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MYCOBACTERIAL INFECTIONS

It is estimated that there are about 15 million cases of tuberculosis and about 10 million cases of leprosy in the world. These include the infectious and the non-infectious. About three-fourths of these cases are believed to occur in the developing countries. Their importance, thus, is obvious. The etiological factors, pathogenesis, epidemiology, immunological mechanisms, control and therapeutic measures appear to have some common features. For us, the control of these two diseases is not only important for health needs, but it also serves as an index of social development. The physical quality of life index in India is 43 while the average for all the countries is 53, and the index for developed countries is about 90 and above. The physical quality of life index (PQLI) is computed from infant mortality, expectation of life, and the literacy rates reached in the country.

As medical research is vital for finding solutions to human problems, it is incumbent on all bio-medical scientists to probe deep into the mysteries of these two diseases and try to find solutions, in both fundamental and applied aspects. We have waited too long to be benefactors and are content to be beneficiaries of advances made elsewhere and by visiting scientists. It is not only the basic research that is relevant now but also Health Services Research. Inspite of all the advances in the basic aspects, we are failing to use it successfully for human betterment due to lack of interest in Health Services Research in respect of control, alleviation and rehabilitation.

Four main groups of Mycobacteria have been identified, based largely on the pathogenic properties, by John Francis and Ellis W. Abrahams*

i. Tubercle bacillus: three species of genus Mycobacterium that grow slowly on artificial media and produce tuberculosis in man, cattle and birds.

ii. Tuberculoid bacilli are members of the genus Mycobacterium which grow slowly on artificial media. The lesions are indistinguishable from tuberculosis and these do not spread from man to man. The atypical tubercle bacillus belongs to this group. Some use the term 'tuberculoidosis' for these lesions. There are four types of these bacilli: Photo-chromogenic (type I); Scotochromogenic (type 11) Batey Type without pigment (type III) and the rapid growers (type IV).

iii. Saprophytic mycobacteria are members of the genus Mycobacterium that grow rapidly in simple artificial media and are prevalent in nature. M. Phelei and M. Smegmatis belong to this group.

*Tubercle, 1982, 62, 309-310

iv. Leprosy and Johns' bacilli are members of the genus Mycobacterium that do not grow on bacteriological media and grow only when Mycobactin is added. It is considered advisable to include organisms of skin tuberculosis and bubalorium in this group.

Tuberculosis and Leprosy have plagued mankind for thousands of years and continue to do so. The third world suffers the most. The physical quality of life is very low. Nutrition and environmental sanitation are low and the socio-economic conditions are poor. Leprosy thrives in tropical and sub-tropical climes, while both diseases are rampant in countries where economic under-development results in low standards of living.

Leprosy is more chronic, more disfiguring and more repugnant and causes greater social stigma. Leprosy attacks tissues derived from ectoderm e.g. skin and nerves, but all organs may be involved. Tuberculosis affects the lungs predominantly though no organ in the body is exempt.

Mycobacterium Lepra was discovered by Hansen in 1873, nine years earlier than the Tubercle bacillus by Robert Koch in 1882. Lepra bacillus is difficult to grow but the discovery of the growth of M. Lepra in the foot pad of mice and the discovery that the nine-banded armadillo is susceptible to leprosy have provided a break-through. However, leprosy research has lagged behind Tuberculosis.

Specific leprosy vaccine is yet to be found. B.C.G. has been used with mixed results and doubts are being expressed even in respect of its utility in tuberculosis. The recent reports on BCG trials in India are an eye-opener. It is, however, advocated in the prevention of childhood tuberculosis.

Immune spectrum in Tuberculoid leprosy T T is high and in Lepromatous Leprosy LL, it is low. Even in tuberculosis there is a possible immune form reaction RR and Non reactive UU which are analogous to TT and LL in Leprosy, Both M. Lepra and M. Tuberculosis become drug resistant to Dapsone and anti-tuberculosis drugs respectively. Both have cell mediated immunity. However, there is real need for more work in this respect. It is disconcerting that so few basic scientists are interested in this aspect.

The ICMR survey in the late fifties showed tuberculosis morbidity to be 1.3 to 2.5 per cent. It is estimated that there could be about 8 million clinical cases requiring treatment, 1.5 million of whom could be infectious requiring priority treatment. The number of deaths from tuberculosis would be about half a million annually. Leprosy cases are estimated to be about 4 million, of whom about I million are likely to be infectious. Lepromatosis occurs when resistance is poor. Tuberculoid type occurs when the immunity is high. The intermediate and borderline cases are between lepromatous and tuberculoid types.

These two diseases which are a blot on our society and nation require attention. Solution to problems will have to be found by Indians for diseases predominantly prevalent in India. Basic as well as clinical scientists will have to develop new techniques for their control. Let us take up the challenge and make the goal 'Health for all by 2000' a reality.

—K. N. Rao

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SURGERY IN ABDOMINAL TUBERCULOSIS—RESULTS IN 137 CASES

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Summary: During a 17J year period 137 patients underwent surgery for abdominal tuberculosis. Ages ranged from 14 months to 75 years 56% were males.

Based upon symptomatology, patients were classified into four groups—obstructive (61 cases), masses (29), perforation (21) and atypical (26). 10% of the patients were on antitubercular treatment at the time of operation. Symptomatology and physical findings varied widely between the four groups, the only common finding being abdominal pain. A correct pre-operaiive diagnosis was made in 69%. At laparotomy 64% were found to have localized lesions and in 51 patients 109 strictures were found. Definitive surgery was required in 115 patients. Mortality in elective cases was 3 % and in emergency cases, 18%.

Abdominal tuberculosis remains a problem in the developing world and in countries having a large immigrant population. It produces a wide variety of symptoms and frequently is neither diagnosed pre-operatively nor recognized at operation, ft is our purpose to review our experience in the management of 137 cases.

Material and Methods:

The case records of all patients operated upon for abdominal tuberculosis during the period January, 1965 to July, 1982 were reviewed. Two patients who underwent abdominal surgery, one for the closure of a colostomy and the other for repair of a hernia, were found to have tubercles in the peritoneum. They were excluded as they were not operated upon because of tuberculosis. One patient underwent operation on two occasions 13 years apart. Both times active disease was proven. This has been considered as two separate cases.

Criteria for diagnosis included the presence of caseating granulomatous lesions in the bowel, isolation of tubercle bacilli in biopsy material, gastric washings or sputum, or histologically proven lesions in regional lymph nodes.

"Based upon the clinical presentation, the patients were divided into four groups. The largest group consisted of 61 who presented with obstructive symptoms, these being acute in 26. Twenty nine patients were treated for a mass in the right iliac fossa, 21 patients for perforation of the bowel and the remaining 26 had either tubercular peritonitis or atypical symptoms.

Results:

Age and Sex

Ages ranged from 14 months to 75 years (Table 1) with a mean of 29 years. 71 % of the patients were in the 2nd, 3rd or 4th decade of life. There was no age difference between males and females. Patients with a right lower quadrant mass averaged 9.4 years older than patients with obstructive symptoms ($t=2.94$, $p<0.01$). The proportion of women with perforation was significantly greater than in other groups ($X^2=5.9$, $p<0.02$).

Symptomatology

Symptoms depended upon the type of presentation (Table 2). Except for pain, there was no common finding. Indeed, the only patients who showed any consistent pattern were those with perforation, having the triad of pain, constipation and vomiting. Melena was most common in patients having atypical presentations or right lower quadrant masses. Alteration in the menstrual cycle or amenorrhoea was present in 12% of women.

The duration of symptoms ranged from a few hours up to 35 years. Patients with perforation or acute obstruction generally had previous symptoms of less than six weeks and often none before the acute episode.

Physical findings also varied with the presentation (Table 3), distension being the most frequent. Only 24% had abdominal masses.

Only four patients gave a family history of tuberculosis. Thirteen patients were under

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TABLE 1

*Age and **Sex** Distribution*

Age	Obstructive	Mass	Perforation	Atypical	Total
0- 9 years	8	0	1	1	10
10-19	12	2	3	5	22
20-29	23	11	6	8	48
30-39	11	8	5	3	27
40-49	2	4	3	6	15
50-59	3	1	2	1	7
60-69	1	1	1	1	4
70+	1	2	0	1	4
	61	29	21	26	137
Mean age	24.9	34.3	31.4	31.4	29.1
% Male	64	55	33	58	56

TABLE 2

Symptoms (Expressed as percent)

	Obstructive	Mass	Perforation	Atypical	Total
Abdominal pain	89	93	100	62	86
Altered bowel habits	49	41	86	35	50
Vomiting	59	34	67	15	47
Colic	41	31	19	23	32
Distension	33	21	43	27	31
Fever	36	17	29	27	2}
Menstrual Irregularities*	5	23	0	27	12
Anorexia	8	21	0	21	10
Abdominal mass	3	31	0	8	9
Weight loss	11	17	0	0	9
Melena	2	10	5	15	7

***Percent of** women

TABLE 3

Physical Findings (Expressed as Percent)

	Obstructive	Mass	Perforation	Atypical	Total
Abdominal distension	56	7	86	8	41
Abdominal tenderness	16	24	95	8	28
Visible peristalsis	28	7	5	0	15
Mass in RIF	3	100	5	4	14
Increased bowel sounds	23	0	19	4	14
Mass other than RIF	3	0	19	35	10
No abdominal findings	0	0	0	15	3

treatment for tuberculosis, the majority for less than three months. Seven patients had received incomplete treatment earlier.

Among those in whom chest x-rays were taken, half had signs of active pulmonary tuberculosis. Abdominal x-rays including barium studies were done in 70, and in 64 the findings were compatible with tuberculosis. In three patients a diagnosis of carcinoma of the large bowel was made and in three the x-rays were interpreted as normal.

Diagnosis

Although this review was made in an area where the disease is endemic, a pre-operative diagnosis of tuberculosis was made in only 69% of the patients (Table 4). In patients with subacute obstruction or an ileocaecal mass, the diagnosis was more often correct than in those undergoing emergency surgery for perforation or acute obstruction. The most common diagnoses other than tuberculosis were those of intestinal obstruction of undeter-

TABLE 4
Accuracy of Diagnosis

Group	Diagnosed as Tuberculosis %
Obstructive	79
Acute	62
Subacute	91
Mass	90
Perfoation	29
Atypical	52
Total	69

mined cause (8 cases) or carcinoma of the large bowel (7 cases).

Pathology

Fifty patients (36%) had diffuse disease cular peritonitis and frequently associated with ascites.

The single most common finding was of stricture (Table 6) there being a total of 109 in 51 patients. Masses occurred in 44, usually

TABLE 5
Site of Disease

	Obstructive	Mass	Perforation	Atypical	Total
Diffuse Localized	27	5	3	15	50
Gastroduodenal	2	0	0	2	4
Jejunal	2	0	3	1	6
Ileal	16	1	15	0	32
Ileocolic	9	20	0	3	32
Colic	3	2	0	3	8
Nodal	1	1	0	2	4
Unknown	1	0	0	0	1
Total	61	29	21	26	137

TABLE 6
*Operative Findings**

	Obstructive	Mass	Perforation	Atypical	Total
Cases	61	29	21	26	137
Tubercules	28	9	4	15	56
Patients with strictures	26	8	14	3	51
Number of strictures	65	13	28	3	109
Enlarged lymph nodes	22	11	3	5	41
Massive adhesions	21	1	2	4	29
Masses	8	25	1	10	44
Ileocaecal	2	21	1	1	25
Other	6	4	0	9	19
Ascites	17	2	0	3	22

*Many patients had multiple findings

Operative treatment

One hundred and fifteen patients underwent definitive operative procedures—bowel resections, stricture-plastics, bypass procedures, lysis of adhesions or closure of perforations (Table 7). Many required more than one procedure. Two patients in the obstructive group had extensive matting of the bowel, probably from tubercular peritonitis, and operation was abandoned (both died). The remaining 20, mostly associated with atypical presentations, had either only a biopsy or miscellaneous procedures such as appendectomy.

Morbiciity and mortality

Operative morbidity was high, 49 patients (36%) having one or more complication. These were more frequent in those undergoing emergency surgery (66%). The most common complications were wound infections and pulmonary infections. One patient developed a faecal fistula and two returned later with intestinal obstruction requiring re-operation.

Eleven patients died, a mortality of 8%. Nine of the deaths occurred among the 50 patients who underwent emergency procedures and two among the 87 operated upon electively. Those who died following emergency operation generally had multiple complications. The two deaths among those operated upon electively followed faecal fistula and recurrent obstruction. Both had massive adhesions and were thought inoperable.

