which he will best be able to demonstrate the best medicine to his students: but also that to the teaching process itself, to conferences and evaluation, he is prepared to give proportionate time and attention. I also believe that, so that he can give the time and application required, he will, sooner or later, have to be rewarded financially for doing so. Our faculties themselves have learned the necessity of this in other subjects: it is no less necessary in relation to general practice.

I believe that the medical schools are interested only in the attainment by the general practitioner of the sort of standards, interests, and achievements for which this College itself was originally created. Our topic today is of great relevance and very much alive at the present time, I am sure. The active thinking of the College's Committee on Undergraduate Education under Dr. Tweddell's leadership, following the fine work done by Dr. Murray Stalker in the first years of the new Preceptorship schemes in more than one school; the munificent prizes offered to medical students by Messrs. Bengers through the College—all these are witness to a lively interest.

If the general practitioner is to retain his place in the medical hierarchy, to improve upon it, and also to remain that cornerstone of medicine as the members of this College see him, then he must decide upon what is his main and principal role: it is from that role that he will be able to give so much in the training of medical students. I believe that a majority of the members of this College would be able to contribute something of substantial value to the training of medical students, if they were given the opportunity to do so.

There is no use whatever in our saying as a College (and here I say "our" with pride since I was admitted to membership a few months ago) that we must be involved in the teaching of medical students, unless we know what we have to offer: unless our role is clearly defined in our own minds; unless we are convinced and can convince the medical schools that what we have to offer is of value to the potential doctor.

We shall never as a College attain any place in the recognition of the medical faculties simply because we feel we ought to, because we feel that it is "owed to us", because of the need to preserve the prestige of general practice or because we have "demanded" Chairs of General Practice to put alongside those of Medicine, Surgery, Obstetrics, and the rest.

If, however, we successfully perform that self-examination which is so essential to all professional groups in society, and come out from it with a certain degree of definition of our role in the future; if we accept that the greatest challenges of present-day medicine are ours; if we are concerned so to improve our understanding of the early diagnosis, the prompt treatment and good management of disease that prevention becomes much more of a reality than is today the case; if we accept responsibility for the overwhelming, and fascinating, and often new problems that exist in the social and psychological areas of medicine; then not only shall we promote that aim of the College of General Practice which directs us to improve the prestige and standing of the general practitioner, but we shall also be sure that the general practitioner has indeed a worthy contribution to make to medical education.

RESULTS OF THE TREATMENT OF TUBERCULOSIS BEFORE AND SINCE THE INTRODUCTION OF CHEMOTHERAPY*

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THE PURPOSE of this report is to indicate briefly the results of modern treatment of tuberculosis compared with the results before the introduction of chemotherapy. Tuberculosis of the lungs, pleura, bones, kidneys, meninges and the miliary type will be considered.

There has been a striking improvement in the outcome of treatment, when chemotherapy is properly administered. If, however, patients with active disease have received inadequate chemotherapy, the cure rate will be lower and the relapse rate higher. All new cases of active tuberculosis, irrespective of the site, should receive combined continuous chemotherapy for about 18 months or longer. Bed rest is indicated during the early active phase and, in certain selected cases, surgical measures are also necessary.

Three antimicrobial agents have proved to be of great value, namely isoniazid (INH), streptomycin (SM) and para-aminosalicylic acid (PAS). It is generally agreed that these drugs should not be prescribed alone, but should be given in a combination of at least two, or all three may be given concurrently. If any one of them alone is prescribed to a patient with open cavitary disease, the tubercle bacilli in the host rapidly develop resistance to the drug, so that it is no longer effective in combating

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*From the Toronto Hospital for Tuberculosis, Weston, Ontario.
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the tuberculous infection. If, on the other hand, two or all three of these antimicrobial agents are given concurrently, the development of resistance by the tubercle bacilli to the drugs administered is markedly delayed, and they continue to be effective in combating the infection for a much longer period.

