CAVITATING PULMONARY TUBERCULOSIS BELOW AGE OF 2 YEARS

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ABSTRACT

A prospective study was conducted on 75 consecutive cases of primary cavitary pulmonary tuberculosis in hospitalized children below 2years to determine the spectrum of the disease. Diagnosis was based on clinical, radiological, tuberculin test and histopathological findings and not on isolation of tubercle bacilli. Peak age was 7-12 months. Ten mothers suffered from pulmonary fibrocavitary disease and 73% of cases were severely malnourished. Presenting symptoms' were fever and cough, at times dyspnea and often followed by measles. Unlike adults, hemoptysis was seldom encountered. Cavitary lesions were characterized by protean radiological manifestations and varied in size and appearance. They were more often multiple than solitary, bilateral or distributed in one or more lobes, usually in the right lung. Loculation within consolidation and other associated pulmonary pathology was frequent with miliary nodules in 45.3%. Widespread hematogenous infection was common with tuberculous meningitis in 28%. The accepted diagnostic features of tuberculosis, viz., hilar and mediastinal lymhadenopathy and positive tuberculin test were often absent. Mortality was 34.7% and in inverse proportion to age. The observations stress the difficulties in diagnosis.

Key words: *Tuberculosis, Infants, Primary cavitating pulmonary tuberculosis, Miliary tuberculosis.*

One of the manifestations of progressive primary tuberculous lung lesion is the occurrence of necrosis and liquefaction of the caseous material within the primary focus. This material may discharge into a bronchus resulting in a cavity which is defined as primary cavitating tuberculosis (PCT). The definition represents a controversial subject with reference to inclusion as "primary", those cavities located in pulmonary lesions resulting from either bronchogenic or lymphatic spread from the primary focus or caused by erosion of caseous lymph node into the bronchus.

PCT, a devastating disease with a high mortality, is a rare complication of primary tuberculosis. However, it is not uncommon during infancy and early childhood. The diagnosis is often overlooked as there is lack of awareness regarding this entity. The clinical features of the disease are different from those in other age groups. Most published literature on PCT consist of individual case reports and detailed account of the spectrum of the disease is seldom available. We report the clinical observations, radiological features and the outcome in 75 cases of PCT presenting before the age of 2 years.

Material and Methods

Cavities besides those in the primary focus itself were diagnosed as PCT. Seventy five consecutive patients with PCT admitted to the Pediatric Department of Goculdas Tejpal Hospital, Bombay between 1973 and 1990

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were prospectively studied. A detailed history and physical examination was conducted on each case. Nutritional status was defined using standards of Indian Academy of Pediatrics(l). Postero-anterior and lateral chest X-rays were performed. Tuberculin test was administered using ITU PPD RT23 with Tween 80 and induration of 10 mm or more at 48-72 hours was interpreted as positive reaction. Attempts to isolate tubercle bacilli with gastric lavage were made on smear examination.

A diagnosis of tuberculosis was considered in cases with:

1. History of exposure to an open case of tuberculosis.
2. Radiographic pulmonary changes such as miliary tuberculosis and hilar and/or mediastinal lymphadenopathy.
3. Extrapulmonary lesions suggestive of tuberculosis.
4. Positive skin reaction to tuberculin test.
5. Clinical and radiological response to anti-tubercular chemotherapy. All cases were advised treatment for minimum period of one year. As a rule streptomycin and isoniazid were used throughout the study and were the only drugs used from 1972-1974. During 1975, ethambutol was added for a period of 2 years. From 1976 rifampicin and 1982 onwards pyrazinamide was introduced.

Tuberculous etiology was established on the basis of the presence of two or more of the above factors in 62 cases whilst in 13 cases a single factor was considered adequate for diagnosis, *viz.,* miliary tuberculosis in 7, response to specific treatment in 6. Tubercle bacilli were isolated in only 2 cases, one on gastric lavage and another on autopsy. In 10 cases on autopsy, histopathological evidence of tuberculosis was detected in the lungs with hematogenous dissemination in 9.

Results

Of 14,281 total admissions, 75 (0.525%) were PCT. Of these 48 (64%) were below 1 year and 27 (36%) between 1-2 years. Only 5 cases were less than 3 months of age and the youngest were two infants aged 1.5 months. The peak incidence was between 7-12 months. Boys were 39 (52%) and girls 36 (48%). Twenty four (32%) had received BCG vaccination as confirmed by presence of a scar.

