 gm%, erythrocyte sedimentation rate ESR: 67 mm at 1st hour. Mantoux test was positive. The radiograph showed irregular swelling with sclerosis of the underlying bones. Radiograph of

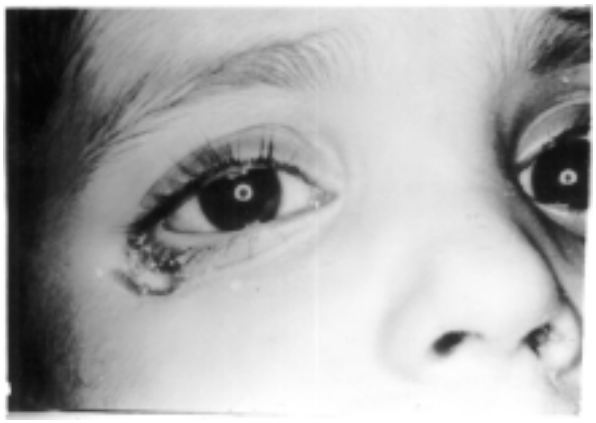

**Figure 1.** Photograph of the patient's eye showing ulcerated and discharging lesion over the lateral canthus of right eye.

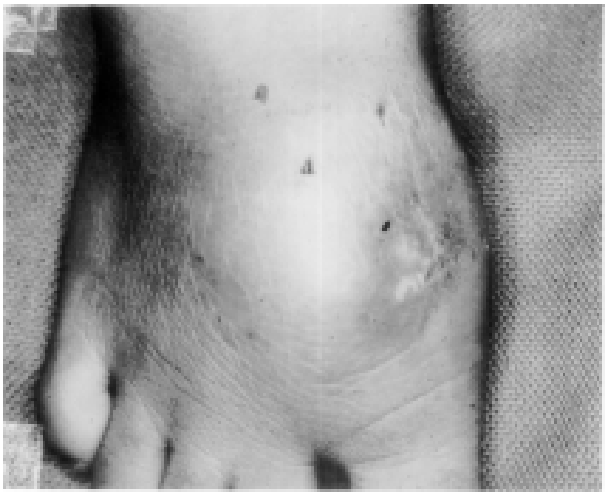

**Figure 2.** Photograph of the patient's right toe showing swelling with discharging sinus of right great toe.

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the right hand showed cortical destruction, sclerosis and cystic expansion or right second metacarpal, (Figure 3). Chest radiograph and ultrasonography of the abdomen were normal.

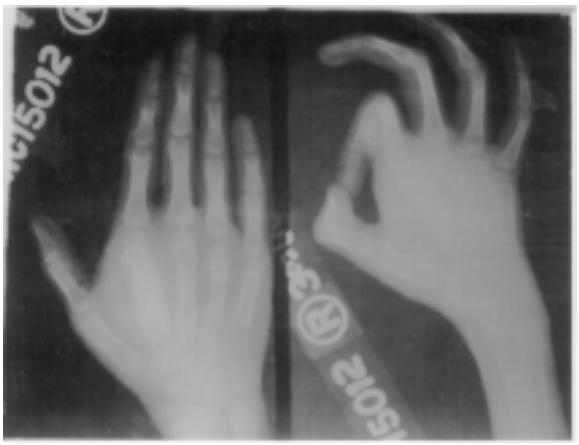

**Figure 3.** Radiograph of the right hand showing cortical destruction, sclerosis and cystic expansion of right second metacarpal.

Histopathology examination of specimen from foot and lateral canthus confirmed tuberculosis. The child was put on intensive phase four drugs (rifampicin, isoniazid, ethambutol and pyrazinamide) anti-tubercular therapy for two months. A follow-up after six weeks of intensive treatment showed healing lesions. Ethambutol was omitted and the rest three drugs continued for four months. The patient is being followed up.