Discussion

Gastro-intestinal tuberculosis is usually divided on the basis of the pathological findings into ulcerative and hyperplastic types. In addition, peritoneal involvement may produce gastro-intestinal symptoms. From the viewpoint of the surgeon, it would seem more suitable to consider it according to symptom complex. There is an obvious correlation for the ulcerative lesions are more likely to produce obstructions whereas the hyperplastic lesions produce masses, usually in the right iliac fossa. On the other hand, tubercular peritonitis results in ascites, adhesions (often followed by

TABLE 7

Operative Procedures in 135 *Patients**

	Obstructive	Mass	Perforation	Atypical	Total
Cases	59*	29	21	26	137
Resections					
lleocaecal	6	12	0	0	18
Hemicoiectomy	1	8	0	3	12
Small bowel	12	0	16	3	31
Colon	0	0	0	1	1
Stricture-plastics	30	2	4	0	36
Lysis of adhesions**	13	6	0	1	20
Bypass	6	4	5	3	18
Biopsy only	1	4	0	13	18
Closure of perforation	0	0	5	0	5
Miscellaneous	1	0	7	3	11

* Two patients in the obstruction group were inoperable.
** As the primary procedure—many others had lysis as secondary procedures.

obstructive symptoms) or masses consisting of rolled up omentum or enlarged lymph nodes. Although any age group may be involved, the disease is most common in the third and fourth decades (Prakash, 1978).

While Prakash (1978) reported a 2:1 female to male ratio, others have found a more nearly equal distribution (Novis et al 1973, Bhansali 1977). In our series, males predominated in all groups except in those having perforations. The reason for this difference is not clear.

Bhansali (1977) stressed that in patients with acute symptoms the abdominal signs differed depending upon the type of presentation- A similar differentiation can be made between those with chronic obstruction and ileocaecal masses. In all series, however, pain is the most common symptom, being present in from 63 % (Sambrianides et al, 1980) to 100 % (Bhansali, 1977). In children, the incidence is less (Johnson and Aderele, 1979).

Prakash et al (1975) found that only 32 of 92 patients with ileocaecal disease had healed pulmonary disease, an incidence similar to ours. In the series reported by Novis et al (1973) the incidence was 34%. However, their population is racially different from ours.

Abdominal tuberculosis frequently presents as a surgical emergency. Bhansali (1977) reported an incidence of 25% and Khoury, Payne and Harvey (1978) 37%. These emergencies consist of perforations, acute obstruction, appendicitis or massive bleeding (1979). Diagnosis is more difficult in this group.

Diagnosis is also difficult in the absence of pulmonary involvement. Shukla and Hughes (1978) made a correct diagnosis in one of eight cases and Johnson and Aderele (1979) reported that a diagnosis was made only at autopsy in 26%. Mandal and Schofield (1976) working in Great Britain pointed out that 20% of those dying of abdominal tuberculosis were undiagnosed during life. Das and Shukla (1976) working in an area where the condition is endemic reported that the diagnosis was made in only 50% of 182 cases. In the current series, 69% were correctly diagnosed. The nature of the obstruction may go unrecognized, particularly in patients having acute symptoms, or caecal masses may be thought to be malignant (Taylor and Brooman 1976, Murillo et al 1978).

When surgery is done, it must suit the pathological findings (Pujari, 1979). Resection of an ileocaecal mass can be of a limited extent rather than the classical hemicolectomy (Prakash et af, 1975) and strictures can be treated by strictureplasty (Katariya et al, 1977) We believe that bypass procedures should be limited to patients in poor general condition in whom strictureplasty is not possible and resection is deemed inadvisable. Since 1975, we have had no occasion to do a two stage resection (Prakash et al, 1975). Perforations are best handled by resection rather than oversewing (Eggleston et al, 1983).

Wound infection is common (Pujari, 1979). The incidence of faecal fistula is low despite the presence of active tuberculosis in the area of anastomosis. Specific antibiotic therapy probably accounts for this.

Mortality is low in elective cases but high in emergency procedures. Bhansali (1977) had a 2% mortality in patients treated electively, but 24% under emergency conditions. Our results were similar—3% and 18% respectively.

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AGRANULOCYTOSIS DUE TO THIACETAZONE

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Summary: Out of 6819 cases of pulmonary tuberculosis who had taken Isoniazid and Thiacetazone with or without Streptomycin for at least 4 months, 5 developed agranulocytosis. In 4 cases, thiacetazone was the offending drug, whereas in fifth case the exact cause of agranulocytosis could not be ascertained.

Introduction

Thiacetazone is one of the oldest known anti-tuberculosis drugs, which, along with isoniazid. is today the sheet anchor of treatment in India and other developing countries of the world. In early 1950's, owing to relatively high dosages used in those days, side effects and toxicity with thiacetazone were frequent. Since isoniazid also became available about the same time, thiacetazone was soon forgotten. In early 1960's, thiacetazone was reinvestigated in a series of studies, as a companion drug to isoniazid. The intention was to find an alternative drug to PAS, that would equally prevent development of drug resistance to Isoniazid and be less bulky as well as less expensive. As a result of number of such studies, a daily dose of 150 mg. of thiacetazone was found to be as effective as PAS and with minimal side effects (East African BMRC, 1960).

Low toxicity of thiacetazone has been reported in a number of trials conducted by various workers (Patel, 1966; Mehrotra et al., 1966) as well as in national and international cooperative trials (Miller et al., 1966; Miller et al. 1970; Pamra, 1971). Various toxic effects to thiacetazone include gastric, hepatic, cutaneous and haematological. Agranulocytosis is a rare but serious and sometimes fatal toxic effect of thiacetazone. Five cases of agranulocytosis due to thiacetazone are being reported, with a view to caution the users of the drug.

Material and Methods

Records of all patients of pulmonary tuberculosis who were treated with isoniazid and thiacetazone with or without streptomycin at this hospital during the 5 year period {from 1st November 1976 to 31stOctober 1981) were scrutinized to find out cases of agranulocytosis. Since most of the toxic reactions attributable to thiacetazone appear in first 8 weeks of treatment (Miller et al., 1966), only those cases who had completed a minimum of 4 months of therapy were included for analysis. But cases of agranulocytosis noted earlier amongst those who had not completed 4 months' treatment were also included.

Observations

A total of 11-549 patients of pulmonary tuberculosis during the 5 year study period (1st November 1976 to 31st October 1981) were put on isoniazid and thiacetazone with or without streptomycin. Of these, 6819 patients (59%) completed 4 months of therapy and were thus eligible for analysis. A total of 5 cases (0.07%) developed agranulocytosis, in which thiacetazone was thought to be the offending drug. Details of these cases are given in the following table.

Out of five case, three cases developed agranulocytosis in first 4 weeks of therapy, whereas other two cases were detected in 12th week. Ftver was the main presenting feature in all cases followed by generalised weakness and toxaemia (4 cases) and ulcers of vesicles (2 cases). One patient developed diarrhoea along with other complaints.

In all these cases anti-T.B. drugs were stopped immediately. Treatment consisted of parenteral penicillin, corticosteroids, repeated blood transfusions and supportive measures. Despite best efforts, only two out of five cases survived.

Discussion

Agranulocytosis is a rare but serious toxic manifestation of thiacetazone, which can be fatal if not recognised at an early stage. Thiacetazone is the most common anti T.B. drug known to cause agranulocytosis though it has very rarely been reported with streptomycin and isoniazid also (Davies, 1981).

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TABLE

Details of 5 cases of Agranulocytosis Due to Thiacetazone.

Case	Age & Sex	Regimen	Time of detection of Agranulocytosis after start of 'T'	Presenting Complaints	TLC DLC	Remarks
S.K.	45 F	STH	4th week	Fever & small vesicles near nose.	TLC 1600/ P-0% L-98% M-2%	Survived and tolerated S & H.
N.D.	16 F	TH	12th week	Fever; generalized weakness.	TLC 3200/ P-0% L-97% M-3%	Survived and tolerated H.
R.P.	50 M	STH	3rd week	Fever, ulcers in oral cavity toxaemia.	TLC 1300 P-0% L-98% M-2%	Expired; Agranulocytosis appeared after adding T to S and H
P.L.	18 M	TH	12th week	Fever, diarrhoea, generalised weakness.	TLC 1200 P-0% L-98% M-2%	Expired; He had used 'H' earlier along with PAS.
S.S.	60 M	TH	3rd week	Fever, toxaemia.	TLC 2400/ P-8% L-89% M-2% E-1%	Expired.

S-Streptomycin
T-Thiacetazone
H-Isoniazid
'T -Treatment

P-Polymorphs
L-Lymphocytes
M-Monocytes
E-Eosinophils

Out of five cases reported, thiacetazone was the cause of agranulocytosis in four cases. Two cases who survived (Cases No. 1&2) tolerated other drugs (isoniazid and/or streptomycin) later on, thus proving thiacetazone as the offending drug. In Case No. 3, treatment was started with streptomycin and isoniazid, with which patient improved and thiacetazone was added after one month. Soon his condition started deteriorating and agranulocytosis was detected within 3 week of start of thiacetazone. Fourth case was being treated with isoniazid and thiacetazone, when he developed agranulocytosis. This patient had taken isoriiazid earlier along with PAS and thus isoniazid could not be the likely offending drug in this case. In Case No. 5, who was also on isoniazid and thiacetazone, offending drug could not be ascertained, as patient expired within three days of admission. No doubt, isoniazid is very rarely known to cause agranulocytosis (Davies, 1981), it is much more common with thiacetazone. In all these cases, there was no history of any other drug intake, to which agranulocytosis could be attributed.

Hinshaw and McDermott (1950) reported *&* cases of agranulocytosis among 2000 patients who received thiacetazone (Cortteben). In the same report, Boehm and Brecke reported one case of agranulocytosis out of 245 patients treated with thiacetazone, thus giving an incidence of 0.41%. Preheim and Peck (1952) reported a case of agranufocytosis amongst 5 cases who were being treated with amithiozone (Thiacetazone). The diagnosis of agranulocytosis was verified by bone marrow study.

In view of conflicting reports about thiacetazone toxicity from different parts of world, an international double blind cooperative study was carried out to fmd out incidence of thiacetazone toxicity (Miller et at, 1966), in which a total of 2077 patients from 13 countries including India participated. Out of 1002 patients on streptomycin, isoniazid and thiacetazone regimen, 2 cases developed agranulocytosis. Both these cases were from Czechoslovakia and both recovered rapidly. One case developed agranulocytosis in 3rd week and other in 6th week. Govindraj (1968) reported a ca sc o

tuberculosis with multiple drug reactions who developed agranulocytosis on 18th day of therapy with thiacetazone. Aquinus (1968), while reporting about toxicity of thiacetazone and isoniazid regimen in Hongkong/BMRC investigation, described one case out of 150 patients on thiacetazone isoniazid regimen, who developed reversible agranulocytosis. Bhatia and Harbans Lai (1969) reported 2 cases of thiacetazone induced agranulocytosis among 3000 patients in whom thiacetazone was used from 1965 to 1967, thus giving an incidence of 0.06%. Both these patients died. Muthuswami (1969) reported 3 cases of agranulocytosis amongst 143 cases who had completed at Least 12 weeks' treatment with thiace a-zone and isoniazid wither without streptomycin.

In the second international co-operative study into thiacetazone side effects, in which 25 hospitals from 10 countries participated, 2 cases out of 1165 patients taking thiacetazone with isoniazid developed agranulocytosis (Miller et al, 1970). Sarveshananda and Parsad (1978) reported a case of progressive fatal bone marrow depression due to thiacetazone.

These cases of agranulocytosis were those who came back to us because of toxicity features. Drug toxicity is an important cause of default as was shown by Gothi et al, (1966) when they reported the side effects which occured in 127 patients on isoniazid and thiacetazone in a district tuberculosis programme. None of their 5 patients who developed agraaulocytosi reported voluntarily at the centre with side effects. They were all discovered at home when a visit was made to retrieve the defaulters. In this study there were 2516 patiens who had completed four months treatment and whose homes could not be visited as they did not belong to Patiala district. Thus if there was a case of serious toxic reaction among them who did not voluntarily visit the centre, it would have remained undetected.

Aim of this paper is not to frighten the users of thiacetazone, but to caution them that this potentially fatal toxic effect should always be kept in mind while using this drug. Patients should be properly educated about various drug reactions so that they can report back to the centre as soon as any such reaction appears and thus necessary action can be taken and unnecessary loss of life prevented.

