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The Management of Genito-urinary Tuberculosis in the Special Hospital

PRESIDENT'S ADDRESS

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WITH 92 empty beds in East Fortune Hospital at Edinburgh, I am presenting a series of cases of genito-urinary tuberculosis which have been observed, treated and followed during the past five years, and which I believe may be the last regional series of statistical significance.

In any survey of focal tuberculosis, it is necessary to recall that the four stages in the evolution of the disease are: (1) the period of incubation, (2) the period of invasion, (3) the period of visceral spread and (4) the period of advanced caseo-cavernous pulmonary tuberculosis.

In the management of genito-urinary tuberculosis, tubercle bacilluria must be regarded as evidence that the second invasive stage of tuberculosis has been successful and that the third stage of visceral spread has begun. Nevertheless, adequate measures taken to build up the patient's resistance, and antibiotic or other therapy directed towards such tuberculous lesions as are demonstrable, may lead to permanent cessation of tubercle bacilluria and to the return of the patient to health and strength. Frank renal tuberculosis following tubercle bacilluria occurs in a very low percentage of patients. Therapeutic measures for the treatment of bacilluria should be as intensive and prolonged as for the treatment of any other clinically recognizable focus of tuberculous infection.

In an earlier series (1935–1945) of 50 cases of genito-urinary tuberculosis in the male, 20% suffered from a lesion which clinically was limited to the genital tract, and few, if any, of those cases would have been recognized had there been no involvement of the epididymis. In order of frequency, clinical genital tuberculosis was recognized (1) in the epididymis (100% of cases), (2) in the seminal vesicles (75%) and (3) in the prostate (17·8%). However, these figures were at variance with those reported elsewhere. Moore (1937) made an autopsy study of the genital tract in 20 cases of tuberculous prostatitis and found vesicular lesions in only 15%. He believed that in tuberculous disease of the prostate the lesions were blood-borne because they were distributed in the peripheral zones of the prostate, whereas a urethral spread by contiguity produced lesions close to the lumen of the prostatic urethra. In an autopsy study of 62 cases of genital tuberculosis, Menville and Priestley (1938) found renal and prostatic tuberculosis closely associated. At the same time they noted that the epididymis was frequently involved whereas the prostate remained normal. Hammond (1941) stressed the difficulties in attempting to assess the pathogenesis and mode of spread in genital tuberculosis. However, it should not be forgotten that the testis and epididymis have a generous blood supply through the spermatic artery and the artery to the vas deferens, the one from the aorta and the other from the internal iliac through its inferior vesical branch. Similarly the prostate, seminal vesicles and ampulla of the vas deferens are all supplied by the inferior vesical and middle rectal branches of the internal iliac artery. The close relationship of these structures to one another in the median line in front of the rectum, and the inter-communications in the lymphatic drainage as well as the intraluminal connexions through the ducts, provide alternative routes for the spread of infection in the genital tract once a tuberculous focus has become established and activated. Thus tuberculosis may (1) occur in the prostate as a peripheral lesion, (2) ascend from the posterior urethra via the ejaculatory duct to the vesicles and prostate, or by way of the vas to the epididymis, (3) descend from

the epididymis via the vas to the vesicles and prostate and by the ejaculatory ducts to the urethra.

Coincidence of renal and genital lesions is relatively common in genito-urinary tuberculosis. Although infection may spread within the genital system, or within the urinary system or both via the lumina of their ducts, that is, by direct extension, the co-existence of the disease may not be due entirely to direct extension from one to the other, as is sometimes stated. Coincidence of renal and genital lesions should be regarded as possible evidence of independent yet co-existing focal manifestations of the disease. The abundant arterial supply to the genital tract, the frequency of genital tuberculosis in the young adult, and the anatomical distribution of certain of the lesions would seem to favour blood-borne implantations.