## DISCUSSION

Bone tuberculosis is always the result of lymphohaematogenous spread from a distant focus. In occurs in one to five percent children who have untreated initial pulmonary tuberculosis[1]. Disseminated skeletal tuberculosis without primary foci is rare. It occurs mostly in infants and children due to massive infection[2]. The skeletal infection often becomes symptomatic within 1-3 years after initial infection. The bones of the hands are more frequently affected than bones of the feet, with proximal phalanx of the index and middle fingers being most often affected[4]. This disease occurs secondary to a primary focus which can be in the respiratory renal or alimentary tract. In about 75% cases the primary focus is in the lungs[4].

Lesions are distributed in the peripheral skeleton in children unlike axial in adults[3]. Metaphysis of a bone is often the site of infection and diaphyseal lesions are uncommon[5]. Sclerosis occur in some long-standing cases, though it is not a common feature except in the healing phase[6]. Radiographic features of cystic expansion of the short tubular bones has led to the name of "Spina Ventosa" for tuberculosis dactylitis of the short bones[3]. Our case showed gross sclerosis and thickening of the involved bones suggestive of a pyogenic infection. Secondary infection in such affected bones leads to a confusing picture. Good prognosis in most of the cases has been noted worldwide if diagnosed and treated correctly.

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BOOK REVIEW

# Metabolic Cardiomyopathy

*Editors: Hansjosef Bohles and Adrian C. Sewell; Published by: Medpharm GmbH Scientific Publishers, Germany; 2nd Revised Edition; 2004; Hardcover; Pages: X1-166 [46 b/w figures 11, colour figures]; Price : 64,-[D]/sFr 102, 40; ISBN 3-88763-104-8*

*With contributions of:* M. Beck, H. Bohles, V. Hesse, C. Kampmann, E. Kauf, W. Kienast, G. Mall, T. Marquardt, E. Mengel, H. Przyrembel, R. Santer, A.A. Schmaltz, A.C. Sewell, W. Sperl, C.F. Wippermann

***[Indian J Chest Dis Allied Sci 2004; 46 : 297]***

During the last few years, the understanding for the aetiology of cardiomyopathies has greatly improved. A great deal of information has accumulated in the field of inherited metabolic diseases, whch provides a new basis for our understanding of many heart muscle problems and their corresponding clinical disease entities.

The authors have done a remarkable job in bringing out the revised second edition of this book updating the recent advances in the field of inborn errors of metabolism. This book is meant to give the reader a comprehensive overview of the cardiological manifestations of inborn errors of metabolism. There are fifteen chapters in this book including the latest information, such as cardiomyopathy in Fabry disease or in patients with congenital disorders of glycosylation (CDG) syndrome. It should be helpful, not only to cardiologists, paediatricians, internists and general practitioners, but also to all those interested in a better understanding of the metabolic basis of clinical disease entities.

Internet:http: // www.medpharm.de

**Dr V.K. Vijayan**
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*Editor-in-Chief (IJCDAS)*
*V.P. Chest Institute*
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*Delhi-110007*
*India*

## National Seminar on Tuberculosis and Chest Diseases

**Institute of Medical Sciences, BHU, Varanasi**

***February 20, 2005***

Contact: Dr J.K. Mishra, Department of TB and Respiratory Diseases, Institute of Medical Sciences, Banaras Hindu University, Varanasi-221 005 (U.P.); Tele.: 91-0542-2366185 (Resi.), 91-0542-2307526 (Off.); Fax: 91-0542-2316483.

## Emergency Medicine Update 2004

**All India Institute of Medical Sciences**

***October 30, 2004***

Contact: Dr Sanjeev Bhoi, Organising Secretary, and Assistant Professor, Department of Emergency Medicine, A.I.I.M.S., New Delhi-110 029; Tele.: 91-11-26589029 (Off.), Mobile: 9811044309, 91-11-26169307 (Resi.); Fax: 91-11-26588663, 26588641;
E-mail: <aiims@rediffmail.com>

COMMUNICATION TO THE EDITOR

# Tuberculosis and Pregnancy

*[Indian J Chest Dis Allied Sci 2004; 46 : 299-300]*

**To the Editor:** This is in reference to review article "Tuberculosis and Pregnancy" published in April-June, 2004 issue[1]. The article states that pyrazinamide should be avoided in pregnancy as there is lack of sufficient studies to ensure its safety during pregnancy.