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COLONISATION OF ATYPICAL MYCOBACTERIA IN THE NORMAL RESPIRATORY TRACT

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Summary: Sputum samples and throat washings were obtained from 200 randomly selected persons free from chronic upper or lower respiratory diseases. Five percent of these normal healthy individuals from the coastal region of Karnataka harboured species of atypical mycobacteria in their respiratory tract. In all of them, colony count was low on L..J Media and isolation was better in Kirchners media. This shows that isolation of atypical mycobacteria may be a normal finding in some individuals. These atypical mycobactena found as commensals could be transported to the lungs causing nontuberculous pulmonary disease particularly in patients with chronic nonspecific respiratory diseases (CNSRD) or with healed lesions of pulmonary tuberculosis.

Introduction

After the advent of antibiotics non tuberculous mycobacterial diseases are frequently reported in world literature (Beck 1959; Kamat, Rossister and Gilson 1961; Black and Chapman 1964). Predisposing conditions are also important in the pathogenesis of pulmonary disease due to nontuberculous mycobacteria; the most common are pneumoconiosis, chronic obstructive pulmonary disease and healed tuberculosis. Two species or complexes have emerged as the predominant agents of disease, M. Kansasii and M. avium-intracellulaeascrofulaceum complex (Wolinsky 1979). In a recent study these potential pathogens were found in the sputum cultures of 13.17% of selected patients hospitalized for relapsed tuberculosis and chronic nonspecific respiratory diseases (CNSRD) (Mohan Kotian, Sarvamangala, Vasavi, Shivananda and Achyutha Rao 1981). It is well known that many of these pathogens are frequently present in the environment. But the problem yet to be solved is how the necessary aerosols are produced to effect a transfer of the bacilli from the environmental sources to the lower respiratory tract of man as person to person transmission usually does not occur.

In this study attempts were made to determine the prevalence of respiratory colonisation with atypical mycobacteria in a normal healthy population around Manipal, a rural educational campus situated in the west coast region of Karnataka. A substantial number of normal people harbour these atypical mycobacteria including species commonly considered to be potential pathogens in debilitated individuals.

Material and Methods

A total of 200 normal healthy individuals were included in this study. Most of them were on the staff of the Kasturba Medical College and Hospital and were residing in the suburbs of Manipal. A small number of healthy individuals including students attending the out patient department of Kasturba Medical College Hospital for routine medical check up were also included. Persons selected were neither suffering from any respiratory illness nor having any inflammatory disease preceding 8 weeks of our study.

Early morning coughed up sputum was collected and in those individuals who could not expectorate any sputum, throat washings with 30 ml sterile saline were thoroughly gargled out. These specimens were collected in a screw-topped wide mouth bottle. Single specimen was obtained from each of the 200 subjects.

The specimens were examined for AFB by direct smear and by concentration method using Petroff's method (Cruickshank, Duguid, Marmion and Swain 1975). They were cultured on two L.J. Media and two Kirchner's liquid media and incubated at 37°C. The cultures on L.J. media were observed once a day in the first week to pick up the rapid growers and then twice a week for 8 weeks before discarding as negative. The Kirchner's culture tubes were centrifuged at 3,000 r.p.m. at the end of second week and fourth week. The deposits were inoculated into L.J. Media, incubated at 37°C and observed as above. Any growth of AFB including rapid growers seen were run through the following tests and identified as; described by

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TABLE 1

Species of atypical mycobacteria isolated from 200 *specimens from respiratory tract of normal healthy individuals*

Species of atypical mycobacteria	L. J. Media	Kirchner's media
Myco. Scrofulaceum	4	4
Myco.avium intracellularecomplex	3	3
Myco.fortuitum	0	1
Myco.xenopi	0	1
Myco.mariunm	0	1

Allen and Baker 1968; Runyon, Wayne and Kubica, 1975; Barksdale and Kim 1977.

The tests performed were rate of growth (slow or fast) Niacin test, Nitrate reduction, Catalase 20°C, Stability of catalase to 68°C 20 minutes, growth on PNB, growth at 25°C and 37^0C, Photochromogenicity, Pigmentation in dark, Oleate tolarance, Arylsutphatase (3 days), Tween hydrolysis (10 days), Tween opacity (4 weeks), Peroxidase, growth on MacConkey, growth on media containing 5 % (Wt/VoI) Nacl, Tellurite reduction and Amidase tests. The results were compared with strains of atypical mycobacteria species obtained from Tuberculosis Reference Centre, Cardiff.

Results

Direct and concentration smears from all the specimens were negative for AFB. Ten out of 200 cases, revealed the isolation of atypical mycobacteria (5 %). Single species of atypical mycobacteria was isolated among 7 positive cultures grown on L.J. media.

Same species had grown both on L.J. media and Kirchner's media from 7 specimens. The remaining 3 specimens yielded mixed growth of two species in Kirchner's media and corresponding growth of one of these species among the mixed growth was seen on L.J. media where concentrated materials were directly inoculated. The pattern of isolation of atypical mycobacteria is given in Table 1.

Discussion

It is now well established that mycobacteria other than mammalian tubercle bacilli and M, leprae are important human pathogens. A wide varity of tissues may be involved, especially the lungs, lymph nodes, skin, soft tissues and bones, joints and tendons of the skeletal system. Although encountered in immunosuppressive patients, life threatening disseminated diseases sometimes occur in previously healthy individuals. The mechanism by which the lung becomes infected and the fate of these mycobacteria once inhaled into the lungs are obscure (Wolinsky-Loc cit).

Non-tuberculous mycobacteria are found in the environment (Gangadharam, 1980). Water has emerged as a source of contamination (Goslee and Wolinsky 1976) certainly for M. marinum and M. xenopi disease and probably for M. kansasii and M, simiae. However diagnosis of disease may be suspected by the clinician, the radiologist and pathologist but it is the microbiologist who must establish the precise cause. It is difficult to decide the aetiological role of atypical mycobacteria causing disease. Contamination of specimens with environmental AFB is common (Maniar and Vanbuckenhout 1976). We checked the tap water and also the distilled water used in our laboratory and found it free from mycobacteria. Care has been taken to sterilise the reagents used in the PetrofTs method for the culture of AFB.

Higher incidence of atypical mycobactcrial disease had been reported in the wide spread coastal region of India (Kaur and Chitkara 1964; Patel, D' souza and Sayed 1966). Recently, the mode of transmission of this disease from aerosolised sea water bubbles had been reported (Gruft, Loder, Osterhout, Parker and Falkinham 1979). Epidemiological study at Madras revealed that one of the causes of failure of BCG protection against tuberculosis in the

coastal region of India could be the sensitisation of these individuals with atypical mycobacteria (Trial of BCG vaccines in South India for Tuberculosis Prevention 1979).

This study showed the colonisation of 5% of the healthy individuals of coastal region of Karnataka, with different species of atypical mycobacteria some of which are potential pathogens. It is stated that even repeated isolation of a single species from the sputum may be due to prolonged colonisation of respiratory tract without relation to disease (Wolinsky-Loc cit). Jt gives an awareness when deciding the aetiological role in the causation of non-tuberculous mycobacterial diseases, and repeated isolation of these organisms with clinico-bacteriological correlation must be the criterion. However it is suggested that like many other commensal organisms of the pharyngeal flora, these AFB are also found associated with normal human respiratory tract. They could be transported to the lung causing non-tuberculous pulmonary disease particularly in those debilitated patients with-chronic nonspecific respiratory diseases, or with healed lesions of pulmonary tuberculosis.

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SERUM CERULOPLASMIN LEVELS IN RELATION TO ACTIVITY OF PULMONARY TUBERCULOSIS

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Summary: Serum ceruloplasmin activity has been measured by colorimetric method of Ravin (1961) in 80 patients of pulmonary tuberculosis and in 30 healthy individuals. Serum ceruloplasmin in sputum positive patients was more than double of that in controls. Significant increase also occurred in patients with tubercular toxemia even though sputum negative. The ceruloplasmin levels per se did not bear any relationship to the radiological extent of disease and tend to decline after chemotherapy.

Introduction

Activity of pulmonary tuberculosis can be judged by clinical manifestations, sputum for acid fast bacilli and by radiological investigations. Ceruloplasmin is a blue alpha globulin of plasma synthesised in liver microsomes. It oxidises a number of polyamines and polyphenols such as benzdinc, para-phenylenediamine (PPD), dopamine, serotonin in presence of monomine oxidase (Homberg and Laurall, 1948, 1950.

Estimation of serum ceruloplasmin levels can be of value in the measurement of activity of tubercular process, if the other conditions which tend to alter the levels of serum ceruloplasmin are ruled out. Normal adult levels of serum ceruloplasmin vary from 30-34 mg% according to Turey et al (1964). Diane, Wilsom Cox (1966), found that the levels in adults showed little variations from day to day and were not influenced by body weight or menstrual cycle.

Decreased levels of serum ceruloplasmin were observed in various diseases (Cartwright et al, 1960; Plum, 1962; Chitra et al, 1962 and Deabreu, I960).

Increase in the level of serum ceruloplasmin has been reported in various disease processes (Hauftova and Slaviok, 1963; Borotolotti, 1964; Borisova, 1965; Shelevich, 3963; Kriegal and Muller, 1965 and Singhvi and Maitrya, 1977). Singhvi and Maitrya (1977) observed increased level of serum ceruloplasmin in untreated patients of pulmonary tuberculosis, which came down with antitubercular treatment in due course of time. The average value of ceruloplasmin activity in normal subjects observed by them was 78.50 units with a range of 30-115 units.

The present study was undertaken to correlate the activity of pulmonary tuberculosis with serum ceruloplasmin level and its value in prognosis of pulmonary tuberculosis.

Material and Methods

One hundred and ten cases included in this study were selected from the different wards and O.P.D. of the hospital for Chest and Tuberculosis, Jaipur, Rajasthan. Cases with associated conditions likely to alter the ceruloplasmin levels were not included in the study. The cases were divided into the following groups:

Group- A : Controls (30 cases)— Normal healthy individuals, without any history, clinical radiological or bacteriological evidence of pulmonary tuberculosis.

Group-B : (40 cases)— Patients of pulmonary tuberculosis with sputum positive for acid fast bacilli by smear examination of sputum stained with Ziehl Neelsen stain.

Group-C : (20 cases) — Patients of pulmonary tuberculosis with sputum negative for acid fast bacilli, but having symptoms of tubercular toxemia, fever, cough with or without expectoration, hemoptysis. Radiological picture was suggestive of active pulmonary tuberculosis.

Group- D . (20 cases)— Old treated cases of pulmonary tuberculosis with sputum negative for acid fast bacilli and without any clinical evidence of activity of pulmonary tuberculosis. These cases were selected to find out any relationship between radiological extent of disease and serum ceruloplasmin levels.

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Serum ceruloplasmin levels were estimated in all the groups. In group 'B' cases, levels were again estimated after 12 weeks of antitubercular chemotherapy to determine the effect of chemotherapy on serum ceruloplasmin levels,

Radiological criteria of minimal, moderately advanced and far advanced lung lesion were in accordance with the classification based on the diagnostic standards of the American Thoracic Society (Medical section, National Tuberculosis Association, Hinshaw, 1969).

The treatment regimen for cases in Group B was—Streptomycin 1 gm intramuscular daily (25 mg per Kg body weight) Isoniazid 5 mg per Kg body weight in single daily dose, Ethambutol 25 mg per Kg body weight in single daily dose.

Estimation of serum ceruloplasmin level was carried out by colorimetric method of Ravin (1961). One unit of activity was defined as an increase in absorbance of 0.001 per O.I ml of scrum per hour.

Results

Scrum ceruloplasmin levels in controls (Group 'A') ranged from 180 units to 370 units with a mean of 274 units (Table 1). In group *B' the levels ranged from 440 units to 840 units with a mean of 680 units, of the 40 cases in Group 'B', 2 were minimal, 21 moderately and 17 far advanced. Serum ceruloplasmin levels ranged from 560-840 units in minimal, 480-820 units in moderately and 440-840 units in far advanced disease (Table II) The difference between mean values in group 'B' cases as compared to controls (Group 'A') is highly significant ($p<0.001$).

In Group 'C' cases serum ceruloplasmin levels ranged from 420 units to 560 units with a mean of 490 units. The difference between the mean levels in Group 'C and Group 'A' is also highly significant ($p<O.OOI$). Levels of serum ceruloplasmin in Group 'D[1] cases ranged from 240 units to 440 units with a mean of 350 units. The difference between the mean levels in group 'D' and group 'A' was not significant ($p>0.1$).