Before the last war I believed that the only treatment for renal tuberculosis was nephrectomy in conjunction with sanatorium life for six months or a year. I considered that surgical removal of the tuberculous kidney was necessary to avoid the continued reinfection of the bladder below, and that when the ureter was involved, it should be removed along with the kidney. In a five-year follow-up of 30 cases of renal tuberculosis treated along these lines between 1935 and 1940 (Band, 1942), I had found that the operation deaths from nephrectomy were negligible and that the recovery rate was good as regarded the immediate future. But as the follow-up continued over a longer period, recurrence of bladder ulceration, reactivation of extra-urinary foci or persistent contracture of the bladder and consequent backward pressure on the remaining kidney began to take their toll. When a complete recovery was taken to mean complete rehabilitation of the patient and a return to employment, I found that the recovery rate of 86·4% in 30 nephrectomized patients was reduced to 50%, and that the ultimate mortality rate was 13·6%. When to the series of 30 cases of unilateral renal tuberculosis which were subjected to nephrectomy were added 11 cases of bilateral renal tuberculosis, the complete recovery rate fell to 36·5%, cases with residual disability amounted to 39%, and the late mortality rose to 24·5%. Of patients with bilateral renal tuberculosis, over 50% died within five years, even when treated under sanatorium conditions.

These pre-war figures were discouraging, but during the past five years, from 1950 to 1955, I have been able to observe the effects of chemotherapy in a series of 106 cases treated in East Fortune Hospital and subsequently followed up by re-examination at regular intervals.

Analysis of Cases

Sex incidence.—Of the 106 patients 74 were males and 32 females. Of the male patients 10 suffered from genital tuberculosis without associated urinary lesions; 40 males as compared with 21 females suffered from unilateral renal tuberculosis; and 12 males were, as compared with 7 females, admitted with the subclinical lesions of tubercle bacilluria. In my earlier investigation into the incidence of tubercle bacilluria I had noted that of 158 males examined in a sanatorium population suffering from extra-urogenital tuberculosis, 12·6% exhibited tubercle bacilluria, whereas of 142 females examined, 30·9% exhibited tubercle bacilluria. The recovery rate from tubercle bacilluria in both sexes was the same (23·4%) and the ultimate mortality rate in those patients with extra-urogenital tuberculosis and with tubercle bacilluria during those years (1930–1940) was high in both sexes (59%).

Age.—In the present series, the highest incidence of urinary tuberculosis occurred in the third, fourth and fifth decades in males and in the fourth decade in females (Table I). This is similar to the age distribution of pulmonary tuberculosis in the two sexes.

Table I.—Age Distribution

Decade	Males	Females	Total
10–20	5	3	8
20–30	20	7	27
30–40	17	14	31
40–50	25	5	30
50+	7	3	10
	74	32	106

Frequency of micturition as a symptom was taken as a frequency greater than three-hourly during the day and rising more than once at night. On admission, 58, or just over half the total number of patients, had frequency, and in all pus cells were present in the mid-stream or catheter specimen of urine. On discharge, 70% were symptom-free.

The total period of *bed-rest and hospitalization* is shown in Fig. 1 and it will be seen that most patients were given complete bed-rest for three to six months and remained in hospital for three to nine months. An adequate number of hours of rest in bed each day is an essential part of the hospital treatment, and the transition from complete bed-rest to a more active

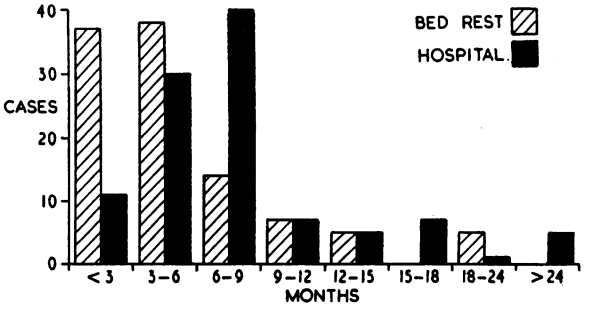


FIG. 1.—Total period of bed-rest and of hospitalization. Two patients transferred as bed-patients.

share in the social activities of the hospital is carefully graded. Any delay before admission to hospital has been due to delay on the part of the patient before medical examination is sought, and not to a waiting list.

The *operative interventions* undertaken in the entire series are shown in Table II.

TABLE II.—OPERATIVE TREATMENT

Nephrectomy	22
Nephro-ureterectomy	32
Partial nephrectomy	1
Uretero-colic anastomosis	4
Orchidectomy	2
Epididymectomy	1
Cordotomy	1
Excision of hydrocele	1
Cutaneous ureterostomy	1

In the *distribution of lesions* (Table III), 51 patients, or 53·6%, with renal lesions had associated cystitis.