What combination of these three drugs has the greatest therapeutic effect? Although there is not much difference in the effect of the different combinations, it is generally agreed that isoniazid should be one of the drugs given. It has established itself as the most powerful agent in the treatment of tuberculosis. In other words, the combination of streptomycin and PAS is slightly less effective than is isoniazid and PAS, or isoniazid and streptomycin, or all three. For the average case, receiving all three drugs concurrently, the dose of isoniazid is 300 mg. daily, of PAS 12 g. daily and of streptomycin 1 g. twice weekly. Larger doses are indicated for the more acute severe infections. Treatment should be given continuously for about 18 months.

In assessing the results of the modern treatment of such a chronic disease as tuberculosis, we are handicapped by the fact that adequate chemotherapy, as we know it, has been in use for little more than seven years – insufficient time for an adequate long-term follow-up. However, since relapses usually occur within a period of five years, the following results should be a fair indication of the ultimate prognosis.

PULMONARY TUBERCULOSIS

Before the results of treatment are described, the National Tuberculosis Association definitions of certain terms which are used in this report should be recalled. In reference to the *extent* of the pulmonary disease, *minimal tuberculosis* indicates that there is no evidence of cavitation and that the total extent of the lung involved is not greater than the equivalent of the lung volume above the level of the second chondro-sternal junction on one side. In *moderately advanced* disease, cavities if present must not be greater than 4 cm. in diameter and the total extent of lung involvement must not be greater than the equivalent of one lung. *Far advanced* tuberculosis indicates any case where the extent is greater than the above. A case may be described as *inactive* if the following conditions are present for at least a six-month period: repeated examinations of the sputum or fasting gastric contents are negative for tubercle bacilli on culture, the chest radiographs have remained stable in appearance, and there is no evidence of cavitation.

Before antimicrobial therapy was available, the mortality rate of active pulmonary tuberculosis was estimated to range from 5%,[1] in cases of minimal extent, to 20%,[2] if the disease was moderately advanced, and to 70%,[3] if far advanced. The majority of patients with persistent cavitation in their lungs died within five years.

TABLE I.—MORTALITY RATE OF ACTIVE PULMONARY TUBERCULOSIS.

Chemotherapy	*Reference*	*Period treated*	*Length of observation*	*No. of cases*	*Extent of disease*	*Death rate from tuberculosis: percentage of cases*
None	Trudeau Sanatorium[1]	Before chemotherapy	20 years	589	Minimal	5%
	Herman Biggs Hosp.[2]		10 years	211	Mod. adv.	20%
	Herman Biggs Hosp.[3]		10 years	223	Far adv.	70%
Adequate	Toronto Hospital for Tuberculosis	1953	5 years	25	Minimal	0
				61	Mod. adv.	0
				54	Far adv.	11%
				140	All cases	4%
Adequate	London Hospital[4]	1952-1956	1 to 5 years	75	All types	4%
Adequate	Vet. Admin., U.S.A.[5]	1950-1954	2 to 7 years	550	All types	5%
Many inadequate	Edinburgh Hospital[6]	1953	3 to 4 years	305	All types	9%

Modern treatment has resulted in a striking reduction in the mortality rate and the relapse rate. At the Toronto Hospital for Tuberculosis we have analyzed the results of treatment of all patients with active pulmonary tuberculosis who were admitted to that hospital in 1953, had sputum positive for tubercle bacilli, had not been given antimicrobial therapy before, and received streptomycin, isoniazid and PAS continuously for at least nine months. The average duration of triple drug therapy given to the 140 patients in the series was 17 months. In Table I is shown the mortality rate in series of cases treated before the introduction of chemotherapy as compared with the rate in our group of cases and other comparable series. With adequate chemotherapy, and resectional surgery where indicated, the mortality was strikingly reduced and almost all the deaths were in the far advanced group.

As indicated in Table II, most of our patients ceased to have positive sputum within six months of starting chemotherapy, and all were sputum-negative in 18 months. Others have reported similar results on similar regimens.

The proportion of our series of 140 patients who attained an inactive status at intervals of one, two

TABLE II.—TORONTO HOSPITAL FOR TUBERCULOSIS, 1953: SPUTUM CONVERSION RATE IN 138 PATIENTS RECEIVING ISONIAZID, STREPTOMYCIN AND PAS FOR NINE MONTHS OR LONGER.