Mean levels of serum ceruloplasmin in group 'B' and 'C' were also compared and the difference was found statistically significant ($p< 0.001$). Similarly the difference between the mean levels of scrum ceruloplasmin in Group 'B[1] and 'D' as well as between Group C and Group D was found statistically significant ($p<0.001$).

TABLE 1

Serum Ceruloplasmin levels in Group 'A' Subjects

No. of Cases	Serum Ceruloplasmin Units Range	Mean
30	180—370	274

TABLE 2

Serum Ceruloplasmin levels in Group 'B 'in Relation to Radiological Extent of Disease

S.N.	No. of cases.	Extent of Disease	Serum Ceruloplasmin Units Range	Mean
1.	2	Minimal Disease	560—840	700
2.	21	Moderately advance	480—820	670
3.	17	Far Advanced	440—840	700
Total	40		440—840	680

The difference in the mean levels of serum ceruloplasmin in minimal cases of group 'B' and Group 'C' was found to be statistically not significant ($p>0.2$); but it was highly significant ($p<0.001$) in the moderately advanced cases. The comparison between the far advanced cases is not valid as there was only one such case in group 'C'.

The differences in mean levels of serum ceruloplasmin in minimal, moderately and far advanced cases in group 'D' as well as in Group B were not statistically significant,

Table 5 shows the level of serum ceruloplasmin in 14 patients of group 'B' after 12 weeks of antitubercular chemotherapy. The

TABLE 3

Scrum Ceruloplasmin levels in Group 'C" *in Relation to Radiological Extent of Disease*

S.N.	No. of cases	Extent of Disease	Serum Ceruloplasmin Range	Units Mean
1.	4	Minimal Disease	420—520	490
2.	15	Moderately advance	420—560	490
3.	1	Far Advanced	440	440
Total	20		420—560	490

TABLE 4

Serum Ceruloplasmin levels n Group 'D' in *Relation to Radiological Extent of Disease*

S.N, Cases	.No. of	Extent of disease	Serum Ceruloplasmin Units Range	Mean
I.	3	Minimal disease	240 — 440	340
2.	13	Moderately advance	280—440	360
3.	4	Far Advanced	280—440	320
Total	20		280—440	350

TABLE 5

Serum Ceruloplasmin in 14 Patient so Group 'B' after 12 weeks of Chemotherapy

Serum Ceruloplasmin Levels					
No. of cases	Extent of disease	Before Chemotherapy Units Range	Mean	After 12 weeks of Chemotherapy Units Range	Mean
14	Moderate	480-520	670	440-720	537

level of serum ceruloplasmin before the initiation of chemotherapy ranged from 480 units to 520 units with a mean of 670 units. After 12 weeks of chemotherapy, the level ranged from 440 units to 720 units with a mean of 537 units. Serum ceruloplasmin levels declined considerably after 12 weeks of chemotherapy. The difference between mean values of serum ceruloplasmin before and after chemotherapy was statistically significant ($p<0.01$).

Discussion

Pulmonary tuberculosis can be diagnosed by a thorough clinical evaluation of history and clinical, bacteriological and radiological features, in some cases it becomes difficult to predict the activity of a tubercular lesion where precise information about one or other parameters is not available.

The significant rise, of levels of serum ceruloplasmin in Group 'B' and group 'C' as compared to controls suggests its relationship with activity of tubercular process. Increased activity of tubercular process in group 'B' where sputum is positive for acid fast bacilli is accompanied by increased levels of serum ceruloplasmin in comparison to group 'C', where sputum was negative. The difference between the mean levels of serum ceruloplasmin in group 'B' and 'C[1] is statistically significant. Rise of serum ceruloplasmin level in group 'D' was, however not significant. This is further suggestive of the relationship of serum ceruloplasmin level with activity of the tuberculous lesion. These findings also suggest that levels of serum ceruloplasmin are related with the activity of the disease process only but not with the extent.

Singhvi & Maitrya (1977), found the levels of serum ceruloplasmin in untreated patients of pulmonary tuberculosis to be increased. Levels were reduced considerably after 6 months of chemotherapy with Streptomycin and Isoniazid.

Fourteen cases of group 'B' with moderately advanced disease showed considerable decline in the ceruloplasmin levels after 12 weeks of chemotherapy. This further substantiates the relationship of serum ceruloplasmin level with the activity of the tubercular lesion.

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FOLATE DEFICIENCY HYPERMELANOSIS DURING PULMONARY TUBERCULOSIS

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Summary: A case of pulmonary tuberculosis with diffuse hypermelanosis is reported. The hyperpig-rnentation was possibly due to folic acid deficiency.

Introduction:

Occurrence of hypermelanosis i.e. increased amount of melanin in the skin is known to occur in many chronic infections like malaria, kala-azar and tuberculosis {Wasserman, 1979) hut the relative role of infection, malnutrition or other factors in its causation is difficult to determine.

Folate deficiency is often associated with pulmonary tuberculosis (Robberts, Hoffbrand & Mollin, 1966; Klipstein, Berlinger & Read, 1967; Markkanen, Levanto, Sellinen et al, 1967; Cameron & Home, 1971). Deficient dietary intake (Robberts et al, 1966), overutilization of folate (Markkanen et al, 1967 and Cameron & Home, .1971), and drugs like cycloserine (Klipstein et al, 1967) & para-aminosalicylic acid (Cameron & Home, 1971) have been incriminated in the causation of folic acid deficiency in pulmonary tuberculosis. To the best of our knowledge, folate deficiency hypermelanosis during pulmonary tuberculosis has not been reported. In the present case hypermelanosis was possibly due to folic acid deficiency.

Case Report:

P.D., a 35 years old Hindu lady was admitted in the Hospital for Chest Diseases and Tuberculosis. Jaipur with the complaints of fever, cough, chest pain and loss of appetite for 4 months. She was a non-smoker, vegetarian housewife, who never took alcohol,

One month before admission, the patient was diagnosed as a case of pulmonary tuberculosis in the out-patients department of this hospital and was put on streptomycin, isoniazid, ethambutol and pyrazinamide in the usual daily dosage. With this drug regimen, the patient had partial relief only and was, therefore, admitted in the hospital.

The patient who was fair coloured at the time of admission was put on the same drug regimen in the hospital. On the 10th day of admission, the patient noticed blackish discoloration over her face. Within 5 days, the blackish discoloration of her skin extended to neck, trunk and extremities. It was more marked over the face, neck and extremities as compared to the trunk. The change in complexion made the patient apprehensive.

The patient was of average build but poorly nourished. She had mild anaemia. Her skin was black in colour but its texture was normal. Respiratory system examination revealed findings of cavitary disease on the right side with coarse crepitations on the left side. Examination of other systems revealed nothing abnormal.

Blood examination revealed haemoglobin 9.0 gm. %, and packed cell volume 26.2%. Peripheral blood film showed macrocytosis with hypersegmented neutrophils. Total and differential leucocyte count were within normal limits. Sputum smear was positive for acid fast bacilli. X-ray chest postem-anterior view revealed bilateral heterogenous shadows with areas of break-down.

The patient was referred to the dermatologist where she was diagnosed as a case of vitamin B_{12} and/or folic acid deficiency hypermelanosis. She was advised folic acid 5 mg. daily orally in addition to her anti-tuberculous drugs.

After 15 days of treatment with folic acid, the blackish discoloration gradually diminished and within 21 days she regained her original fair complexion. At this time her haemoglobin was 11,2 gm. % and packed cell volume was 30.4%.

Serum levels of folic acid and vitamin B_{12} could not be measured.

Discussion:

Only a few case reports are available in the literature, which implicate folate deficiency in the causation of hyperpigmentation. Baumslag & Metz (1969) described 5 cases of mottled hyperpigmentation of the palms, soles and

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tongue in women who had megaloblastic anaemia of pregnancy. Gilliam & Cox (1978) reported the case of a child with mottled hyperpigmentation that was shown to be secondary to vitamin B_{12} deficiency. They suggested that reduction of the tyrosinase inhibiting effect of reduced glutathione on melanin production was responsible for hyperpigmentation in vitamin B12 deficiency. Downham, Rahbein & Taylor (1976) while reporting a case of folate deficiency anaemia with hyperpigmentation suggested that the hypothesis of GiEliam & Cox could well apply to folic acid deficiency hyperpigmentation also.

Though the essential serum folic acid levels were not estimated, in the present case, the findings from the patient's history, physical examination, laboratory tests and response to therapy ruled out pellagra, thyroid disease, Addison's disease, pernicious anaemia, porphiyrea cutanea tarda, drug ingestion and other known causes of gray or brown hyperpigmentation. The complete response to folic acid in 3 weeks probably indicates hyperpigmentation being due to folic acid deficiency.

The other possible mechanism of hyperpigmentation in the present case could be an excessive stimulation of the rericuloendothclial system, as has been suggested by Wasserman (1979) in the hyperpigmentation associated with chronic infections. Excessive stimulation of reticuloendothelial system according to him results in reduced adrenocorticai activity, which leads to hyperpigmentation.

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TUBERCULOSIS OF THE SPLEEN

A.K. HANDA* AND F.C. EGGLESTON**

Summary: Tuberculosis **of** the **spleen** in an **80** year old male presented as a cold abscess. Diagnosis was made at operation. Recovery was uneventful. The condition is **rare** and the mode of presentation was **unusual.**

Introduction:

Tuberculosis of the spleen may be the only manifestation of disease without any evidence of the presence of a tubercular lesion elsewhere in the body or it may be the result of miliary or disseminated disease. The former is rare. We have had one such case.

Case Report:

G.B., an 80 year old man of poor means, was admitted with complaints of low grade fever and dry cough of four months' duration. This was accompanied by anorexia and weight loss. For one week he had noticed a mass in the left lateral chest wall. There was no past or family history of tuberculosis.

Examination showed a chronically ill, malnourished man. The only positive finding was a 7.5 x 5 cm swelling over the left 9th, 10th and 11th ribs in the midaxillary line. The local temperature was not raised, the mass was fluctuant, non-tender and did not transilluminate. The spleen and kidneys were not palpable. A diagnosis of cold abscess was made.

Haemoglobin was 10.6 mg/dl. TLC was 9.8 x 109/l with 7% eosinophils. Urine, stool and chext x-ray were normal. Abdominal x-ray showed a calcified round opacity 10 cm in diameter under the left dome of the diaphragm. There was a mass pressing on the greater curvature of the stomach seen on barium meal examination. The splenic calcification and the absence of pulmonary findings suggested a diagnosis of hydatid cyst of the spleen. Hydatidosis is common in this area.

At laparotomy a 10 x 10 cm splenic abscess that had eroded through the overlying interspace was found. Splenectomy was done and the abscess was curetted. Recovery was uneventful. Pathological examination revealed caseating tuberculosis of the spleen. The patient was given anti-tuberculosis therapy and remains well two years later.

Continents:

Splenic tuberculosis was first described as a clinical entity by Winternitz (1912). He thought the gastrointestinal tract was the portal of entry. Subsequent reports have consisted either of isolated case reports (Chapman, et al. 1954; Soo et al. 1972) or experience with a limited number of cases (Engelbreth-Holm, 1938).

Although the disease may occur at any age, most of the cases are seen in the 2nd to 4th decade (Winternitz, 1912). Both sexes are affected equally. While the condition can run an acute or subacute course, chronicity is more common. Patients usually present with vague pains, loss of weight, anorexia, a dragging sensation or occasionally with a mass in the left hypochondrium (Winternitz, 1912; Cummings, et al. 1978). Rarer modes of presentation include pyrexia of unknown origin, a discharging sinus (Soo et al. 1972) or repeated infections because of severe neutropenm (Chapman et al. 1954).

A correct clinical diagnosis is possible only if there is a past history of tuberculosis or evidence of healed lesions in other parts of the body. This is rare and the diagnosis is usually made either postoperatively or on post-mortem (Engelbreth-Holm, 1938).

Laboratory investigations are not of much value. Calcified nodules in the splenic area are considered diagnostic.

Splenectomy is the treatment. In some renal transplant centres, splenectomy is done to protect against the leukopenic effects of azothiopurine. The findings of primary splenic tuberculosis in these patients necessitates antituberculous therapy in addition to the immunosuppressive therepy (Cummings, et al. 1978).

With more patients from areas of the world where tuberculosis is endemic being accepted for renal transplantation, this entity is likely to be more frequently observed in the future.