In 24 patients there was a history of contact with an individual with active tuberculosis. Of these 10 were mothers with fibrocavitary pulmonary disease. The other 14 comprised 4 fathers, 8 relatives and 2 neighbors. In 7 instances there were multiple household contacts. Sixteen (28%) cases aged between 7-24 months followed measles. Fifty five (73.3%) patients suffered from severe protein-energy malnutrition, of these 44 had Grade IV and 11 Grade III malnutrition. Anemia with a hemoglobin level below 8 g/dl was seen in 21 (28%) and Vitamin A deficiency and active rickets in 4 cases each.

The commonest presenting symptoms were fever (67; 89.3%) and cough (51; 68%). The cough was nonproductive. It was either persistent and weak or paroxysmal and loud which at times sounded brassy or hoarse. Occasionally, bouts of cough were followed by a "whoop" resembling pertussis. Other symptoms consisted of dyspnea with wheezing or inspiratory stridor in 14 (18.7%), convulsions in 13 (17.3%), diarrhea in 12 (16%), vomiting in 10 (13.3%), and weight loss and failure to thrive in 5 (6.7%). Drowsiness and irritability were present in 2 cases each; hemiparesis, VII nerve paraly-

sis and hemoptysis in 1 case each. Signs on examination of the chest were often limited to rales.

Radiological Appearance

PCT was characterized by marked variation not only in the size and position but in the appearance of the cavity itself. The cavities were seen more frequently in the right lung (45 cases, 60%) as compared to the left (13 cases, 17.3%) and were bilateral in 17 (22.7%). The right lower and upper lobes were the most common sites of involvement. The size of the cavities varied greatly from few mm to 5 cm diameter which occupied almost half the lung.

PCT presented with or without surrounding consolidation/collapse. In 53 (70.7%) the cavities appeared independently and were either multiple (37 cases) or single (16 cases). Multiple cavities were usually small, bilateral and associated with miliary tuberculosis *(Fig. 1a)*. Single cavities were spherical or oval and often thin-walled, one of which was a tension cavity *(Fig.2);* only in 2 cases they had thick ragged walls *(Fig. 3)*. In 22 (29.3%) cavities were situated, within consolidation/collapse which was either limited *(Fig. 4)* or extensive *(Fig. 5*). Usually, these cavities appeared as irregular highlights but in one case air-fluid level was detected within a cavity *(Fig. 6)*. Serial X-rays showed considerable change in size, distribution and character of the lesion.

Miliary tuberculosis was present in 34 cases, of which 5 were detected on autopsy; spontaneous pneumothorax and pneumomediastinum *(Fig. lb)* was seen in 2 cases. Forty cases had consolidation/collapse, 30 hilar and/or mediastinal lymphadenopathy, 4 bronchopneumonia and 2 lobar emphysema. Thickened pleura *(Fig. 6)* was confirmed in one case on autopsy. Pleural effusion and empyema were conspicuous by their absence.

Tuberculous meningitis was present in 21 (28%) patients, of which one was serous meningitis. Thirteenscases with tuberculous meningitis had miliary tuberculosis. Superficial matted and caseated lymph nodes were found in 6 cases, 5 were cervical and one axillary. Otomastoiditis was present in 2 cases and resulted in VII cranial infranuclear nerve paralysis. On autopsy tubercular mesentric lymphadenitis and tubercles in the liver and spleen were seen in 6 cases. In 23 (30.7%) cases hepatosplenomegaly and in 10 (13.3%) only Hepatomegaly were found which although not proved on biopsy, could have been a manifestation of tuberculosis. Phlyctenular keratoconjunctivius and erythema nodosum were not detected.

The tuberculin test was more often negative (45 cases) than positive (23 cases). The BCG test was positive in presence of a negative .tuberculin test in 5 cases.

Mortality was 34.7%. Of the 26 deaths, 4 were within a day of admission and 3 more within 3 days. Besides the condition on admission various factors governed the prognosis of which age and associated miliary tuberculosis and tuberculous meningitis were important. Younger the child, the higher was the mortality. In infants below 6 months the mortality was 70.6% as compared to 41.9% in 7-12 months and only 3.7% above 1 year. Between the age group below 6 months and above 1 year there was no significant difference in the incidence of miliary tuberculosis and tuberculous meningitis; severe malnutrition was less (47%) in early infancy as compared to 85% in the older age group. Twenty two (84.6%) of total deaths occurred when miliary tuberculosis and tuberculous meningitis were associated features.