Interval since starting chemotherapy in months	*Percentage with positive sputum*
0	100%
3	27%
6	8%
9	4%
12	2%
18	0

NOTE: An additional two patients, not included in this series, died of tuberculosis within six weeks of starting chemotherapy.

and three years after starting chemotherapy is listed in Table III. Some form of resectional surgery was necessary in 22% of the group. It is evident that if cases of minimal or moderately advanced disease are treated as above, one can be confident that the process will in almost all cases become inactive within two years. With far advanced disease, however, a favourable outcome is less certain.

We wish to sound a note of warning in reference to patients with pulmonary tuberculosis who have had prolonged chemotherapy, whose sputum has become negative and who are apparently well, but in whom a radiograph reveals that the cavity in the lung is still open. These are the so-called "open negative" cases and since a cavity is still present they are not to be classed as inactive. In a series of 123 such cases reported by Raleigh[8] of the Veterans Administration, 31% "relapsed" at the end of one year and 50% "relapsed" after 3½ years. In other words, the presence of a persistent cavity in the lung is always a great menace to the patient, whether he has had chemotherapy or not. The presence of a cavity in the lung that has failed to close after six to eight months of chemotherapy is the cardinal indication for surgical resection.

In the 1953 series of 140 patients at the Toronto Hospital for Tuberculosis described above, pulmonary resection was performed in 31 cases or 22% of the group. The resection was segmental in 20 cases; a lobectomy was performed in 10 cases and a pneumonectomy in one case. All these surgically treated cases became inactive; there were no deaths, but one relapse occurred.

Since 1953, artificial pneumothorax has been abandoned as a method of treatment, and a thoracoplasty is rarely performed. It is interesting also that the proportion of patients requiring major pulmonary surgery has decreased to about 12%.

TABLE III.—RESULTS OF TREATMENT OF 140 PATIENTS WITH ACTIVE PULMONARY TUBERCULOSIS AND POSITIVE SPUTUM WHO RECEIVED ISONIAZID, STREPTOMYCIN AND PAS FOR NINE MONTHS OR LONGER (AVERAGE 17 MONTHS)* ADMITTED TO TORONTO HOSPITAL FOR TUBERCULOSIS IN 1953.

Extent of disease	*Number of cases*	*Number of deaths from tuberculosis*	*Percentage with inactive tuberculosis at intervals after starting chemotherapy*		
			1 year	*2 years*	*3 years*
Minimal	25	0	36%	100%	100%
Mod. advanced	61	0	31%	95%	97%
Far advanced	54	6	2%	69%	81%

* NOTE: Pulmonary resection was necessary in 22% of the above series.

Having attained an inactive status, what proportion of cases will subsequently relapse? In an attempt to answer this question, data on series of patients studied before and after the introduction of chemotherapy are listed in Table IV. The striking reduction in the relapse rate from about 30% to 4% is notable.

TUBERCULOUS PLEURISY WITH EFFUSION

So-called primary tuberculous pleurisy with effusion has been known as a sinister disease.

TABLE IV.
RELAPSE RATE OF PULMONARY TUBERCULOSIS PATIENTS SENT HOME FROM HOSPITAL WITH ARRESTED OR INACTIVE TUBERCULOSIS

Period in hospital	*Hospital*	*No. of cases*	*Chemotherapy*	*Time followed up after discharge*	*Relapse rate*
1947-52	Vet. Adm. Hosp.,[7] Memphis	900	None or inadeq.	3 years	30%
1953-55	Vet. Adm. Hosp.,[7] Memphis		Adequate	3 years	14%
1951-56	Fitzsimons Army[7] Hospital	2500	Adequate	1 to 5 years	4%
1953-54	Toronto Hosp. for Tuberculosis	125	Adequate	2 to 5 years	4%

Although it is apparently a benign process, tuberculous lesions developed in the lungs or elsewhere in about 25% of patients during the subsequent five years, in the absence of chemotherapy. When, however, chemotherapy is given for about one year after the onset of the effusion, tuberculous complications seldom appear during the follow-up period.