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The International Conference under the auspices of Commonwealth Medical Association will be hosted by Indian Medical Association from December 3-5th 1983. The theme of the Conference is: "The Funding of the Health Care: Problems and Solutions". This will be followed by the Academic Seminar under the auspices of IMA Academy of Medical Specialities on 6th December, 1983 and IMA College of General Practitioners on 7th December, 1983. The preliminary programme has been published in IMA News, September 1983 issue. Further details can be had from Dr. Harish Grover, Organising Secretary General, IMA House, I.P. Marg, New Delhi-110 002.

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CONGENITAL TUBERCULAR HEPATITIS IN A 15 DAYS OLD NEONATE

GAURI BAZAZ-MALIK* AND D.N. MALIK**

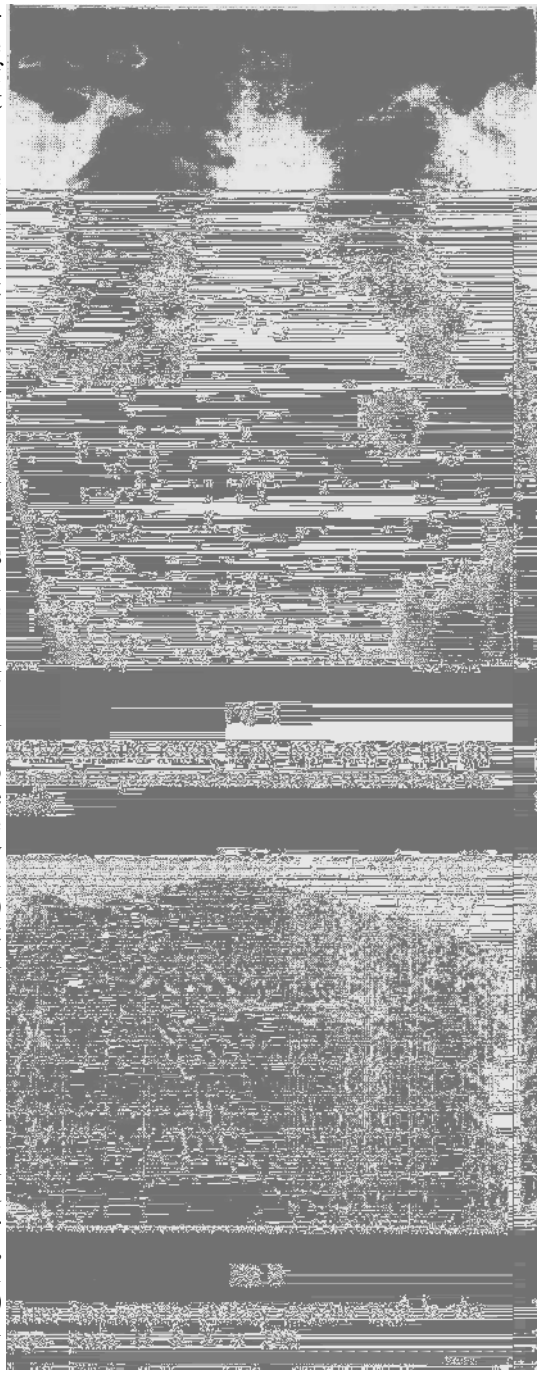
Summary: A case of tubercular hepatitis in a 15 days old full term nconate who had jaundice associated with hepatosplenomegaly is reported. Mother was a case of chronic pulmonary tuberculosis.

Tuberculosis is a major health problem all over the world, but in developing countries it is more acute with a disease prevalence of 4/1000 population and infection rate of almost 30% (W.H.O., 1974).

With very rare exceptions, children are born free from infection with tubercle bacilli. Therefore the neonatal period is the only period of life when people of any generation are free of tuberculosis (Dingley, 1980). But a neonate is highly vulnerable to congenital as well as acquired tubercular infection (Pope, 1942). It is said that a lesion proving fatal during neonatal period is almost certainly congenital (Morrison, 1963).

A case is piesented here with possibly such a lesion.

Case Report: A 15 days old male child was admitted to the Kalawati Saran Children Hospital, associated with Lady Hardinge Medical College, New Delhi, on 14-7-82 with complaints of fever, yellow discoloration of conjunctiva and high coloured urine for 7 days and marked distension of the abdomen and difficult respiration of 5 days duration. The child, a full term normal home delivery to a 4th gravida mother had developed severe symptoms within seven days of birth. The mother was later found to have radiologically active looking lesion in the left lung with Caries spine and a para vertebral abscess (Fig.l) Father too had a minimal inactive looking lesion at the riglet apex. Bacteriological status of both was not known. Siblings were poorly nourished.



On examination, neonate revealed Icterus +; Liver 6-7 cm. and spleen 4 cm. below costal margins. Cardiovascular, respiratory and C.N.S. systems were unremarkable. Provisional diagnosis of neonatal hepatitis was made and the case was treated with antipyretices, neomycin cap. 1½b.d., ampicillin l00mg. T.V. 6 hourly, gentamycin 5 mg, o.d. I.M., but died within 1½ days of admission. Liver biopsy (4951/82) revealed areas of caseation with minimal inflammatory response (Fig. 2). On Ziehl

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Neelsen's stain a heavy component of acid fast bacilli was demonstrated in the caseous areas (Fig.3). The lesion was diagnosed as tuberculosis of liver. Autopsy was not allowed.

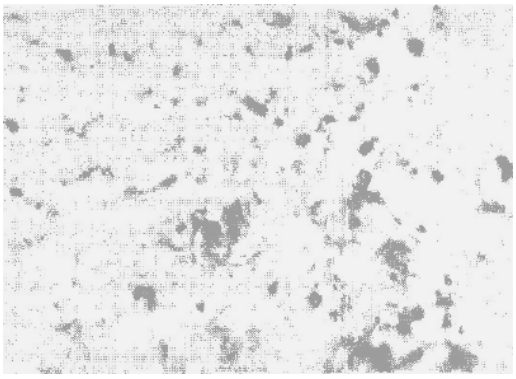

Fig. 3

Caseous material with pyknotic nuclei and abundant acid fast bacilli.Ziehi Neelsen's stain x 1000.

Comment: Congenital tuberculosis is rare. Only 158 convincing cases have been accepted (Davis et al. 1960) and a few more have been added to this list during the last two decades. The primary complex in congenital tuberculosis is found in the liver and portal lymph nodes. The infection is usually blood borne and less often by swallowing the infected amniotic fluid leading both to intestinal and liver lesions. In neonatal tuberculosis the clinical presentation of the case may be of acute meningitis, typhoid fever, acute bronchopneumonia, encephalopathy and occasionally marked hepatosplenomegaly, the last often mistaken for viral hepatitis or cirrhosis (Dingley, 1980). In the present case clinical presentation lead to a diagnosis of neonatal hepatitis.

In a sensitised person tubercle bacilli are engulfed by neutrophils within a few hours of entry but these become obscured by macrophages by the end of first day which ingest majority of the organisms by the second day. Weil developed granuloma with Langhan's giant cells appears only after a week (Raticliffe & Wells, 1948). In a nonimmunised host as in the present case the typical morphological features of a granuloma do not develop and obscure the real nature of the lesion which can be confirmed only by the demonstration of the micro-organism. Tuberculin sensitivity in a neonate takes about a month to develop (Gasford & Griffith, 1951) and caseation is observed in the lesion (Morrison, 1963). In the present case marked clinical symptoms were observed within the first week of life. As the granuloma takes at least a week to develop it will be obvious that lesion was congenital. According to Morrison (1963) a lesion proving fatal during neonatal period is almost certainly congenital. Therefore this case is presented as a case of congenital tubercular hepatitis.

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ADVERSE REACTIONS WITH MULTIPLE ANTI-TB DRUGS

S.K. GUPTA*, V.K. MAINI** and R.S. BEDI***

Summary: Twelve cases of tuberculosis developing adverse reactions with multiple anti-TB drugs are reported. The offending drug was identified on The basis of disappearance of reaction on withdrawal of the drug and its recurrence when challenged with the offending drug. In eleven cases, reactions were noticed in the first eight weeks of therapy. Thiacetazone was the commonest drug producing untoward reactions. Deseensitization was tried in seven cases with mild type of adverse reactions and was successful in five.

Introduction

It is not very uncommon to have adverse reactions to a single anti-TB drug, but the number of those who get such reactions with more than one drug is very small (Smith and Zirk, 1961). A few case reports of patients developing untoward reactions with multiple anti-TB drugs are available from India (Mital et al, 1976; Mathur et al. 1979; Jhamaria and Gupta, 1981). We report 12 cases of tuberculosis who developed adverse reactions with more than one anti-TB drug.

Observations

The 12 cases reported have been taken up from the cases put on anti-TB drugs during one year from March 1981 to February 1982. Salient features of these patients are given in the table. Five cases were males and seven females. Their ages were between 20 and 60 years. In 6 patients, the reactions were noticed in the first four weeks of therapy and in 5 cases, reactions occurred within the first eight weeks. One case developed reaction during the seventh month of treatment.

In two cases (described below), four drugs produced adverse reactions and in 5 cases, reactions were noticed with three drugs. In the remaining 5 cases, two drugs produced untoward reactions.

Thiacetazone was the commonest offending drug producing reactions in 10 cases. Other offending drugs were P.A.S., Streptomycin, Isoniazid, Rifampicin, Pyrazinamide and Ethambutol.

Skin reactions in the form of itching, maculo-papular rash, urticaria or bullous eruptions were the commonest adverse reactions noted in all twelve cases. Jaundice (4 cases) and gastro-intestinal disturbances in the form of abdominal pain, diarrhoea and vomitting (4 cases) were the other common reactions observed. Eosinophilia and giddiness occurred in 2 cases each. Arthralgia, circumoral numbness, "flu-like syndrome", difficulty in breathing and hypotension were the other uncommon reactions encountered.

Desensitization was tried in seven cases where reactions were of a mild nature. In the remaining five cases, who developed serious types of adverse reactions like generalised skin eruptions or severe hypotension, desensitization was not tried. It was possible to desensitize five patients successfully against Isoniazid and Ethambutol.

Two cases who developed adverse reactions with four drugs, being illustrative, are described in detail:

Case No. 1 M.S., 60 year old male was diagnosed as a case of pulmonary tuberculosis and put on Rifampicin, Ethambutol, Pyrazinamide and Isoniazid, as he had already taken Streptomycin, Tsoniazid and PAS irregularly for one year and his sputum was still positive for acid fast bacilli. He had eczema over the legs for many years. He tolerated these drugs well for seven months, till he reported with generalised itching and rash on 30.9.81. All drugs were stopped and the reaction subsided. On 7.10.81, he was given Isoniazid which he tolerated well. Two days later, a challenge dose of Ethambutol was given with which itching and rash reappeared. Reaction subsided in two days and on 16th, itching and skin rash recurred when a challenge dose of Pyrazinamide was given. Rifampicin was tried on the 21st, but the patient complained of itching, maculopapular rash and vertigo and the drug was withdrawn. On the 25th, Thiacetazone was given in a challenge dose, but had to be

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ADVERSE REACTIONS WITH MULTIPLE ANTI-TB DRUGS

TABLE

*Salient features of 12 cases developing multiple **drag** reactions*

Sr. No.	Name	**Age & Sex**	**Time** of **appearance** of adverse Reaction	**Drugs** causing reaction	Reactions encountered	Desensitiza-tion
1.	M.S.	60M	7th month	**EMB, TH, PZA, R1F**	itching, skin **rash,** vertigo.	**N.D.**
2.	**J.S.**	27M	2nd **week**	**TH, PAS, EMB, SM**	itching & skin rash, acute pain abdomen, diarrhoea, arthralgia.	Successful with **EMB.**
3.	M.	30F	2nd week	**SM, R.1F, TH**	circum-oral numbness, urticaria, hypotension, nausea & vomiting.	**N.D.**
4.	V.K.	26F	6th week	**TH, INK, EMB**	skin rash, jaundice	Failed
5.	H.K.	35F	5th week	**TH, INH, RTF**	skin rash with bullous eruptions, eosinophilia	N.D.
6.	B.K.	22F	2nd week	**SM, TH, PAS**	erythematous rashes all . over body.	Successful with SM
7.	R.S.	22M	4th week	**TH, INH, EMB**	skin rash with eosinophilia	Successful with I**NH**
8.	S.L.	30M	6th week	**INH, TH**	Itching with skin rash, **jaundice.**	Failed
9.	S.D.	35F	4th week	**TH, PAS**	Jaundice and skin rash	N,D.
10.	N.	41F	7th week	**INH, TH**	itching	Successful with INH
11.	S.	35F	1st week	**SM, INH**	giddiness with vomit-ing, difficulty in breath-itching	Successful with **INH** ing;
12.	**T.R.S.**	**22M**	6th week	**RIF, EMB**	**"Flu-like** syndrome", skin rash, jaundice	**N.D.**

RIF	Rtfampicin	TH	Thiacetazone
EMB	Eihambutol	SM	Streptomycin
INH	Isortiazkl	**PZA**	Pyrazinamide
PAS	**Para** amino salicylic acid	K	Kanamycin
N.D.	Desensitization not done due to severe reaction		

stopped because of recurrence of rash and itching. Thus, this patient had adverse reactions with Ethambutol, Pyrazinamide, Rifampicin and Thiacetazone.