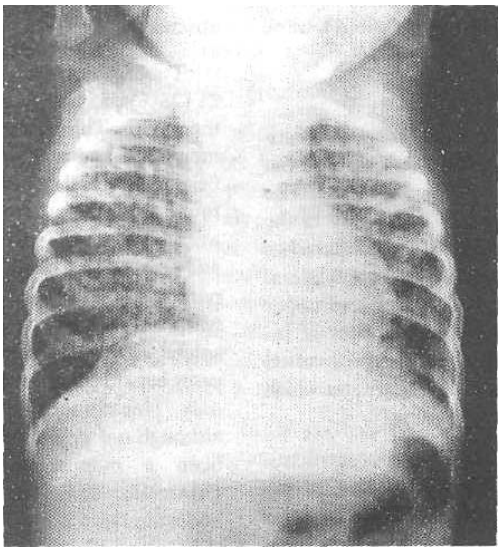

Fig. 1a. Multiple small cavities with miliary tuberculosis confirmed at autopsy.

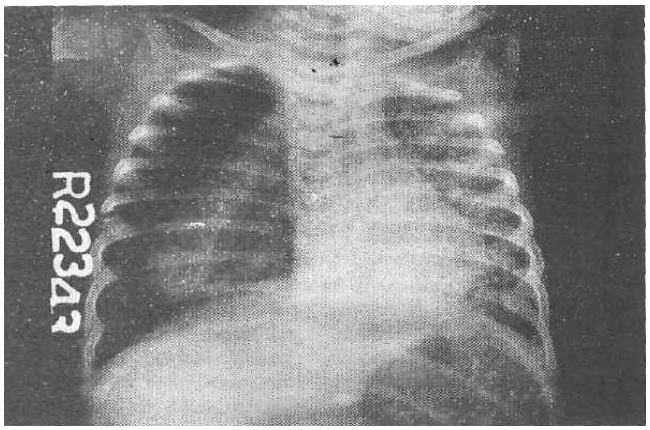

Fig. 1b. Right pneumothorax and pneumomediastinum a week after admission in 9-month-old infant with marasmic kwashiorkor, tuberculous cervical lymphadenitis and hepatosplenomegaly.

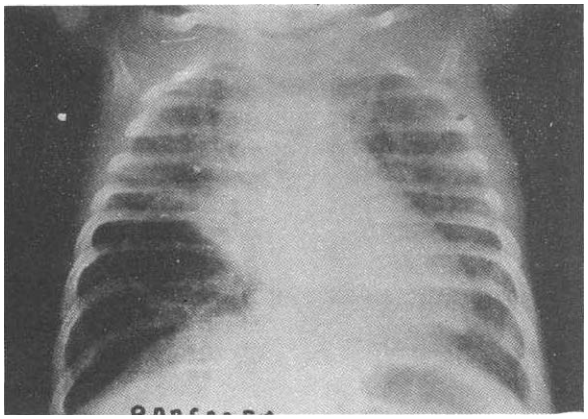

Fig. 2. Thin-walled tension cavity in an emphysematous right lower lobe, military tuberculosis and hilar/ mediastinal lymphadenopathy. The subject was a 4-month-old marasmic, cyanosed infant in respiratory distress with weak persistent cough and hepatosplenomegaly and died within hours of admission.

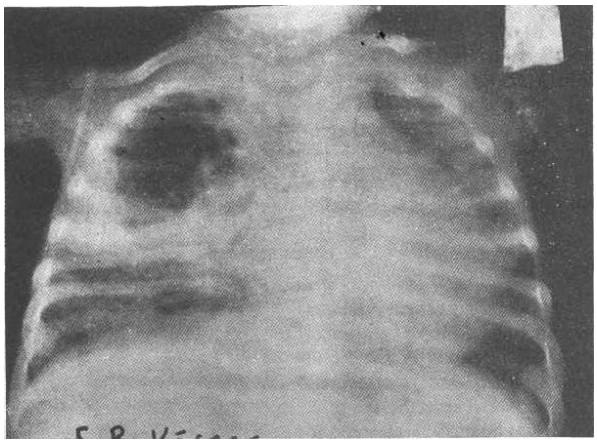

Fig. 3. Thick-walled cavity right upper lobe military tuberculosis and hilar/mediastinal lymphadenopathy confirmed at autopsy. This was a 7-month-old marasmic infant with tuberculous meningitis hepatosplenomegaly who died within hours of admission.