The Veterans Administration of the United States[9] reported a series of 114 patients who were given chemotherapy after the onset of the pleural effusion and were followed up for five years. The incidence of tuberculous complications was 4% during the follow-up period, as compared with 23% in a previous series of 138 patients who did not receive chemotherapy. Others have reported similar findings.

cases of bone and joint tuberculosis admitted to the Toronto Hospital for Tuberculosis in 1945, with the results in those admitted in 1953. The former year was selected because all the patients admitted in 1945 had completed their treatment before the advent of antituberculous drugs. The year 1953 was chosen because most of the patients admitted in that year received adequate chemotherapy.

Follow-up in the two series of cases was excellent. Of the 58 cases admitted in 1945 and the 33 admitted in 1953, all except four have been followed up to 1959 or to death; the remaining four cases were followed up for two to eight years. The mortality rate in the two series is shown in Table V. Sixteen patients (27.5%) in the 1945 group died of tuberculosis; all except one of the deaths occurred within five years of admission. There were no deaths from tuberculosis in the 1953 series.

TABLE V.—MORTALITY RATE OF BONE AND JOINT TUBERCULOSIS, THE TORONTO HOSPITAL FOR TUBERCULOSIS.

Year admitted to hospital	*Number of cases*	*Chemotherapy*	*Death rate (percentage of cases)*		
			Tuberculous	*Non-tuberculous*	*Total*
1945	58	None	27.5%	5.2%	32.7%
1953	33	Adequate in most	0	6%	6%

TUBERCULOSIS OF BONE AND JOINT

Tuberculosis of bones and joints is a manifestation of a disseminated hæmatogenous infection. About 25% of cases have lesions in more than one joint and over 20% have tuberculosis of the genitourinary tract; many also have active pulmonary tuberculosis.

Before the introduction of chemotherapy the mortality rate was about 28% and though excellent results were obtained in the majority of the remainder by rest and surgical fusion, prolonged treatment, stretching into years, was usually necessary.

Adequate chemotherapy has resulted in—

(a) Marked reduction in mortality.

(b) More rapid subsidence of active disease with disappearance of abscesses, closing of sinuses and reduction in joint damage.

(c) Decrease in length of hospital stay, and

(d) Marked reduction in relapse rate.

To illustrate these changes, a comparison has been made between the results of treatment of all

The average duration of immobilization for spinal tuberculosis was reduced from 20 months in the 1945 series to 14 months in 1953, and for tuberculosis of the hip from 27 months to 15 months. Excluding those patients who died before surgery could be applied, an arthrodesis or grafting operation was necessary in 80% of the 1945 series and in just 33% of the 1953 group.

In the 1945 series a relapse occurred in 34.5% of the patients and 60% are well and working now, whereas in the 1953 group just two patients (6%) relapsed, both of whom had inadequate chemotherapy, and 88% are well and working. It is worthy of emphasis that of the 1953 group, 40% have ended up with a wide range of joint movement which has not led to any relapse in the succeeding six years. Before chemotherapy, this could only be achieved in the rare patient who presented with a juxta-articular lesion which could be drained before it ruptured into the joint.

TABLE VI.—TORONTO HOSPITAL FOR TUBERCULOSIS: MORTALITY RATE IN PATIENTS WITH RENAL TUBERCULOSIS EXTRARENAL TUBERCULOSIS ALSO PRESENT IN TWO-THIRDS OF THE CASES.

Chemotherapy	*Period when diagnosed*	*Number of cases*	*Length of follow-up in years*	*Death rate (percentage of cases)*		
				Tuberculous	*Non-tuberculous*	*Total*
None*	1922-36	82	20 to 35	58%	10%	68%
None	1931-47	347	0 to 16	46%	6%	52%
Inadequate, SM or SM-PAS for less than 6 months	1948-49	175	10 to 11	21%	8%	29%
Adequate, INH-PAS-SM for over 1 year	1952-57	163	1 to 7	1%	3%	4%

* Includes cases from The Hospital for Sick Children and Christie Street Hospital.

RENAL TUBERCULOSIS

The prognosis of renal tuberculosis has improved remarkably with chemotherapy. Untreated tuberculosis of the kidney probably never heals, though in some cases its progression may be very slow.