TABLE III.—DISTRIBUTION OF LESIONS

	Males	Females	Total
Bacilluria	12	7	19
Restricted unilateral	6	2	8
Widespread unilateral	34	19	53
Bilateral	8	2	10
Residual cystitis	4	1	5
Renal with associated genital lesions ...	40	—	40
Renal with associated cystitis			51

Classification.—We have now adopted the following modification of the categories described by Jacobs and Borthwick (1950):

(1) Tubercle bacilluria without pyelographic evidence of calyceal ulceration.
(2) Restricted unilateral renal tuberculosis.
(3) Widespread unilateral renal tuberculosis.
(4) Bilateral renal tuberculosis.
(5) Persistent or residual tuberculous cystitis.
(6) Genital tuberculosis.

A follow-up system has been adopted which includes, for each category, the duration and variety of chemotherapy used, the duration of bed-rest and hospitalization, the length of time required to achieve conversion of the urine, the relief of symptoms of frequency, as well as the total period of treatment and observation required before the patient can return to employment.

(1) *Bacilluria.*—The total number of patients with bacilluria and no detectable renal lesion was 19. Of these, 11 of the 12 male patients suffered from associated genital lesions. About 25% suffered from a mild frequency of micturition. The time for conversion was relatively short (Fig. 2), and followed the pattern of the entire series. Similarly the delay before return to work after discharge followed the same general trend. The majority in this group had bed-rest for over three months and were in hospital for six to nine months. The duration of chemotherapy followed the general pattern and was continued for several months. Of the 11 patients with associated genital lesions, orchidectomy was carried out in 2 because of

widespread tuberculous epididymo-orchitis, and in a third patient hydrocelectomy was undertaken, though on histological examination of the thickened hydrocele sac evidence of tubercle was not found and at operation the testis and epididymis appeared normal.

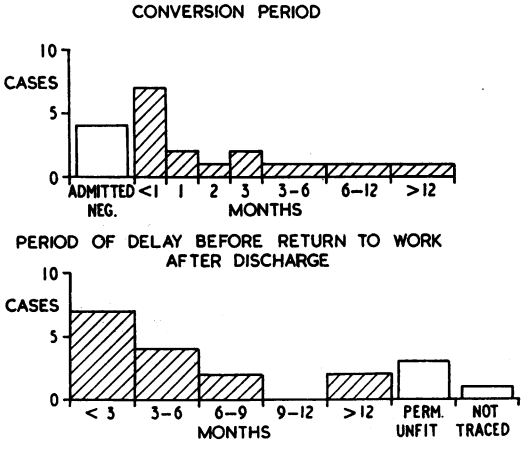


FIG. 2.—*Bacilluria:*

Total number of cases	19
Frequency present on admission	5
on discharge	1
Associated genital lesions	11

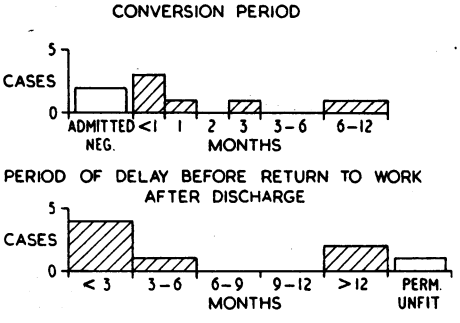


FIG. 3.—*Restricted Unilateral:*

Total number of cases	8
Frequency present on admission	3
on discharge	1
Associated genital lesions	3
Associated cystitis	3

(2) *Restricted unilateral renal tuberculosis.*—In this group there was a total of 8 patients. In 3 there was associated cystitis, and in 3 males there were associated genital lesions. The 3 patients with associated cystitis suffered from frequency on admission. In this small group, 6 of the 8 patients had conversion of the urine within a month of admission, and 5 of the 8 patients were able to return to work within six months of leaving hospital (Fig. 3). The duration of total bed-rest and hospitalization followed much the same pattern as in the whole series. Similarly, chemotherapy was given for a period of nine months to a year, including the continued administration of Pasinah for a short time after discharge from hospital. Nephrectomy was carried out in 2 patients and nephro-ureterectomy in one.