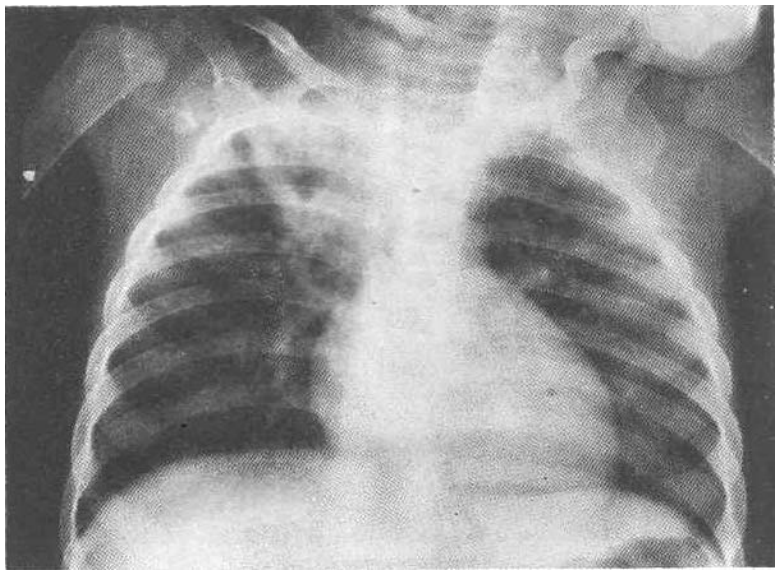

Fig. 4. Cavity surrounded by consolidation in the right upped lobe and hilar/mediastinal lymphadenopathy confirmed at autopsy in a 12-month-old marasmic infant in respiratory distress with tuberculous meningitis.

Mortality was 84.6% if both were present, 50% with tuberculous meningitis, 33.3% with miliary tuberculosis and 12.1% if both were absent. Only 4 deaths occurred in the absence of miliary tuberculosis and tuberculous meningitis of which 3 were below the age of 5 months and in 1 specific chemotherapy was introduced late due to missed diagnosis.

Discussion

From the present study certain persistent findings have emerged evolving a pattern of PCT which would be useful in arriving at a diagnosis. A typical case is a severely malnourished infant between the age of 7-12 months who may be BCG vaccinated and whose mothers suffer from active pulmonary tuberculosis. The illness follows an attack of measles and the presenting symptoms are fever and cough. Hilar and/or mediastinal lymphadenopathy could be absent and tuberculin test negative. Associated lesions are miliary tuberculosis, tuberculous meningitis and hepatosplenomegaly. The cavitary lesions, usually in the right lung or bilateral are either solitary or multiple, within consolidation or isolation. Clinical picture and prognosis are linked with age. In the younger age group below 1 year as compared to above 1 year, the differences are reflected in higher mortality (52.1% and 3.7%, respectively), maternal tuberculous contact (18.7% and 3.7%, respectively) miliary tuberculosis along with tuberculous meningitis (22.9% and 7.4%, respectively) and hepatosplenomegaly (31.2% and 11.1%, respectively).

The present series is characterized by a remarkably high incidence of associated

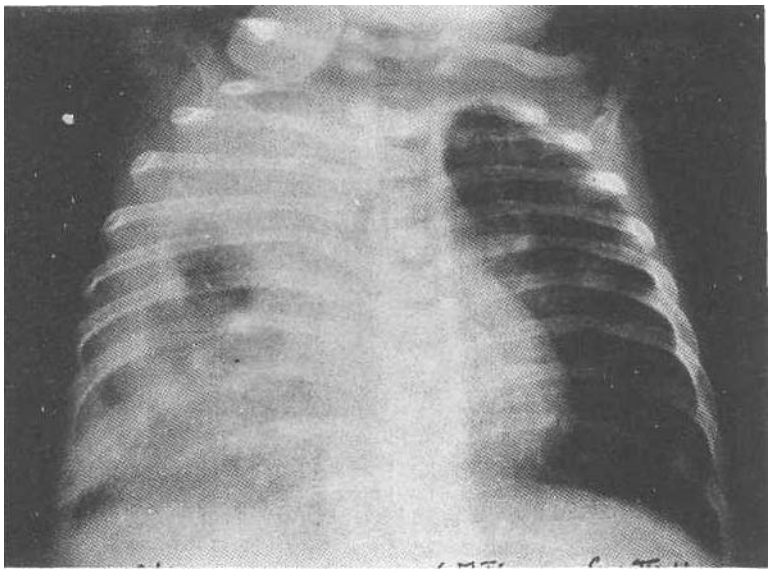

Fig. 5. Multiple cavities within massive consolidation of the right lung in a 6-month-old infant with marasmic kwashiorkor and hepatosplenomegaly. There was history of tuberculosis in mother and 2 siblings. At the age of 2 months, anti-tubercular chemotherapy advised for segmental consolidation of the right lower lobe was not administered.