Pyrazinamide is a good bactericidal drug with a unique and very effective sterilizing action. If pyrazinamide is omitted from an anti-tuberculosis regimen the duration of treatment is extended from six months to nine months which will reduce compliance of the patients to treatment. Also it will increases the work load for directly observed treatment under the Revised National Tuberculosis Control Programme guidelines.

Although detailed teratogenicity data for pyrazinamide are not available, major international organisations recommend that pyrazinamide can be safely used during pregnancy. These international organizations include World Health Organization (WHO), the International Union Against Tuberculosis and Lung Diseases (IUATLD) and American Thoracic Society[2,3]. Central Tuberculosis Division, Ministry of Health, Government of India has also approved the use of pyrazinamide in pregnancy under the Revised National Tuberculosis Control Programme Guidelines.

Therefore, it is requested that the message to the practising doctors should be loud and clear that pyrazinamide can be safely used during pregnancy.

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3. American Thoracic Society / Centers of Disease Control and Prevention / Infectious Diseases Society of America. Treatment of tuberculosis. *Am J Respir Crit Care Med* 2003; **167**: 603-62.

**The Authors Reply:** It is well known that pyrazinamide (PZA) is a very useful drug of anti-tuberculosis therapy and is used among the first line drugs. In the context of pregnancy the review has provided the factual scientific information. It is clearly mentioned in the review that International organizations have recommended the use of this drug during pregnancy, however, there are inadequate data on teratogenicity. This is backed by sufficient literature and reviews, which have been quoted in the literature.

In one of the recent review following statements would clarify the issue[1] "Pregnancy and breastfeeding: The initial treatment regimen should consist of INH, RIF and EMB. Although all of these drugs cross the placenta, they do not appear to have teratogenic effects. Although detailed teratogenicity data are not available, PZA can probably be used safely during pregnancy and is recommended by the World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (IUATLD). If PZA is not included in the inital treatment regimen, the minimum duration of therapy is nine months.

In can be inferred from the existing information that wherever primary resistance to INH resistance is less than 4% in the community, then three drugs regimen can be used in patients[2]. In

the context of pregnancy, in such case, pyrazinamide may be omitted. In India, the level of primary resistance to INH is much above this level, therefore, the four drugs regimen including pyrazinamide should be used and this would be applicable to pregnancy also. It would not be out of context to mention that data of teratogenicity due to pyrazinamide are inadequate till date.

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## RADIOLOGY FORUM

It is proposed to extend the scope of the Radiology Forum of our Journal by inviting our readers as well as other workers in the field or Respiratory Medicine to submit brief report of patients with interesting clinical and radiological features for publication. These will be published, provided that :

(*a*) the condition is of sufficient clinical and radiological interest;
(*b*) photographs (10 cm × 8 cm) are of excellent quality for printing (Maximum : 3 photographs);
(*c*) the diagnosis in each case has been confirmed;
(*d*) the chest radiograph is accompanied by brief clinical account, not exceeding one page typescript.

All the material received for publication in the Radiology Forum will be evaluated to judge the suitability for publication by our experts panel.

***Editor-in-Chief***

*[Indian J Chest Dis Allied Sci 2004; 46 : 301-305]*

ABSTRACTS' SERVICE

## Central Airway Obstruction

**Armin Ernst, David Feller-Kopman, Heinrich D. Becker, and Atul C. Mehta**

*American Journal of Respiratory and Critical Care Medicine 2004;* ***169*** *: 1278-97*

Central airway obstruction is a problem facing all medical and surgical subspecialists caring for patients with chest diseases. The incidence of this disorder appears to be rising because of the epidemic of lung cancer; however, benign causes of central airway obstruction are being seen more frequently as well. The morbidity is significant and if left untreated, death from suffocation is a frequent outcome. Management of these patients is difficult, but therapeutic and diagnostic tools are now available that are beneficial to most patients and almost all airway obstruction can be relieved expeditiously. This review examines current approaches in the workup and treatment of patients suffering from airway impairment. Although large, randomized, comparative studies are not available, data show significant improvement in patient outcomes and quality of life with treatment of central airway obstruction. Clearly, more studies assessing the relative utility of specific airway interventions and their impact on morbidity and mortality are needed. Currently, the most comprehensive approach can be offered at centers with expertise in the management of complex airway disorders and availability of all endoscopic and surgical options.