(3) *Widespread unilateral renal tuberculosis.*—This group of 53 patients was the largest in the series. Of these, 38, or 71·7%, had associated cystitis, and 19 of the 34 males (56%) suffered from associated genital lesions. Those with frequency on admission had cystoscopic evidence of tuberculous cystitis, and on discharge 9, or 24·3%, had some residual frequency. Although the disease was unilateral and widespread, the conversion period under chemotherapy was most satisfactory, and 46 of the 53 (86·8%) achieved conversion of the urine within three months. Of the 53 patients, 40, or 75·5%, were able to return to work less than twelve months after discharge from hospital (Fig. 4). Chemotherapy was used for a longer

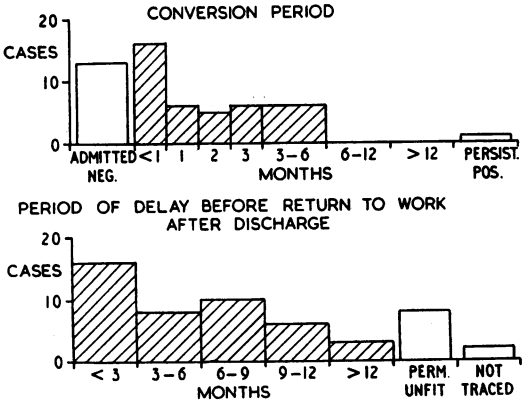


FIG. 4.—*Widespread Unilateral:*

Total number of cases	53
Frequency present on admission	37
on discharge	9
Associated genital lesions	19
Associated cystitis	38

period in this group, and 40 patients, or 75·5%, received such treatment for six to twelve months. In nearly one-third of these patients, chemotherapy was continued for a few months following discharge from hospital. The operation of choice was nephro-ureterectomy with two incisions, the first a sub-umbilical mid-line approach to mobilize the lower third of the ureter extraperitoneally and to divide it just above the bladder; thereafter the patient was turned on his side and the kidney and ureter were removed through a lumbar approach: the last rib was usually excised. Nephro-ureterectomy was performed in 27 patients, nephrectomy in 17, and in 2 a subsequent uretero-colic anastomosis became necessary. Operation was not undertaken when symptoms of genito-urinary tuberculosis were relieved by auto-nephrectomy after calcification, and when the extra-urogenital lesions were active.

(4) *Bilateral renal tuberculosis.*—This group included only 10 patients. Unfortunately the bilateral lesions occurred in a young age group, the majority males. In these young men associated genital lesions were common and in nearly all accompanied cystitis. All achieved conversion of the urine in six months, and 6 of the 10 patients were placed in some form of employment (Fig. 5). In 8 patients, complete bed-rest was continued for from six to nine

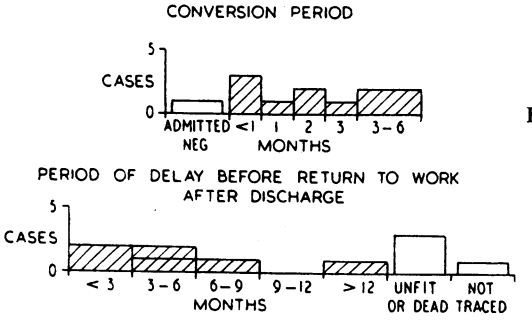


FIG. 5.—*Bilateral:*

Total number of cases	10
Frequency present on admission	8
on discharge	5
Associated genital lesions	6
Associated cystitis	8

months, and in 6 patients hospitalization was continued for as long as one to two years. In 8 patients chemotherapy was administered for nearly a year. In the operative treatment of these patients, the more seriously diseased kidney was removed in 7 cases. In 3 patients a persistently contracted bladder led to repercussions on the remaining kidney. Uretero-colic anastomosis of the remaining ureter was done in 2, and in the third patient, cutaneous ureterostomy, because of the extensive ureteric disease.

(5) *Residual cystitis.*—5 patients previously treated elsewhere for genito-urinary tuberculosis were admitted on account of reversion of the urine and recurrence of tuberculous ulceration of the bladder. 4 of the 5 patients again achieved conversion of the urine and a negative culture for tubercle bacilli. 3 patients were able to return to a modified form of employment within a year of discharge from hospital (Fig. 6). All had complete bed-rest for

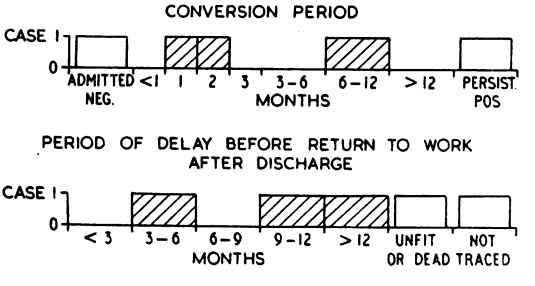


FIG. 6.—*Residual Cystitis:*

Total number of cases	5
Frequency present on admission	4
on discharge	1
Associated genital lesions	2

three months or less, and 4 were discharged in six months. The combination of bed-rest and chemotherapy was the treatment of the greatest value, and it was not considered advisable to attempt to apply diathermy to the solitary residual vesical ulcer. In 2 patients, bladder instillations of 5% isoniazid solution seemed to give some relief. Ureterocolic anastomosis for the remaining ureter was necessary in one case.