miliary tuberculosis and tuberculous meningitis which has been reported infrequently from the industrialized countries. An unexpected feature was the relatively low incidence (40%) of hilar and/or mediastinal lymphadenopathy. However, there is considerable disagreement in their interpretation and these are known to be missed antemortem and detected on autopsy. The evidence of malnutrition with PCT has been reiterated in the literature and 3/4th of the cases suffered from severe PEM. Tuberculin test was of limited diagnostic assistance and was more often negative than positive.

The role of measles in the etiology of PCT has not received sufficient attention from most authors. Measles was a predisposing factor in about l/4th of the cases above the age of 6 months. Prevention of PCT should include measles vaccination preferably as early as 6 months and infants after recovery from measles must be observed closely for the development of progressive tuberculous disease.

Review of the literature on pulmonary tuberculosis in infancy shows preponderence of right lung involvement(2-4) and the same is also true for PCT(5-7). In the present series the right lung was involved thrice as often as the left and the lesions were most frequently detected in the lower and upper lobes. Merrit(6) reported the commonest site of lesion to be the lower and Joffe(5) upper and middle lobes. The striking feature was the extensive distribution of multiple cavities in both lungs (22.7%), due to poor host response as a result of malnutrition and disseminated tuberculosis.

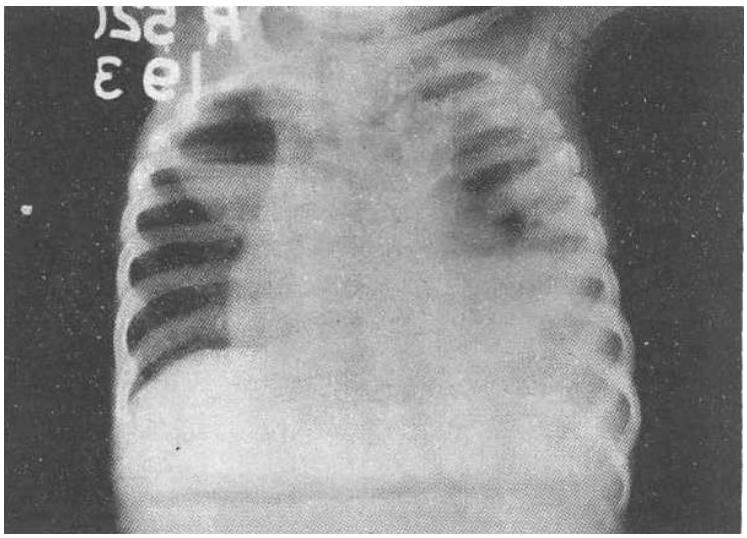

Fig. 6. *Cavity with air-fluid level right upper lobe (lI1d homogenous density of the left lung with cavities. The subject was a 12-month-old infant with fever following measles. A normal X-ray chest with rapidly changing appearance was suggestive of staphylococcal pneumonia. On the basis of hepatosplenomegaly and failure to respond to antibiotics anti-tubercular chemotherapy was introduced. The child expired after* 1 *month. On autopsy the cavity in the right lung measured* 3.5 *cm in diameter, contained thick whitish yellow material, was lined by necrotic slough and surrounded by consolidation with tubercles. The left lung pleura was thickened and adherent, the entire lung was destroyed by numerous cavities and the upper lobe had areas of caseated consolidation with tubercles. Bilateral caseated hilarjmediastinallymphadenitis was detected.*

The definition of PCT is disputed by various authors with reference to inclusion of cysts associated with tubercular bronchiectasis, bronchopneumonia, tension cysts(8) and those situated within segmental lesions(9). It is argued that the differentiation between them and necrotic cavities can be determined only by pathological examination. As in the present series other reports on PCT include cavities within consolidation(4,5,10), those associated with bronchopneumonia(7) and tension cysts(5).