## Early Therapy Improves Outcomes of Exacerbations of Chronic Obstructive Pulmonary Disease

**Tom M.A. Wilkinson, Gavin C. Donaldson, John R. Hurst, Terence A.R. Seemungal, and Jadwiga A. Wedzicha**

*American Journal of Respiratory and Critical Care Medicine 2004;* ***169*** *: 1298-03*

Treatment of chronic obstructive pulmonary disease (COPD) exacerbations improves outcomes; however, responses to treatment are variable, and patients with COPD often delay presentation or fail to seek therapy. The impact on exacerbation outcomes, hospitalization, and health status of delaying or failing to seek treatment is poorly understood. We studied between 1996 and 2002 a cohort of 128 patients with COPD, mean (SD) $FEV_1$ of 1.07 (0.43) L. Patients recorded respiratory symptoms daily and reported exacerbations to the outpatient-based study team or to their primary care physician; 1,099 exacerbations were recorded by the patients, of which 658 were reported to a physician. The time between exacerbation onset and treatment was a median (interquartile range) of 3.69 (2.0-5.57) days, and the exacerbation recovery time was 10.7 (7.0–14.0) days. Earlier treatment was associated with a faster recovery (regression coefficient 0.42 days / day delay) (confidence interval, 0.19–0.65; $p<0.001$). Patients who reported a higher proportion of exacerbations for treatment had better health-related quality of life than those patients with more untreated exacerbations (rho=–0.22, $p=0.018$). Failure to report exacerbations was associated with an increased risk of emergency hospitalization (rho=0.21, $p=0.04$). Patient recognition of exacerbation symptoms and prompt treatment improves exacerbation recovery, reduces risk of hospitalization, and is associated with a better-health-related quality of life.

## The Clinical Skills Laboratory as a Learning Tool for Medical Students and Health Professionals

**Nada H. Al-Yousuf**

*Saudi Medical Journal 2004; **25** : 549-51*

Clinical skill laboratories (CSL) have become one of the essential facilities in an undergraduate medical curriculum. A wide range of training skills were recently introduced which includes clinical examination, diagnostic and therapeutic skills as well as communication skills. Although the educational value of the CSL is very well recognized, very little is written about it in the literature. The purpose of this paper is to provide an overview of the skills laboratory integrated in an undergraduate medical curriculum, highlight the nature of this trend, look at the advantages and disadvantages and suggest some guidelines for implementation.

## Bronchiolitis Obliterans Organizing Pneumonia

**Abdullah H. Al-Saghir and Abdullah E. Al-Mobeireek**

*Saudi Medical Journal 2004; **25** : 57-65*

Bronchiolitis obliterans with organizing pneumonia (BOOP) is now established as a distinct clinicopathologic entity, yet it may be overlooked by clinicians due to unfamiliarity and its non-specific presentation. It can be either idiopathic or associated with a variety of causes, such as infections, drugs, radiation or connective tissue diseases. A lung biopsy is needed to provide histopathologic confirmation. Usually prognosis is good, and the response to steroids may be dramatic, but occasionally BOOP may be fatal or runs a chronic relapsing course. This article is an updated review on current knowledge regarding BOOP.

## Knowledge of and Attitudes Towards Tobacco Control Among Smoking and Non-smoking Physicians in 2 Gulf Arab States

**Nasser N. Behbehani, Randah R. Hamadeh and Nejma S. Macklai**

*Saudi Medical Journal 2004; **25** : 585-91*

***Objective.*** The global health professional survey is a project organized by the World Health Organization, to determine the smoking habits, knowledge and attitude towards tobacco control of health professionals in several countries around the world. This paper presents data from Kuwait and Bahrain.