Still in hospital under treatment and therefore not included in this series is one patient with residual cystitis and stricture at the lower end of the remaining ureter for whom uretero-ileostomy has been performed with success. A grossly dilated ureter and kidney have shrunk to normal dimensions and the intravenous pyelograms give evidence of good concentration. The blood urea has fallen to 50 mg. % from a figure which at one time reached 150 mg. %.

(6) *Genital tuberculosis in the male.*—Of all male cases reviewed, there were combined lesions in 41, or 55·4%, as compared with an incidence of 51·3% in the earlier series.* In 10, or 13·5%, the lesion was confined to the genital organs. In 23 cases, or 31%, the lesion was confined to the urinary tract. These figures are comparable to those I had observed before chemotherapy was available, and the slight alterations in the percentages may be accounted for by more accurate personal observation and investigation. Furthermore, in the present series all examinations, cystoscopic, pyelographic or bimanual, have been made under Pentothal anæsthesia. In my earlier series bimanual examination under anæsthesia had not been carried out in every case, and involvement of the prostate, with irregularity in its consistence, had not always been detected.

In the present series, whereas involvement of the vesicle was noted in 64% of cases which was comparable with the incidence of tuberculous seminal vesiculitis in the earlier group, my records now show a marked rise in the incidence of tuberculous prostatitis, that is, 70% as compared with 17·8% in the earlier group observed. There was a relatively high incidence of a combination of genital lesions (34 patients, or 68%) (Table IV). In a certain number,

TABLE IV.—GENITAL TUBERCULOSIS IN THE MALE: DISTRIBUTION OF LESIONS IN 50 CASES

	Cases	Per cent
Epididymis	35 (8)	70 (16)
Seminal vesicle	32 (2)	64 (4)
Prostate	35 (6)	70 (12)
Combined genital lesions ...	34	68

(Figures in brackets indicate sole lesion.)

the pelvic genitalia, vesicle or prostate were alone involved. That the prostate and vesicle alone should be involved in 8 patients, or 16%, provides evidence of the possibility of a primary lesion in the pelvic genitalia in genito-urinary tuberculosis. 16, or 32%, of patients with genital tuberculosis suffered from tuberculous epididymitis with sinus formation in the scrotum, and I would like to stress the fact that out of 50 cases of urogenital tuberculosis in which the genitalia were involved, orchidectomy was considered necessary in only 2, and epididymectomy in only 1 patient. There can be no doubt that the scrotal lesion with sinus formation will heal under conservative measures alone. The response to chemotherapy, bed-rest with a scrotal support, and aspiration when necessary, is quite dramatic. In 34 of the patients (68%) there was conversion of the urine or of the discharge from the scrotal sinus in one month or less, and of all the patients with urogenital lesions, only one remained with a positive culture after treatment for six months (Fig. 7). This would appear to provide further support to the view that the treatment of genital tuberculosis should primarily be comparable to that of tuberculous pulmonary or osseous lesions.

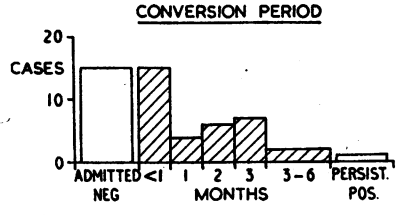
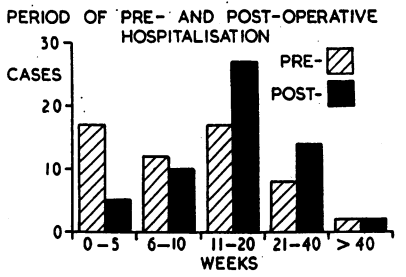


FIG. 7.—*Genital Tuberculosis in the Male:*
Genital without associated urinary lesions 10
Genital with sinus 16
Genital without sinus 34