Case No. 2: J.S., 24 years male, a case of pulmonary tuberculosis, was put on Streptomycin, Isoniazid and Thiacetazone in standard dosages on 2.2.1982. On llth February, he developed itching and maculopapular rash all over the body, which disappeared when all anti-TB drugs were stopped. On the 15th, rash and itching reappeared with a challenge dose of Thiacetazone and this drug was stopped. Two days later PAS was added but had to be withdrawn as it caused acute abdominal pain and

diarrhoea. Ethambutol was added on 19.2.82, but it also caused mild itching and rash. However, desensitization with Ethambutol was tried starting with an initial dose of 25 mg. and increasing it daily by 25 mg. The patient was able to tolerate the full dose of Ethambutol within 2 weeks. Next week, he started complaining of pain and swelling of small joints of hands and feet after Streptomycin injection. Arthralgia disappeared when Streptomycin was stopped but recurred when a challenge dose of Streptomycin was given. Streptomycin was stopped and he was discharged on Isoniazid and Ethambutol,, which he tolerated well. Thus, this patient developed untoward reactions with Thiacetazone, PAS, Ethambutol and Streptomycin,

Discussion

The offending drugs in these cases were proved by giving challenge doses of various drugs, one by one, and eliciting the so-called '"Light switch phenomenon", i.e. reappearance of reaction on challenge with the offending drug (Bianchine et al. 1968). Majority of cases (11 out of 12 cases) developed adverse reactions within the first two months of treatment. Smith & Zirk (1961) reported majority of reactions within first five weeks.

One patient developing reaction to Streptomycin, Thiacetazone, Isoniazid and Cycloserine was reported by Govind Raj (1968). Mital et al. (1976) reported 3 cases in which there were adverse reactions to four or more drugs. In our study, two patients developed adverse reactions of many types. In one case (Case No 2) the patient developed itching and skin rash with Thiacetazone and Ethambutol, acute abdominal pain and diarrhoea with P.A.S. and arthralgia with Streptomycin. *In* the second case (Case No.l), there was skin rash with Ethambutol, Thiacetazone and Pyrazinamide and itching and vertigo with Rifampicin. Multiple reactions of such diversity in one individual are extremely rare. Wayne (1958) stated that people who get allergic reactions to drugs are predominently individuals with allergic diathesis. In the present series, except for one (Case No. 1), who had long standing eczema, none had any history of bronchial asthma, allergic rhinitis, eczema or urticaria etc.

Five of our patients had severe adverse reactions in the form of generalised skin eruptions or hypotension and in these cases desensitization was not tried. Out of the remaining 7 cases, where desensitization was tried, we succeeded in five cases. Smith & Zirk (1961) observed that desensitization rarely fails, if a satisfactory technique is employed.

As most of the adverse reactions to various anti-TB drugs usually occur within the first 8 weeks of therapy, it is of the utmost importance that all patients should be properly educated about the possible adverse reactions at the start of treatment so that prompt action can be taken in cases developing such reactions and unnecessary morbidity, occasional mortality and drug default can be prevented. Secondly, drugs producing mild reactions should not be changed unnecessarily before giving a fair trial to desensitization.

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ANNUAL MEETINGS OF THE INTERNATIONAL UNION AGAINST TUBERCULOSIS (16TH TO 18TH SEPTEMBER, 1983)

A Brief Report

by DR. S.P. PAMRA*

Meeting of the Executive Directors

The main subjects discussed during the meeting were as follows:-

(a) Fund-raising: The IUAT has procured the services of a specialist in fund-raising from USA for a short period. A suggestion was made that a consultative committee be set: up for guiding the National Associations in respect of fund-raising. Some, however, felt that a consultative committee may not serve much purpose as every State will have to adopt measures best suited to it. The decision regarding consultative committee was postponed to next year,

(b} Mutual Assistance Programme: There was some doubt about the continuation of this programme as specific grants from some constituent members which made this programme possible were likely to be withdrawn. The Canadian representative assured that the funds from Canada will continue to be provided. Switzerland was of the opinion that mutual assistance, as far as they were concerned, is likely to be made available in future directly to a country on government to government basis rather than being canalised through the ITUAT. Switzerland was assisting Tanzania in this connection. Norway and Sweden were also likely to follow the same pattern.

A suggestion was made that the IUAT may make drugs available to the developing countries at subsidised rates rather than providing monetary assistance for any other activity. The Executive Director of the IUAT informed the members that the assistance in the shape of drugs is already being provided to some countries and the other countries who need such assistance can ask for it from the IUAT.

(c) Non-tuberculous respiratory diseases:-The representatives from some of the developed countries of North America and Europe made a strong plea for changing the name of the IUAT and enlarging its activities to include non-tuberculous respiratory diseases also. The representatives of the developing countries on the other hand were not in favour of diluting the activities of the IUAT in respect of tuberculosis atleast for some more years to come. No final decision was therefore taken in this connection.

(d) *Health Education:* There was a general agreement amongst the members that the health education material produced by all the countries should be made available to others for their guidance, though finally each country will have to design its own material in a shape[1] and form that is most likely to be acceptable to its population.

(e) A point was made that the teaching to the undergraduates is not satisfactory even in developed countries and students pay little attention to tuberculosis during undergraduate study since tuberculosis is not included usually in the examination for the basic medical qualification. It was felt that the constituent members may take up this question individually with the authorities controlling medical education,

The Executive Directors were finally requested to submit proposals for next year's Agenda expeditiously. The emphasis should be on specific proposals rather than general points for discussion.

Scientific Committee on Treatment

The meeting was attended by 50 ordinary and corresponding members. Half a dozen papers on various aspects of short-course chemotherapy, viz. treatment of sputum negative patients, elderly patients, children and serum levels of drugs in relation to toxic reactions were presented. The Committee felt that no further change in its recommendations as formulated at the last meeting in December, 1982 was called for in the light of the fresh studies that were reported at this meeting.

Bulk of the time was utilised in discussing problems of chemotherapy in children about which there is paucity of controlled trials. A working paper was presented by Dr. Vennema of USA, but most of the members did notagree with his views. After long discussion, some members of the Committee were asked to

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report on various aspects of the problem at the meeting of the Committee next year.

Joint Meeting of the council and the Scientific Committees

This meeting was attended by about 100 persons and was presided over by Dr. Shimao, the Chairman of the Executive Committee. Dr. Bado of Argentina and Prof. Dahlstrom of Sweden were the Co-chairmen. Three main subjects were discussed.

a) Structure and budget of Scientific Commi ttees and the Commitment of WHO and IUAT to Primary Health Care.

It was felt that there has been little or no decline in the problem of tuberculosis in developing countries. There was need for more and better tools and stepping up of operational research in the developing countries. There is a vicious circle of poor development and poor health care. New trends in technology are not being fully exploited. There is a paucity of work on behavioural attitudes of people and delivery of new technology which are essential for progress. Delivery of health care has to be so planned that it should win the community's confidence. Progress in the evolution of new vaccines to replace BCG was briefly reported.

b) Non-tuberculous respiratory diseases and smoking

The recommendations of the 5th World Conference on Smoking and Health were briefly reported. It was felt that smoking and its prevention is more of a political than a health problem. The money spent by the multinationals in publicity of smoking and various brands of cigarattes was much more than the health budget in some countries. Replacement of tobacco crop with other crops so that the farmer's interests are not jeopardised, rehabilitation of persons engaged directly or indirectly in tobacco growing, processing, marketing, etc. further complicate the issues. It was reported that whereas health facilities are recommending measures to cut down smoking, some organisations like FAO are recommending measures for improving the tobacco crop, etc. Thus, the problem has to be dealt with not merely on the health front but also on political, economic and other fronts also.

A plea was made for greater attention to non-tuberculous respiratory diseases. There is a strong move to change the name of the Union to bring in non-tuberculous respiratory diseases also in addition to tuberculosis. The linal decision on this matter was postponed till next year.

c) *Some unsolved problems in tuberculosis control in developing countries.*

Dr. Styblo highlighted the wide gap which still exists between the availability of knowledge and its application in the developing countries. Lacunae in diagnosis, availability of diagnostic facilities at the periphery and non-compliance of the patients were particularly referred to. Involvement of the population itself in deciding the best strategy for organising sputum examination at the periphery was stressed.

Results of a pilot project in case-finding and case-holding being carried out in Tanzania under the auspices of the IUAT and WHO were reported. 60-70% of the estimated sputum positive cases were being detected. There is a decline in the proportion of sputum positive to sputum negative cases. Extra-pulmonary cases constitute 7-10% and re-treatment cases are of about 5 %. The number of males is approximately double that of females in all age groups except 0-14 years where males and females are almost equal. The annual risk of infection which was 2% previously has now come down to about 1.5%. The proportion of cases discovered to the estimated cases goes down as the distance from the diagnostic centre increases. In the rural areas, the number of cases detected are about 35 per 100,000 as compared to 60 per 100,000 in the urban areas. Of the persons put on treatment, 7% died. 18% dis-continued treatment prematurely, 10% were still continuing treatment and 40% had completed treatment successfully. In !3% the treatment had failed and 10% were still under treatment.

At the concluding meeting, it was decided that the next International Conference will be held in Singapore in 1986, and Dr. Sen Gupta, representative of the Singapore Tuberculosis Association, took over as President of the International Union in place of the representative from Argentina. The constituent members were requested to suggest suitable topics for the Singapore Conference. It was suggested that the Conference may last three days, the pre-lunch time on each day will be devoted to two plenary sessions each and the free communications will be taken up in three or four rooms simultaneously in the post-lunch period. The Programme Committee for the next Conference will be set up some time next year and will review and select suitable papers.

BOOK REVIEWS

CUNICAL STRATEGIES IN ADULT ASTHMA

by Charles **H. Scoggin and Thomas L. Petty, published by Lea & Febiger, Philadelphia, 1982, Agents in India K.M,** Varghese **Company, Bombay, price $ 9.75.**

The authors have packed a wealth of knowledge within, the short space of 140 pages. It is a comprehensive treatise on the subject dealing with all problems pertaining to Asthma. Complex heterogeneous mechanism of its causes; role of allergy and other trigger phenomenon: the role of clinical findings and laboratory tests in diagnosis and assessment; various clinical types; their distinguishing features and management and management of asthma complicated by other conditions e.g. pregnancy, heart disease, surgery, etc. are all exhaustively dealt with in a very captivating style. Like a good novel, one cannot put it back once having started reading it and having finished it, one cannot help giving it a second and more leisurely reading.

All ambiguities and controversies are scrupulously avoided. Important clinical features are supplemented by selected ease histories. The approach to the problem is intensely practical and rational, even at the cost of cutting down much of theoretical basis of the phenomenon described. The indications for management are clear cut.

With a view to impress the salient points on the reader's mind and memory the text is spiced here and there with tense and apt homilies. A few examples are pertinent;-

"common things happen commonly," "silent chest (in acute asthma) is ominous and when it becomes noisy, it is a good sign"; "dangers of steroids (in the management of Asthma) are too late, too little, too long"; "best time to treat Status asthmaticus is three days before it happens": "nobody ever got the Nobel prize for not giving penicillin": 'most of what we are 'discovering' today is not new": etc.

The indications for treatment of various types of asthma are precise. The strategy in the deployment of various drugs is conveniently mentioned as "ABC approach—A, B & C standing for three different groups of drugs". In short, the subject is dealt with in such a way that it cannot but have a lasting impact on the reader.

A short chapter also deals with the unsolved problems, new drugs and new strategies in managment. The authors also refer to increased need for enlightenment among patients and physicians if this scourge is to be contained.