The general belief is that cavities are infrequent in primary tuberculosis in children as is apparent from most clinical studies. Although, PCT has been reported from the West(ll) the incidence is higher in African(2,3,5,7,8) and Indian(4,10) children. In all probability this is the result of early tuberculization, malnutrition and measles. In Freiman's series(3) of 176 tuberculous African children, 23 had cavitation of which 19 were aged 2 years or younger. From India, Manchanda(4) in a study of 125 cases below 3 years found 7 with PCT and Udani(10) has described various types of cavities encountered in infancy.

In sharp contrast to clinical findings there is a relative high frequency of tuberculous cavities in postmortem studies as proved by a review of numerous documented series in tuberculous infants below 2 years from

technically advanced countries in the early part of 20th century(6). Merritt(6) in a study of autopsy on 75 tuberculous infants below 1 year from 1915-1928 at John Hopkins, found that cavities occurred in nearly 50% of the cases which they were definitely diagnosed by X-rays in only one and were suggestive in two other cases. Such a paradoxical finding can occur if cavities are much more frequent in fatal cases or they are difficult to detect antemortem.

The ultimate proof of confirmation of diagnosis of tuberculosis must be the recover of tubercle bacillus but in infants isolation of the organism is proverbially difficult. In 1954 Miller and McDougall(12) stated that in children under 2 years diagnosis is usually made by a combination of clinical findings, tuberculin test and radiogrphy. After nearly 4 decades their observations still hold true. Since, PCT is prevalent in developing countries with limited facilities this approach to diagnosis is widely accepted. Whether the cavity is tubercular or not, is at times extremely difficult to determine, particularly in the very young infant. Several cases of suspected PCT with a typical clinical profile have not been included in the series when they failed to meet the criteria required for diagnosis. These had nonspecific pulmonary lesions such as consolidation/collapse or bronchopneumonia without hilar and/or mediastinal lymphadenopathy, absence of extrapulmonary tuberculous lesions, negative tuberculin test and response to chemotherapy could not be appreciated due to death or discharge against medical advice soon after admission. Diagnostic difficulties were increased when history of contact was not available.

Bacillary pneumonia and in particular staphylococcal pneumonia was the most important differential as PCT often had an acute onset with fever, cough and dyspnea. A changing deteriorating picture on serial radiography was observed especially in the absence of specific chemotherapy. Massive consolidation and thickened pleura *(Fig. 6)* resembled empyema but these were not associated with a mediastinal shift. Pneumothorax though rare did occur. At times, diagnosis of Freidlander pneumonia was entertained as chest X-rays showed bulging interlobar fissure. Only in one case the cavity had air-fluid level raising the possibility of an abscess. Investigations such as hemogram, ESR, culture studies of blood, throat and ear swabs were not helpful. Newer immunological tests for tuberculosis and lung puncture aspirations were not performed. Biopsy of a lymph node even without clinical characteristic features of tuberculosis may prove to be a valuable diagnostic tool. Besides infective, congenital cysts had to be ruled out. When despite broad spectrum antibiotic treatment clinical condition worsened early introduction of specific antituberculous chemotherapy based on a high index of suspicion was a justified and useful therapeutic test which proved to be a life-saving measure as PCT progresses rapidly with a fatal outcome.

The pattern of tuberculosis is changing rapidly and is likely to change further with widespread use of BCG vaccination, chemoprophylaxis and potent antimicrobial drugs. The prevalence of PCT is on the decline and the number of cases recorded in the first half of the study period from 1973 to 1981 was 0.58% of the total admissions as compared to 0.27% from 1982 to 1990. If in the near future AIDS does become a growing problem in India the infant would be at risk to develop tuberculosis with unprecedented changes in the pattern of disease as the immunocompromized host would be expected to react with higher cavitary and fulminating

disseminated lesions. Of 136 adult AIDS cases reported in a study from US(13), 21% developed tuberculosis. Besides progressive pulmonary disease with cavitary lesions and miliary spread majority had extrapulmonary disease. Unusual manifestations of tuberculosis were frequent.

The optimism that the advent of every new chemotherapeutic agent evokes is often shortlived in the context of young infants with cavitary and disseminated tuberculous disease. Although addition of pyrazinamide to the therapeutic regimen improved survival, of the two infants below 1 year suffering from PCT associated with tuberculous meningitis, one died and the other led a vegetable existence with decerebrate rigidity. In view of the high mortality of PCT, emphasis should be on prevention and all efforts should be aimed at control of the disease in the mothers which is fundamental to protecting the infant.

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