At the Toronto Hospital for Tuberculosis, four groups of cases have been followed up for many years. The mortality rate in the different groups is shown in Table VI. In the first group of 82 patients who had neither chemotherapy nor nephrectomy, 58% died of tuberculosis.[10] In the next group of 347 cases treated by nephrectomy but without chemotherapy, 46% died of tuberculosis. Inadequate chemotherapy in 175 cases led to a moderate reduction of mortality, but in the last group of 163 cases, adequate chemotherapy resulted in a striking reduction in the mortality to 1% and a relapse occurred in only 1% of this group. The renal tuberculosis was bilateral in 32% of cases. The disease is inactive in 98% of the last group. It is possible that more relapses will occur later, since the follow-up period of one to seven years is relatively short.

It should be remembered that renal tuberculosis is hæmatogenous in origin and is associated with tuberculosis at other sites in the body in about two-thirds of the cases. All patients should be admitted to hospital for investigation and for a preliminary period of treatment before returning home to complete their course of chemotherapy, which should be given for 1½ to two years. At the Toronto Hospital for Tuberculosis about 10% of cases require nephrectomy for grossly destroyed or nonfunctioning kidneys. In addition, new surgical techniques have been evolved for the occasional case in which mechanical sequelæ develop during the healing of tuberculosis of the urinary tract; for example, for the relief of progressive hydronephrosis from contracture of the bladder or from ureteral stricture.

MILIARY AND MENINGEAL TUBERCULOSIS

Prior to 1946, before streptomycin began to be used for tuberculous infections, these relatively rare forms of tuberculosis had a mortality rate of almost 100%. It is of interest to note the progressive improvement in the survival rate of miliary and meningeal cases as more potent antimicrobial agents were discovered. For example, in a large series of cases of miliary tuberculosis without meningitis, reported by Williams[11] of the U.S. Veterans Administration, the five-year survival rate when treated by streptomycin only was 52%; when treated by the streptomycin-PAS combination, 80%; and when treated by INH-SM-PAS, 95%. Table VII gives the three-year survival rate in this large series of 772 patients with miliary and/or meningeal disease who received chemotherapy. Moreover, the five-year survival rate is almost as good as the two-year rate, indicating that relapses seldom occur if the patient survives two years.

TABLE VII.—THREE-YEAR SURVIVAL RATE OF PATIENTS WITH MILIARY AND MENINGEAL TUBERCULOSIS, REPORTED BY V.A. AND ARMED FORCES OF U.S.A.[11]

	Three-year survival rate		
Type of disease	*No chemotherapy*	*SM-PAS*	*INH-SM*
Miliary	2%±	80%	95%
Meningeal	0	50%	78%
Miliary and meningeal	0	30%	70%

NOTE: Relapses very rare after the third year; one death from recurrence of meningitis during the fourth and fifth years.

Most of the deaths in this group occur when treatment is started at a late stage, and if patients with meningitis survive this stage, they may be left with permanent disability.

SUMMARY

The results of the treatment of tuberculosis of the lungs, pleura, bones, kidneys and meninges and of miliary tuberculosis have been briefly described. The outcome of modern treatment has been compared with that before the use of chemotherapy. Although the follow-up period is not long enough for final assessment, it is evident that combined continuous administration of isoniazid with PAS or with streptomycin, or all three drugs, for 18 months or longer, has resulted in a striking reduction in the mortality rate and improvement in the relapse rate. When chemotherapy was given for six months or less, the mortality rate and relapse rate were much higher, being not much better than the results observed before chemotherapy was introduced.

We wish to acknowledge our gratitude to Dr. Clare Wicks, medical superintendent, Toronto Hospital for Tuberculosis, for his help in organizing the investigation, and to Professor R. F. Farquharson for helpful comments.