The book is not only a 'must[1] for all medical libraries, but it should also be in the possession of every specialist, post-graduate student and above all a family physician who is called upon to deal with asthma. The general get-up and production is excellent and yet the book is very moderately priced at less than $ 10 which is comparatively much less than the other monograms of the same standard and usefuless.

—S.P. PAMRA

INTENSIVE AND REHABILITATIVE RESPIRATORY CARE (3RD EDITION) EDITED

by Thomas L. Petty, published by Lea & Febiger, Philadelphia, 1982, Agents **in India K.M. Varghese Company, Bombay, Price $ 28.50**

The book is a must not only for medical libraries but also for every chest physician. The popularity of the book is proved by the number of editions and reprints since its first appearance in 1971,

Dr. Thomas L. Petty has himself written 15 out of the 20 chapters and one out of the 3 appendices. Eight other experts have between themselves contributed 5 chapters and 2 appendices. All the experts appear to be from the team working in the Respiratory Care Unit of the University of Colorado Medical Centre, Denver. It is obvious from the detailed illustrative case notes and repeated quotations from observations and research work, that this centre must be doing excellent work.

The beautifully reproduced illustrations of techniques and apparatus used are outstanding. The editor is very particular about diff erent techniques being correctly carried out and choice of the particular apparatus, such as ventilator correctly made to suit the individual needs of the patient. At the very onset a firm case is made for proper study by blood gas analysis, PH estimation etc. to make a correct diagnosis. How clinical judgement may be misleading is proved not just by arguments but by quoting case reports in great detail. The authors believe that it is best to start at

the very beginning and hence the importance given to the technique of taking arterial blood samples and estimation of blood PO2 and PCO2 in the very first chapter of the book.

The book deals adequately not only with the emergency treatment of respiratory failure with all its different causes in the 'acute respiratory unit' but also follow up action in the ward; O.P.D. and even at home.

The most creditable and touching success story is certainly that of the young man of 22 suffering from Duchenne's muscular dystrophy who was given up as hopeless by others. The unit took up the challenge in response to the plaintive cry of the mother—must he die? and not only pulled him through the crisis of acute respiratory failure but taught the mother all the details of how to look after him at home with his permanent tracheostomy, ventilation and all. All the items of apparatus used at home are listed in great detail. That the young man lived to work as a part of the team for rehabilitation of other patients suffering from muscular dystrophy is the biggest tribute to the talented and dedicated team. Dr. Petty and his colleagues adequately deal with not only how to save lives but also how to deal with the patient and relatives where death is inevitable.

One cannot help feeling the marked desparity between the advanced countries with experts like Petty and others and all equipment and drugs available to them and the other less fortunate institutions capable of correctly dealing with respiratory failure in developing countries like ours. **Dr.** Petty has made an excellent case that acute respiratory care is even more profitable and useful then acute coronary care.

This book is a must not only for institutions and chest specialists but also for medical postgraduates and para medical workers working in respiratory care units.

—M.D. DESHMUKH

FUNDAMENTAL CARDIO VASCULAR AND PULMONARY PHYSIOLOGY—AN INTEGRATED APPROACH FOR MEDICINE

by Jerry Frankline Green, Published by Lea & Febiger, Philadelphia, 1982, Agents in India K.M. Varghese Company, Bombay, Price $20.00

The book is divided into 4 Sections. Section I on 'Basic Concepts' covers volume pressure relationship, pressure flow relationship and transport process.

Section H on 'Cardiac physiology' includes heart, its functions, basic anatomy and properties of cardiac muscles, electrophysiology of heart, electro-cardiogram, disturbance in cardiac rhythm, myocardial mechanics, control of cardiac function, pressure flow and volume relationship.

Section III on 'vascular physiology' deals with vascular circuit, circulatory mechanics, determination of venous return, cardiac output, arterial blood pressure and its normal values. Distribution of cardiac output, arterial blood pressure and its normal values, distribution of cardiac output, determination of vascular tone, pulmonary micro-circulation, cardio-vascular disturbances and the blood.

Section IV: gives details of pulmonary physiology which includes pulmonary system, pulmonary mechanics, pulmonary gas exchange, lung water pulmonary disturbances and control of respiration.

The book has four appendices dealing with usual abbreviations and symbols, haemodynamics, quantitative aspects of membrane transport and ventilation perfusion relationships.

The book has been written in a very lucid style and is very well illustrated with schematic drawings, equations and models. The author has substantiated the various theories and haemodynamics of myocardial mechanics and cardiac cycle with graphic illustrations. The various physiological laws, e.g. Booke's law, Poisenille's law have been explained by keeping the background of biochemistry and its variations during the state of health and its variations during disease in view.

Basic concepts of electrocardiogram have been properly outlined for identifying disturbances of cardiac rhythm and specific cardiac abnormalities. There is an excellent chapter on vascular physiology with schematic summary, which will be a very useful guide for understanding the basic concepts of circulation. Similarly the capillary pressure in microcirculation is very well dealt with. Starling's principle of fluid balance and capillary filtration co-efficient has been very well explained by equations.

The book will be of immense value for research workers, post graduate students and specialists in understanding the basic concepts of cardio-pulmonary vascular physiology, its variations and its bearing on clinical medicine.

—H.B. DINGLEY

PROBLEMS IN PULMONARY MEDICINE FOR PRIMARY PHYSICIAN

by Robert H. Poe and Robert H. Israel, Published by Lea & Febiger, Philadelphia, 1982, Agents in India K.M. Varghese Company, Bombay, Price $ 32.50.

This book consists of 18 chapters and aims to analyse the common problems in pulmonary medicine that are faced by a primary care practitioner. The authors have stressed a practical, problem-oriented approach to the diagnosis and management of some important pulmonary diseases. The first three chapters on dyspnoea, cough and haemoptysis are superb in clarity of presentation. The chapter on pulmonary functions is well illustrated and discussed. The evaluation of patient with solitary pulmonary nodule, pulmonary infiltrate etc. are written with an emphasis on those particular aspects which prompt a consultation from pulmonary specialist. All the articles arc comprehensive and well referenced.

The chapters on mechanical ventilator, adult respiratory distress syndrome, sleep apnoea syndromes may not be very helpful to the primary physician—at least in India. A common problem like respiratory infections does not find a place in proper perspective in this book. The chapter on Tuberculosis, which may have been written with the primary physician of developed countries in view, is grossly inadequate for the requirements of his counterpart in developing countries.

The main features of the book arc clear presentation, management plans and good reproduction of roentgenographs. Though the book is highly priced yet it will be excellent resource for the nonspecialists who are dealing with patients with pulmonary diseases. The medical students and house-officers may not lind it so useful,

-D.D.S. KULPATI

Ind, J. Tub., 1983, 30, 170

NEWS & NOTES

34th TB SEAL CAMPAIGN

The 34th TB Seal Campaign, organised by the Tuberculosis Association of India and its affiliates in the States, was inaugurated on 2nd October 1983—Gandhi Jayami Day—by Shri Zail Singh, President of India and Patron, Tuberculosis Association of India at a special function held at Rashtrapati Bhawan, New Delhi. The function was attended by the President and members of the Tuberculosis Association of India and the Delhi TB Association.

In a Message issued on the eve of the inauguration of the Campaign, the President said: 'Tuberculosis is one of the fatal diseases and it is the poorer sections of our society who are victims of its incidence the most. Considerable work has been done to control this disease yet much more needs to be done before this scourge is finally eradicated from the country. 1 hope this campaign will provide further impetus to the selfless workers engaged in this noble cause to redouble their efforts in combating this deadly disease. On this occasion, I appeal to my countrymen to help the movement by donating generously. My best wishes for the success of the Campaign".

Shri S. Ranganathan, President, Tuberculosis Association of India, in his Message appealed to the people to strengthen the TB Associations by buying TB Seals in large numbers and help to intensify the fight against tuberculosis in our country. The Association has printed and distributed through its affiliates in the States about 300 lakhs of Seals for this Campaign.

REFRESHER COURSE IN TB

The Anti-TB Association of Tamilnadu conducted a Refresher Course on TB & Chest Diseases on 23rd July, 1983 at R.K.V. Kaliamandram, Ramalingam TB Sanatorium, Perundurai, Periyar District. The Course was organised under the joint auspices of the District TB Association, Periyar Dist. and Ramalingam TB Sanatorium, Perundurai. Eminent Professors of the Coimbatnre Medical College gave lectures on various aspects of TB. Dr. G. Chandrasekharan, Dy. Director (TB), Dr. V. Rangasamy, Director, Institute of TB & Chest Diseases, Madras, Dr. K. Jagannath, Superintendent, Tambaram TB Sanatorium and Shri S.A. Rajagopalan, Publicity Officer (TB) participated in the sessions. Dr. Chandrasekharan also gave the valedictory address. 76 doctors including 25 private practitioners attended the course.

The TB Association of Pondicherry organised a Refresher Course in TB on 7th August, 1983, at Avvaiyar Women's College, Karaikal. Mr. S. Krishnan, I.A.S., Secretary (Health), inaugurated the Course and Dr. V. Sambasivam, Director of Health & Family Welfare Services, presided. Dr. V.K. Padmanabhan, TB Control Officer, Pondicherry, Professors and Heads of Departments of Radiology, TB & Chest Diseases, JIPMER, Pondicherry, District TB Officers and others participated in the Course.

FREE MEDICAL CAMP

The Sholapur District Anti-Tuberculosis Association, of the Maharashtra State Anti-Tuberculosis Association arranged a Free Medical Camp for Chest Diseases on the 6th and 7th of August, 1983 at Sholapur. 500 persons were examined, 356 M.M.R. X-Rays were taken and 37 new cases with pulmonary lesions were detected.

SEMINARS

M/s Lupin Laboratories (Pvt.) Ltd., organised a Seminar on Tuberculosis at Cuttack on 11th June, 1983 for the benefit of District Tuberculosis Officers. About 50 doctors from TB Hospitals and clinics in Orissa, members of the faculty of the local Medical College and a few general practitioners attended. **Dr. S.P.** Pamra, Hony. Technical Adviser. TB Association of India gave a talk on 'Current Management of Tuberculosis'.

The District Tuberculosis Association^ Raipur, in cooperation with the Raipur Academy of Medical Sciences, organised a Seminar on Tuberculosis on the 26th Junej 1973 at Raipur. The Seminar was attended by over 100 persons including members of the Academy, general practitioners and post-graduate students of the Medical College. Dr. **S.P.** Pamra, delivered twb lectures, one on 'Diagnosis of Pulmonary Tuberculosis' and the'other on 'Recent advances in the management of Tuberculosis'. Dr. H.B. Dingley delivered lectures on tuberculosis in children and surgical treatment of pulmonary tuberculosis.

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ABSTRACTS

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A Controlled Trial of Six Months Chemotherapy in Pulmonary Tuberculosis.

1st Report: Results during Chemotherapy. British Thoracic Association. Brit. J. Dis. Chest, 1981, 75, 141.

Results of six months chemotherapy with daily isoniazid and rifampicin supplemented for the first two months by either streptomycin and pyrazinamide (SHRZ6 regimens) or by ethambutol and pyrazinamide (EHR.Z6) in patients with culture sputum positive have been reported and compared with those of nine month regimen of daily isoniazid and rifampicin supplemented by ethambutol for the first two months (EHR9 regimens).

All patients in three regimens had bacteriological conversion before the end of chemotherapy, but the rate of sputum conversion was more rapid with two pyrazinamide containing regimens. Of the 287 patients on the SHRZ6 and EHRZ6 regimens, who completed chemotherapy, 77% had achieved negative cultures at two months and 98% at three months, compared with 64 % and 88% respectively *o* the 157 patients on the EHR9 regimens. Of the 334 patients who had SHRZ6 and EHRZ6 regimens, 14 (4%) developed hepatitis. Among the 177 patients in EHR9 group (who did not receive pyrazinamide) the jrequeacy of hepatitis was[1] 4%. Thus addition, of pyrazinamide to regimens containing rifampicin and isoniazid did not increase the frequency of hepatitis. But frequency of adverse effects other than, hepatitis particularly skin rashes was more in pyra?in;imide containing regimens.

Eosinophilia as a result of Rifampicin Therapy

Pranesh Nigam, et al., J. Ind.Med. Assn., 1981, 77, 158.

2 cases, one of pulmonary tuberculosis and one of leprosy, are described where a few days after starting Rifampicin along with other drugs, skin rash and increase in absolute number of eosinophilia in peripheral blood were noticed. The eosinophil count returned to normal within a few days of withdrawal ot rifampicin but recurred when a challenge dose of rifampicin was repeated.