***Methods.*** The survey period was between May 2000 and March 2001. A questionnaire was distributed to all physicians in Bahrain and to a random sample from Kuwait. The responses to knowledge and attitude questions were on a scale of 1–5, (1 strongly agree, 2 agree, 3 unsure, 4 disagree and 5 strongly disagree).

***Results.*** Four hundred and seventy physicians from Bahrain and 1095 from Kuwait completed the questionnaire. The prevalence of cigarette smoking in Kuwait was: current smokers 18.4%, previous smokers 15.8%; Bahrain 14.6% and 14.3%, respectively. The prevalence of *shisha* smoking was 12% and 6.4% for Kuwait and Bahrain, ($p$=0.004). The mean scores of agreement with the association between passive smoking and lung diseases, lower respiratory tract infections in children were 1.6, 1.7 and 1.8, 1.9 for non-smoking physicians and smoking physicians ($p$<0.01). The mean scores of agreement with the following policies: large health warning on cigarette packages, complete ban on tobacco advertisement and an increase in the price of cigarette were 1.3, 1.4, 1.7 and 1.7, 1.7, 2.5 for smoking and non-smoking physicians ($p$<0.01).

***Conclusion.*** Smoking physicians have less knowledge and less favourable attitude towards tobacco control compared to non-smokers. There was no difference in the prevalence of cigarette smoking between Kuwait and Bahrain, but the prevalence of *shisha* smoking was higher in Kuwait.

## Tuberculosis in HIV-infected Persons in the Context of Wide Availability of Highly Active Antiretroviral Therapy

**E. Girardi, G. Antonucci, P. Vanacore, F. Palmieri, A. Matteelli, E. Lemoli, S. Carradori, B. Salassa, M. Bruna Pasticci, M.C. Raviglione, G. Ippolito, and the GISTA-SIMIT Study Group**

*European Respiratory Journal 2004;* ***24*** *: 11-17*

Highly active antiretroviral therapy (HAART) greatly reduces the risk of developing tuberculosis for HIV-infected persons. Nonetheless, HIV-associated tuberculosis continues to occur in countries were HAART is widely used.

To identify the characteristics of HIV-infected persons who develop tuberculosis in the context of the availability of HAART, the current authors analysed data taken from 271 patients diagnosed, in Italy, during 1999-2000. These patients represent 0.7% of the 40,413 HIV-infected patients cared for in the clinical units participating in this current study.

From the data it was observed that 20 patients (7.4%) had a previous episode of tuberculosis whose treatment was not completed. Eighty-one patients (29.9%) were diagnosed with HIV at tuberculosis diagnosis, 108 (39.8%) were aware of their HIV status but were not on antiretroviral treatment and 82 (30.3%) were on antiretroviral treatment. Patients on antiretroviral treatment were significantly less immunosuppressed than patients with HIV diagnosed concurrently with tuberculosis, or other patients not on antiretrovirals (median CD4 lymphocytes count: 220 cells/$mm^{-3}$ *vs* 100 cells/$mm^{-3}$ and 109 cells/$mm^{-3}$, respectively). No significant differences in clinical presentation of tuberculosis according to antiretroviral therapy status were recorded.

Failure of tuberculosis control interventions (*e.g.* noncompletion of treatment) and of HIV care (delayed diagnosis of HIV infection and suboptimal uptake of therapy) may contribute to continuing occurrence of HIV-associated tuberculosis in a country where highly active antiretroviral therapy is largely available. However, a significant proportion of cases occur in patients who are on antiretroviral treatment.

## Atypical Pathogens and Respiratory Tract Infections

**F. Blasi**

*European Respiratory Journal 2004; **24** : 171-81*

The atypical respiratory pathogens *Chlamydia pneumoniae*, *Mycoplasma pneumoniae* and *Legionella pneumophila* are now recognised as a significant cause of acute respiratory-tract infections, implicated in community-acquired pneumonia, acute exacerbations of chronic bronchitis, asthma, and less frequently, upper respiratory-tract infections.