TREATMENT

After admission to hospital, chemotherapy was given for a number of weeks in the period of pre-operative treatment (Fig. 8). During this interval when treatment was confined to bed-rest and chemotherapy, it was found that the majority of patients achieved conversion of the urine, and that culture for tubercle bacilli became negative. Thus in 90 patients there was conversion of the urine within three months of their admission to hospital (Fig. 9). The duration of post-operative hospitalization and of chemotherapy largely depended on the length of time it was considered necessary for the period of preparation, and this in turn on the degree of constitutional disturbance or the multiplicity of lesions. After discharge from hospital, patients were called for follow-up examinations at three-monthly intervals and were personally interviewed and examined by the consulting physician and surgeon together. A fresh specimen of urine was submitted for culture for tubercle bacilli, and at intervals the chest was re-X-rayed and a follow-up intravenous pyelogram carried out. Cystoscopy or retrograde pyelography was not repeated at the follow-up examination unless indicated by an alteration in the symptomatology, by pyuria, or by reversion of the urine to a positive culture.



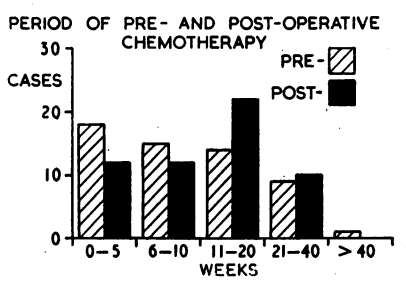
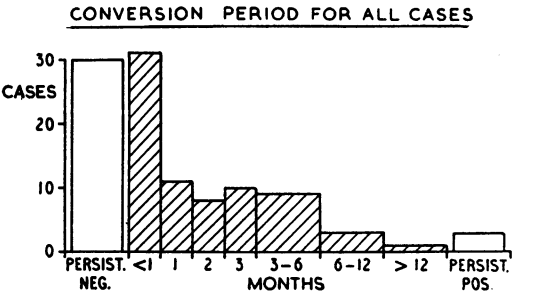


FIG. 8.



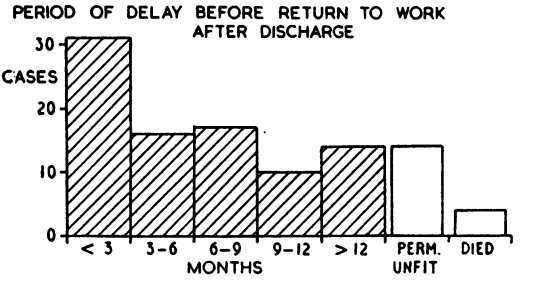


FIG. 9.

A closer collaboration between physician and surgeon in the treatment of genito-urinary tuberculosis has led to an increasingly frequent recognition of the presence of extra-urogenital tuberculous lesions, and in the present series these were found in 94% of cases. Patients with urogenital tuberculosis were accordingly notified as such and contacts were examined by the tuberculosis physician and his staff. It was considered advisable to inform the patient quite frankly that he was suffering from tuberculosis, and that he would ultimately benefit from the long-term follow-up which applied to all cases of tuberculosis, and so, from the beginning, patients were given training which was identical with that provided for the respiratory cases. They were impressed with the need for strict personal hygiene, and instructed in the handling of fomites and the observation of rest hours. There was a planned schedule of treatment which began with complete bed-rest, chemotherapy and operative intervention when necessary, and ended with rehabilitation and after-care. It was felt that patients with genito-urinary tuberculosis should be brought within the rehabilitation schemes already in existence for patients with respiratory tuberculosis, and should thereafter be helped to secure suitable employment without undue delay. In order to achieve this ideal scheme, arrangements were made to admit to East Fortune Hospital with equal priority those suffering from respiratory or genito-urinary disease. For the last four years, since there was no waiting list, immediate admission to hospital of all cases of genito-urinary tuberculosis became possible. Fortnightly supervisory, cystoscopic, or operative sessions were arranged, when the merits of individual cases could be discussed between physician and surgeon. Cases of urogenital tuberculosis were admitted to wards where open cases of respiratory tuberculosis were not normally treated, and it was considered that this segregation had considerable psychological value. The services of the almoner, Ministry of Labour officers, teachers and Local Authority nurses were made available to all. Social, economic and rehabilitation problems could be discussed and the patients were subjected to the same regular review and consultation with the tuberculosis physician as were the respiratory patients. They were also accustomed to the hours of rest and exercise which conformed with the general pattern of the hospital regimen. They entered into the social and recreational facilities of the hospital and were given week-end leave at three-monthly intervals.