Experimental Models To Explain the High Stelizing Activity of Rifampin in the Chemotherapy of Tuberculosis.

Jean M. Dickinson,et al., Amer. Rev. of Res. Dis., 1981, 123, 367.

Model systems were set up *in vitro* to explore the reasons why rifampin is a better sterilizing drug than isoniazid in short-course chemotherapy of tuberculosis. When the growth rate of mycobacterium tuberculosis strain H37 Rv was reduced uniformly by lowering the incubation temperature or the pH of the culture medium, the bactericidal activity of rifampin and izoniazid decreased to a similar extent. However, when a culture was maintained at 80°C and incubated for daily periods of 1 or 6 hours at 37°C, rifampin killed more rapidly than isoniazid. Maintenance of control cultures without antimicrobials at 8°C with or without periods at 37”C, had little or no effect on their viability, ability to commence logarithmic growth at 37°C, or to incorporate (3°C) uridine. Old cultures left undisturbed or to which small additions of fresh culture medium were regularly added were killed more rapidly by rifampin than by isoniazid. These experiments supported tile view that the special part of the bacterial population that is killed more rapidly by rifampin than by isonizaid during short-course chemotherapy consists of bacilli dormant much of the time but occasionally metabolising for short periods.

Pharmacokinetics of Streptomycin (SM) in Patients with Pulmonary Tuberculosis.

A.J. Roncoroni, et al., Amer. Rev. of Res, Diseases,; 1981, 123 (4 Supple), 254.

A pharmacokinetic study was carried out among patients in the age group 22-44 years and weight range 48-82 kgs. All patients were sputum positive and they were administered streptomycin in a dose of 1 gm once a day intramuscular for two weeks in all along with Rifampicin, INH and Ethambutol. Creatinine clearance was within normal limits in all cases. No side effects were observed. The study showed that a streptomycin dose of 15 mg/kg body weight of streptomycin as a single

intramuscular injection daily provides a mean serum peak level of 40 ug/ml one-hour after administration of the drug. This dosage helps to maintain the Trough level" of streptomycin in the 1-2 ug/ml range throughout the two weeks of therapy.

Infectiousness and Pathogenicity of Drug Resistant Mycobacterium Tuberculosis.

D.E. Snider, et al, Amer. Rev. of Res. Diseases.. 3981, 123 (4 Supple), 254.

Primary resistance to anti-tuberculosis drugs is not increasing despite widespread use of drugs. A possible explanation can be that drug resistant bacilli are not as infectious or pathogenic as drugs sensitive ones. To test this hypothesis, prevalence rate among contacts of patients with bacilli resistant to INH/ Streptomycin and contacts of patients with sensitive bacilli were studied. There was no difference between the contacts in these two groups in respect of either prevalence of infection or disease. There was also no relationship between the concentration of drugs to which the patients' organisms were resistant and the rate of infection among the contacts. Contacts of patients whose organisms were resistant to both INH and Streptomycin were significantly more likely to have become infected than contacts of patients whose organisms were resistant to one of the two drugs only. 2 of the 3 bacillary cases arising amongst the contacts had sensitivity test results which were different from those of the index cases.

Studies on lung Disease due to Atypical Mycobacteria in Japan.

Michio Tsukamura, et al, Kekkaku; 1981, 56, 391.

Frequency of atypical mycobacteria among patients admitted to a tuberculosis hospital from April 1979 to March 1980 was studied. Out of 1869 positive cultures 224 or 12% were found atypical. This ratio was 6%, 5.8%, 7.8% and 9.5% in 1971, 1974, 1975 and J977 respectively. Whereas the disease in 141 patients was assessed to have been caused by atypical mycobacteria, the isolation was casual in 46 cases. The frequency showed considerable geographical variation. Most of the disease seemed to be caused by M. avium-M. intracellulare.

Clinicopathologic Manifestations and Differential Diagnosis from Enterocolonic Tuberculosis

Liu Tonghita, et al: Chinese Medical Journal, 1981, 94, 431.

In 40 cases of enterocolonic Crohn's disease (CD), the resected specimens were studied elinicopathologically and were compared with 53 cases of enterocolonic tuberculosis (TB). There are many symptomatic and morphologic overlaps between the two diseases. Nevertheless, fissuring ulcer, widening of submucosa and cobblestone appearance arc distinctive diagnostic features of CD, while caseous necrosis and/or presence or acid-fast tubercle bacillus are the hallmark of TB. Anti-tuberculous therapy may alter the histologic characteristic of TB leading to scarring of the granuloma, yet caseous necrosis never completely disappears even after massive doses of anti-tuberculous therapy. In our series, caseous necrosis in the lymph node and bowel wall was still prominent in 21 cases of enterocolonic TB receiving preoperative anti-tuberculous treatment.

Immune logical Study on the Background Factors of Intractable Pulmonary Tuberculosis Patients.

Shinobu Takenaku: Kekkaku; 1981, 56, 267.

Immunological studies were carried out on patients with intractable pulmonary tuberculosis to evaluate the factors associated with intractability. An intractable patient was considered to be one who had remained unconverted with far advanced cavitary disease in spite of good and adequate chemotherapy, matching cases whose response to chemotherapy was favourable were taken as controls. Intractable patients showed (1) depression of delayed hypersensitivity reaction to DNCB, (2) decrease in the number of monocytes and lymphocytes in peripheral blood, (3) depression in the interaction between monocytes and lymphocytes, (4) decrease in the number of T-lymphocytes and (5) an increase in the number of IgG-FcR T-lymphocytes. On the other hand, the number of B-lymphocytes immunoglobulin levels in peripheral blood and sensitivity to PPD were similar to those in the controls. Monocyte functions were almost the same in the controls with respect to phagocytosis. NBT reduction test and lysosomal enzyme levels. These results suggest that non specific immunity of patients with intractable disease is depressed in respect of the cell-mediated immunity, but not in humoral immunity.

Recent trends in Empyema Thoracis

G.F.A. Benefield.Brit. J. Dis. Chest; 1981, 75, 358.

One hundred and twenty three patients with empyema thoracis have been reviewed. The major cause was pneumonia, next to it was thoracic and gastro-oesophygeal surgery.

Of these 62 (or 63%) had microorganisms chiefly staphaureus strepto, pneumoniae and anaerobes, following pneumonia whilst gram-negative enteric bacilli were frequently isolated in the post-operative cases. Treatment with antibiotics alone or with closed drainage resolved 29% of empyemas but another 64% required major surgery. The former group had a mean duration of symptoms of 28 weeks, whereas the surgically treated patients had symptoms for a mean period of 83 weeks. 83% of patients who required thoracotomy had a history of more than four weeks. Thirty six patients died, 11 of whom had empyema, giving an empyema mortality of 9%. With wide spread use of antibiotics the management of empyema has considerably changed,

Mayo Lung Project: Evaluation of Lung-Cancer Screening

Lewis B, Woolner, et al: Mavo Clinic Proceedings, 1981, 56, 544.

The primary purpose of the Mayo Lung Project is to determine whether screening of 'high-risk' populations by means of periodic sputum cytology examinations in addition to thoracic roentgenograms will result in lower mortality from bronchogenic carcinoma than that found in a control population. The high-risk population screened consisted of men 45 years of age or older who were chronic excessive cigarette smokers. The paper reviews the status of the programme as on December 31, 1979, and cencentrates on three facets of the screening programme; (1) determination of the relative value of the two screening tests in the early detection of lung cancer; (2) documentation of the relative frequency of cell types of lung cancer and the extent of the disease when first detected; and (3) the size and location of all 'incidence' cancers (cancers detected by rescreening after a negative initial screening) and the proportion of these that are'occult' (cytologically positive, roentgenographicaHy negative). Our results show that in an incidence series in cigarette-smoking males, squamous carcinoma is almost equaled in frequency by small cell carcinoma (30% and 26% respectively). Fifty-four percent of incidence cancers in the group being re-screened every 4 months were detected at an early, potentially curable stage of the disease. Contrary to early expectations, chest roentgenography far surpassed sputum cytology as a means of detection of early lung cancer. Sputum cytology is highly effective in early detection of squamous cancer—50% of all early stage squamous cancers are first detected by this means — but is of little use in the early detection of adenocarcinoma or large cell types. In small cell cancer, neither screening modality is of value. Occult lung cancer makes up a rather small fraction of lung cancer as a whole, preliminary data suggesting an incidence of 12 to 15%

Bronchogenic Carcinoma in a Tuberculosis ward.

Kenji Nakamura, et al., Kekkaku; 1981, 56, 403.

Cytological screening of the sputum on three consecutive days was carried out in 479 male patients of pulmmary tubercuiosis, aged over 60 years, admitted in the tuberculosis ward of a chest hospital in Japan between 1975 and 1979. 13 patients (2.7 %) were found to have bronchogenic carcinoma. This rate is much higher than that among the same age group in the general population. The carcinoma was of epidermoid type in 11, adenocarcinoma in 1, and small ceil carcinoma in another. All patients were smokers. The sputum of 9 patients was positive for tubercle bacillus, two patients for atypical mycobactcria and the remaining two were negative by smear and culture. The carcinoma was more often on the same side as tuberculous lesion.

Transbronchial needle aspirations for diagnosis of lung cancer

Ko Pen Wanz-Et-al, Chest; 1981, 80, 1.

Thirty two consecutive patients with mediastinal lesions suggestive of bronchogenic carcinoma had transbronchial needle aspirations. 18 of the 20 patients (90%) with proved bronchogenic carcinoma showed malignant cells in the aspirate. Of the 12 patients with normal cytology, six were subsequently proved to have non-neoplastic disease. Transbronchial needle aspiration is a useful diagnostic procedures in the diagnosis of malignant disease.

Etiologic considerations in superior vena cava syndrome

James M. Parish, ct al., Mavo Clinic Proceedings, 1981, 56, 407.

The Mayo Clinic experience with superior vena cava obstruction during the last 20 years was reviewed. The diagnosis of superior vena cava obstruction is often made at the bedside. Typical symptoms include suffusion, dysponea, cough, and, less commonly, pain, syncope, dysphagia, and hemoptysis. The most important physical findings are the increased collateral veins covering the anterior chest wall and the dilated neck veins with edema of the face, arms, and chest. The chest x-ray film usually shows widening of the superior mediastinum. Of the 86 cases of superior vena cava obstruction, 67 (78 %) were due in malignancy and 19 (22 %)

to benign causes. The cause of obstruction is usually established by bronchoscopy open lung biopsy, or biopsy of the superficial lymph node. Radiotherapy remains the standard approach for the treatment of superior vena cava obstruction due to malignant disease, it is of particular interest to note that of the six benign cases resulting from thrombosis of the superior vena cava, three were due to the use of central venous catheters.

Thoracic complications of amoebic abscess of the liver

Carlo Ibarra—Perez; Chest, 1981, 79, 672.

501 patients of amoebic abscess of liver showed thoracic complications from 1961 to 1979. 175 patients had inflammatory lessions of thoracic structures (165 with pleural effusions and penumonitis and ten with pericarditis). The remaining 326 patients ruptured through the diaphragm (175 into the airways, 106 into the pleural cavity, 5 into the pericardium, 39 into the airways and pleura and one into the pleura and pericardium). The thoracic complication was preceded by a picture suggesting an inflammatory process or a chronic wasting disease. The complication was signaled by increase or change in. character of pain locally or referred to the right upper abdomen, respiratory insufficiency, haemoptysis, expectoration of necrotic material, sepsis, tamponade and shock. Chest roentgnogram showed small to massive effusion, basal pneumonitis and cardiomegaly. Seroiogy, liver scans and pneumoperitoncum were diagnostic. Treatment included metrodinazole and emetine, drainage of pleural or pericardial contents, bronchial aspiration etc. Mortality among cases with rupture was 11.4 percent. All others recovered fully.

Safety of fiberoptic broncho alveolar lavage **in evaluation of interstitial lung** disease.

Jeffry Stninpf-et al; Chest; 1981, 80, 3.

281 fiberoptic broncho-alveolar lavage procedures were performed on 119 individuals with interstitial lung disease and 22 normal volunteers and there were no major complications including fever (25 percent) Pneumonia (0.4 percent) bleeding (0.7 percent) and bronchospasm (0.7 percent). These findings suggest that broncho-alveolar lavage for interstitial disease is a safe procedure associated with minor risks.