Chronic infection with *C. pneumoniae* is common among patients with chronic obstructive pulmonary disease and may also play a role in the natural history of asthma, including exacerbations. The lack of a gold standard for diagnosis of these pathogens still handicaps the current understanding of their true prevalence and role in the pathogenesis of acute and chronic respiratory infections.

While molecular diagnostic techniques, such as polymerase chain reaction, offer improvements in sensitivity, specificity and rapidity over culture and serology, the need remains for a consistent and reproducible diagnostic technique, available to all microbiology laboratories.

Current treatment guidelines for community-acquired pneumonia recognise the importance of atypical respiratory pathogens in its aetiology, for which macrolides are considered suitable first-line agents. The value of atypical coverage in antibiotic therapy for acute exacerbations of chronic bronchitis and exacerbations of asthma is less clear, while there is no evidence to suggest that atypical pathogens should be covered in antibiotic treatment of upper respiratory-tract infections.

## Patient-physician Communication About End-of-Life Care for Patients with Severe COPD

**J.R. Curtis, R.A. Engelberg, E.L. Nielsen, D.H.Au and D.L. Patrick**

*European Respiratory Journal 2004; **24** : 200-205*

Since patients with chronic obstructive pulmonary disease (COPD) infrequently discuss treatment preferences about end-of-life care with physicians, the goal of the present study was to identify which specific areas of communication about end-of-life care occur between patients with severe COPD and their physicians, and how patients rate the quality of this communication.

A total of 115 patients with oxygen-dependent COPD, identified in pulmonary clinics in three hospitals and through an oxygen delivery company, were enrolled in this study. A 17-item quality of communication questionnaire (QOC) was administered to patients, along with other measures, including satisfaction with care.

The patients reported that most physicians do not discuss how long the patients have to live, what dying might be like or patients' spirituality. Patients rated physicians highly at listening and answering questions. Areas patients rated relatively low included discussing prognosis, what dying might be like and spirituality / religion. Patients assessments of physicians' overall communication and communication about treatment correlated well with the QOC. Patients' overall satisfaction with care also correlated significantly with the QOC.

In conclusion, this study identifies areas of

communication that physicians do not address and areas that patients rate poorly, including talking about prognosis dying and spirituality. These areas may provide targets for interventions to improve communication about end-of-life care for patients with chronic obstructive pulmonary disease. Future studies should determine the responsiveness of these items to interventions, and the effect such interventions have on patient satisfaction and quality of care.

## The Use of SPECT in Preoperative Assessment of Patients with Lung Cancer

**D.B. Piai, R. Quagliatto(Jr), I. Toro, C. Cunha Neto, E. Etchbehere and E. Camargo**

*European Respiratory Journal 2004;* ***24 :*** *258-62*

Perfusion scintigraphy is the most frequently used method for the regional assessment of pulmonary function in candidates for pulmonary resection with borderline respiratory function. This method provides two-dimensional images, and it considers all the segments of the pulmonary lobes as having the same volume and function, without considering the spatial overlapping of pulmonary areas with different function. As single-photon emission computed tomography (SPECT) provides tomographic imaging, this could be a more precise method for regional assessment.

In this study, the postoperative predicted forced expiratory volume in one second ($FEV_1$) ($FEV_1$,pp0) was calculated in 26 patients with lung cancer using $FEV_1$, quantitative lung perfusion scan with planar acquisition (PA) and quantitative lung perfusion scan with tomographic imaging (SPECT).

The estimated $FEV_1$,ppo values obtained using both methods were compared with $FEV_1$ values measured after surgery (mean: 48±44 days: range: 15-180 days; median: 32 days). The Pearson's linear correlation coefficient was 0.8840 for $FEV_1$,ppo estimated by PA and 0.8791 for $FEV_1$,ppo estimated by SPECT. The linear correlation coefficient for lobectomy was greater than the coefficient for pneumonectomy using both methods.