Chemotherapy.—An increasing number of surgeons have now accepted the plea that chemotherapy should be administered not in a haphazard fashion but according to a definite plan carried out under sanatorium conditions. Five years ago, when the present series of cases was first observed, the chemotherapy consisted of streptomycin 1 gram with PAS 10 grams, daily for about thirty days, followed after an interval of a few weeks by another course, and later a terminal course of PAS alone. A year later, the superiority of uninterrupted chemotherapy was established, and moreover the problem of drug resistance was being met. Throughout 1952 the use of streptomycin was limited to 1 gram every third day, and the intensive course restricted to a few weeks. In the same year isoniazid became available and it was reported by the Medical Research Council that streptomycin used

intermittently was not entirely safe because of the development of resistance. Throughout 1953 continuous combined therapy with all three drugs—PAS, streptomycin and isoniazid—was used during the period of hospitalization. In patients older than 45 years, dihydrostreptomycin replaced streptomycin to restrict the incidence of vestibular damage. On the whole, however, it may be said that with these drugs chemotherapy has been remarkably free from toxic effects. Following the work of Dick (1954) who found that isoniazid-treated lesions appeared to heal by recapillarization whereas streptomycin-treated lesions apparently healed with a greater degree of fibrosis, PAS and isoniazid in full dosage have proved an effective chemotherapeutic combination, and PH(Pasinah), has been the drug combination of choice for continued use throughout the period of hospitalization and afterwards on discharge when the patient returns to his own home. Streptomycin, or dihydrostreptomycin, 1 gram daily, has been used without additional cover one week before and two weeks after the operative intervention.

We have considered it advisable to maintain out-patient chemotherapy for a varying period of months after discharge from hospital. This is done to cover the time during which a patient freed from the discipline of in-patient treatment must use initiative and restraint as a convalescent, in order to make progress towards rehabilitation. At this stage retrogression may occur, with reversion of the urine to a positive culture, if there is too much freedom and neglect of the regimen imposed in hospital. Pasinah, in the form of the combined cachet, is readily taken by the patient, and, as already stated, has latterly been the drug of choice for post-operative chemotherapy and follow-up domiciliary supervision by the patient's own doctor.

To particularize, the chemotherapeutic programme latterly has been as follows:

(1) PAS 16–20 grams and isoniazid 200–300 mg. daily, beginning at diagnosis or after the first group of three early morning specimens of urine have been submitted for culture.

(2) Streptomycin or dihydrostreptomycin 1 gram daily for seven days before and fourteen days after operation.

(3) Penicillin crystalline $\frac{1}{2}$ mega unit b.d. on day of operation and for six days thereafter.

(4) Vitamins A, D and C added to diet.

(5) Cachets of PAS and INAH combined (as Pasinah or Pycamisan) to provide a full dosage of 15 grams PAS and 200 mg. INAH. This treatment is continued for three months or longer, even up to one year, when there is evidence of chronic disease, genital or elsewhere.

Results

The clinical results of the past five years as compared with those of 1935–1940 have been amazingly good, and as far as we can judge they appear to be maintained. Relapses have been few, and attendance at the follow-up examinations has been almost 100%. When the patient attending at a follow-up clinic meets both surgeon and tuberculosis physician, all that is required of him can be dealt with at one session, and thus, by arrangement with the Tuberculosis Officer, the inconvenience of attendance at two clinics is avoided.

It has been found that these patients have appreciated the frank disclosure that they have become victims to tuberculosis, and that a hospital service is available which will provide all they require for treatment. Moreover, the instruction given to them by a tuberculosis physician and the talks they have had with almoners, Ministry of Labour officers and others, have assured them that while they are incapacitated it is possible for the family to continue at home, and that direction, or if necessary training, will be provided to ensure their return to suitable employment. They have accepted with confidence the prospects of a long-term course of treatment in which operative intervention looms no greater than a therapeutic incident.

We have been most impressed with the high percentage (83%) of our patients who have been able to return to employment within a reasonable interval after their discharge from hospital. The late mortality has fallen to 3·8%, and the number remaining permanently unfit reduced to 13·2%. When these figures are compared with those (24·5% and 39% respectively) of the smaller series of 41 cases which were personally followed up between 1935 and 1940, the contrast is remarkable, and a tribute to the efficacy of chemotherapy in tuberculosis.

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