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RÉSUMÉ

Les auteurs décrivent les divers traitements de la tuberculose pulmonaire, pleurale, osseuse, rénale, méningée et miliaire. Les résultats du traitement moderne sont comparés à ceux que l'on obtenait avant l'emploi de la chimiothérapie. Bien que nous ne possédions pas encore le recul suffisant pour une évaluation définitive de cette thgrapie, il est évident que l'administration continue et combinée d'isonazide avec acide para-amino-salicylique ou streptomycin ou de tous les trois ensemble pendant 18 mois ou plus longtemps a amené une réduction frappante du taux de mortalité et une amélioration dans la fréquence des rechutes. Lorsque l'on administrait la chimiothérapie pour six mois ou moins, le taux de mortalité et de rechutes était beaucoup plus élevé que ce nous voyons à l'heure actuelle et à peine meilleur que les taux que nous obtenions dans le passé avant l'introduction de cette thérapeutique médicamenteuse.

REVIEW ARTICLE

SIGNIFICANCE OF HÆMATURIA

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MODERN PHYSICIANS are fully aware of the potential seriousness of hæmaturia and advise patients who have such a condition to undergo prompt and thorough examination. The tragedy that occurs from delayed diagnosis of malignant lesions of the genito-urinary tract can often be ascribed to a patient who either does not seek advice immediately after hæmaturia appears or ignores the counsel of his physician. The public must be made aware of the seriousness of hæmaturia.

Hæmaturia may be of two types: gross and microscopic. It should be clearly understood that this is purely an arbitrary classification and one based only on degree. In any condition in which microscopic hæmaturia may occur, gross hæmaturia also can occur. The presence of more than an occasional red blood cell in several high-power fields of the centrifuged specimen constitutes hæmaturia. Many variables enter into this conclusion, such as the accuracy of the technician, the speed of centrifuging and the specific gravity of the urine. Dilute urine contains fewer erythrocytes than does an equal volume of concentrated urine.

Grossly bloody urine always demands an accurate explanation and should never be treated merely symptomatically. Gross hæmaturia is seldom constant, so that weeks, months, and occasionally even years may elapse between episodes. Gross hæmaturia always means an abnormal or pathological condition. In approximately one-fifth of the cases the bleeding is not associated with pain or other symptoms.

The physician must first determine whether discolouration noticed by the patient was due to blood in the urine. There are several conditions in which foreign substances excreted by the kidney result in discolouration of the urine. These conditions are paroxysmal hæmoglobinuria, march hæmoglobinuria, nocturnal hæmaturia of Marchiafavar, porphyria and ochronosis. Concentration of urine, certain drugs (Pyridium and phenolsulphonphthalein) and some foods (beets) may produce purplish or reddish discolouration of the urine, which may be mistaken for blood. But in such instances red blood cells are not present in the urine. Red cells in the urine specimen are proof of hæmaturia. If it is established that blood has been passed, the source of bleeding must next be determined. Blood in the toilet bowl or on toilet paper may have come from the anus, rectum, or vagina, as well as from the urinary meatus, and these orifices should be inspected for evidence of bleeding. Catheterization is often necessary to obtain an uncontaminated specimen, especially in females. No opportunity should be lost to locate the source of bleeding while the bleeding is sufficient to produce a distinct red colour.

Careful questioning and observation may provide suggestions as to the site of bleeding. Blood which is seen only at the beginning of urination often indicates a urethral origin. If the blood is evenly distributed throughout the act of voiding, the source is usually above the prostate. If blood is seen only at the end of urination, a lesion of the vesical outlet or prostatic urethra is probably the source. The patient should be instructed to void continuously in equal amounts into one after another of the three specimen glasses. Examination is facilitated by comparison of the three specimens. Bright red colour, especially if accompanied by bright red clots, suggests arterial bleeding; a dark red colour with almost black clots usually indicates venous or old bleeding.

A study of other formed elements in the urine may provide a clue to the possible site of hæmaturia. The presence of tubular casts or of a considerable number of epithelial cells of the renal type microscopically would be suggestive of, while the presence of blood casts would point definitely to, hæmorrhage into the renal tubules as the site of origin.

SITES OF ORIGIN OF HÆMATURIA

There are three main possible sites of origin of hæmaturia: lesions occurring as a part of systemic disease, lesions in organs adjacent to the genito-urinary tract, and lesions in the genito-urinary tract itself. In some instances, hæmaturia may be

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