In conclusion, both methods show good correlation for real postoperative pulmonary function without demonstrating single-photon emission computed tomograpy superiority over planar acquisition, and both methods were more effective for estimating postoperative predicted forced expiratory volume in one second in lobectomies than in pneumonectomies.

*[Indian J Chest Dis Allied Sci 2004; 46 : 306-308]*

# Authors' Index – 2004
## (Vol. 46, Nos 1 – 4)

# Guidance for Authors

*The Indian Journal of Chest Diseases and Allied Sciences* considers for publication original articles dealing with respiratory and cardiovascular diseases and in the fields of anatomy, biochemistry, microbiology, mycology, pathology, pharmacology, physiology, ultra-structure and virology of respiratory, and cardiovascular systems. However, only papers that make a significant contribution to the existing state of knowledge in a particular field will be published. The journal publishes original articles, case reports, radiology forum, short communications and book reviews.

**Submission of Manuscripts.** Manuscripts including figures (in triplicate) should be sent to ***The Editor, The Indian Journal of Chest Diseases and Allied Sciences, C/o Publication Department, V.P. Chest Institute, University of Delhi, Delhi-110007, Post Box No. 2101***.

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Presentation of manuscripts should conform with the uniform requirements for manuscripts submitted to biomedical journals (for further details see *Ann Intern Med* 1988; **108** : 258-265).

Authors are advised to see a recent issue of the Journal to get familiar with the format adopted in respect of various elements of a paper. All the manuscripts should be organised in the order set forth below. *Failure to follow these instructions may result in the manuscript being returned to the author(s) for revision before* it will be reviewed.

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II. *Abstract and Key Words.* The second page should carry a structured abstract of not more than 200 words. It should be written for the readership of both clinicians and basic investigators and should state the hypothesis or central question of the study or investigation, the study subjects or experimental animals, observational and analytical methods, the main findings, and a final statement of the principal conclusions. Three to six key words using, where possible terms of medical subjects headings list from *Index Medicus.*

III. *Introduction.* It should commence on separate page and should briefly review the current state of knowledge strictly concerning the topic of the paper. It should also make a clear statement on the reasons for undertaking the study being reported and what it hoped to achieve. No mention should be made of the

results obtained or conclusions drawn.

IV. *Material and Methods.* The material (patients, experimental animals, etc.) used for making observations must be described along with all other relevant information. The methods used in the study should be described, giving sufficient information to permit the work to be repeated. If a generally accepted technique has been used, only a reference to that is enough. If, however, such a technique has been modified by the workers, the manner in which this has been done should be clearly stated. If statistical analysis of the data has been done, the methods used for analysis should be specified.

V. *Results.* This section should not include materials suitable for inclusion in "Material and Methods' or "Discussion". The results should be presented in logical sequence in the text, tables and illustrations. The data presented in the tables or figures should not be repeated in the text. Only important and significant observations should be included.

VI. *Discussion*. This should be limited to significance of results obtained and what can and what cannot be concluded and why. It should not be a repetition of the findings already given under 'Results'. Results should be discussed in the light of others' work in the field. Speculative and purely theoretical discussion to which results presented are not related will not be accepted.

VII. *Acknowledgements*. Acknowledge the source(s) of support in the form of grants, equipments, drugs; or all of these; as well as the person (s) who have made substantive contributions to the study. All acknowledgements must be grouped into one page after 'Discussion'.

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**Journal**

Kumar S, Mohan A, Sharma SK, Pande JN. Recent concepts in the pathogenesis of bronchial asthma. *Indian J Chest Dis Allied Sci* 1997; **39** : 27-45.

**Book**

Behera D. *Textbook of Pulmonary Medicine.* New Delhi : Jaypee Brothers Medical Publishers (P) Ltd, 1995.

**Chapter in Book**

Niewoehner DE, Sobonya RE. Structure-function correlations in chronic obstructive pulmonary disease. In : Baum GL, Wolinsky E, ed *Textbook of Pulmonary Diseases;* 4th edn; Vol II. New York : Little, Brown and Co.; 1994: 973-993.

*Correctness of the reference list is the entire responsibility of the author (s).*

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