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# MEDICAL JOURNAL

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### MESSAGE FROM THE DEAN

IT is a great pleasure for me to congratulate the Medical Journal on the conclusion of twenty years of continuous publication, and to express the hope that it will be possible for it to continue publication for many years to come.

The successful publication of a Medical Journal entirely under the control of the undergraduate body of the Medical School has many potentialities in an educational way to the students themselves, and also to its readers outside the School. The first essential, of course, is that the Journal should be on a sound financial basis and to accomplish this it would seem necessary for it to be of such quality that it would have appeal not only to the student but to the medical alumni, practitioners and graduates of other schools. It would seem to me that if a formula could be found to raise the paid subscription to the Journal that your financial problems would thereby be largely solved.

To be of educational value to the student body there should be a considerable increase in the number of students taking part editorially in the work of the Journal. Otherwise, only a few are going to profit from the standpoint of learning how to write scientific or clinical articles for publication. While it is to be preferred that as much copy as possible be prepared by undergraduates, it occurs to me that a great deal of assistance might be had from the body of graduate students at this School which now numbers something over sixty.

The continuation of the policy of publishing as many as possible of the manuscripts prepared by the guest lecturers for the Dr. F. R. Eccles Memorial Medical Alumni Lectureships, the B. T. McGhie Memorial Lectureships, the John A. Macgregor Memorial Lectureships, etc., is to be commended. In order for your editorial staff to be assured of getting this material, there should be close liaison between them and those responsible for each of the Lectureships so that the guest lecturers may have ample opportunity to prepare not just a lecture for delivery but a manuscript as well for purposes of publication.

It would seem to me also good policy for the administrative staff of the Journal in their drive to increase the paid subscription list not to overlook the undergraduates and staff as well as the Alumni and practitioners within the fourteen counties, our University constituency.

(Signed) DEAN J. B. COLLIP.

*A Critical Analysis of recent developments in*  
**THE TREATMENT OF MASSIVE  
HAEMORRHAGE OF PEPTIC ULCER  
ORIGIN\***

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**T**HE OLDER METHODS of treating haemorrhage originating in peptic ulcer consisted of rest, sedation with morphine, starvation and expectant optimism. The conservative viewpoint and therapy were adopted; the medical mortality was moderate or low; with the introduction of intravenous therapy, supportive fluids and transfusions it was expected that the mortality figures would be much bettered.

In 1933 Meulengracht<sup>1</sup> suggested the liberal feeding of haemorrhage cases and an entirely new angle in the therapy was thereby initiated. The remarkable improvements in the surgery for ulcer, due to improved anaesthetics, better technique and the use of antibiotics pre-and post-operatively with the significant lowering of mortality rates has led to the invasion of this hitherto entirely medical field by courageous and competent surgeons.

To what extent have these newer thoughts and procedures been reflected in the results of the therapy of haemorrhage from ulcer? The picture has changed materially for the better as reflected in the constant stream of accumulating statistics from both medical men and surgeons. The very profuse literature on this subject and the keen interest evoked is a token of the fact that the topic is a rapidly changing one, but one that still calls for critical analysis both to accept the constructive suggestions and to limit or evaluate the over-enthusiasm of the extremists.

*Definition of Haemorrhage:*

Bleeding from an ulcer may vary from occult seepage to a mild, a moderate, or a massive and exsanguinating haemorrhage. Quite obviously in gathering statistics on the incidence and mortality of ulcer haemorrhage, the outcome will be entirely influenced by the degree and the severity of the bleeding. Haemorrhage may be classified by Grades, 1, 2, 3, and 4, (Raffsky and Weingarten)<sup>2</sup> as slight, intermediate, or massive (Warthin)<sup>3</sup> or as listed by Hoerr, Murphy and Gray<sup>4</sup> as moderate, severe compensated, severe uncompensated, or exsanguinating. Since mild or moderate haemorrhage is simple in its treatment, and is accompanied by practically no direct mortality, all writers have now agreed to concentrate their attention and statistics on only the severe, the massive, or the exsanguinating instances, since in this group resides solely the great responsibility for choice of treatment, and the grave threat to the survival of the patient. By including all the haemorrhage cases in one category one

\* The 10th DR. F. R. ECCLES Memorial Medical Alumni Lectureship, October 26th, 1950.

can draw a bounteous picture of optimism and success with any method of estimating the effects of therapy. By excluding the mild cases and analyzing only the massive haemorrhages, the picture becomes more doleful. And yet, because that latter is the critical group that calls for most help, recent literature has concentrated its attention upon the consideration only of sudden massive haemorrhage of ulcer origin.

Much confusion in the literature has also arisen from the fact that writers on haemorrhage often include in their series all instances of haematemesis and melaena of whatever origin. Thus carcinoma, oesophageal varices, hiatus hernia and gastritis, are lumped with ulcer cases. The uncritical author frequently quotes statistics on ulcer haemorrhage from such more general articles without discriminating between haemorrhage of ulcer and of non-ulcer origin.

#### *Incidence:*

Haemorrhage from peptic ulcer occurs as a complication in approximately 25% of ulcer cases, and may occur at any age, though with greater incidence in the later decades. Haemorrhage from duodenal ulcer occurs approximately four times more frequently than in gastric ulcer cases, but since that is also the relative incidence of duodenal to gastric ulcer, it is apparent that both types of ulcer have an equal tendency to haemorrhage. Haemorrhage as a first symptom of ulcer occurs in 16.2% of the cases (Ivy)<sup>5</sup>. Men are twice as prone to haemorrhage as are women, again to be explained on the greater incidence of duodenal ulcer, particularly in men. Haematemesis is more common in gastric, melaena alone more frequent in duodenal ulcers; the gravity of the prognosis is greatly increased by the presence of haematemesis since the mortality of melaena alone is moderate.

The first haemorrhage is likely to be the most severe and attended with the highest mortality. Subsequent massive haemorrhages may occur in from 60% (Allen)<sup>6</sup> to 74% (Wilkinson and Tracy)<sup>7</sup> of the patients, though the recurrent haemorrhages are less likely to threaten life. The greatest incidence of haemorrhage takes place in the fall months, possibly related to the occurrence of upper respiratory infections which are prone to originate at this season of the year.<sup>8</sup> Arterial hypertension plays little rôle in haemorrhage and has no direct effect on mortality, the mortality figure being 15% for cases with or without hypertension (Raffsky and Weingarten).<sup>2</sup> Ulcer as a psychosomatic disease is particularly prone to haemorrhage. Sudden psychic strain is often the precipitating factor in bleeding.<sup>9</sup>

#### *Mortality of Ulcer Haemorrhage Under Conservative Therapy:*

Statistics on medical mortality from haemorrhage must be scanned with a critical eye lest comparisons become confusing. Only massive haemorrhage that is accompanied by shock and a lowering of the red blood count to three million or less and the haemoglobin figure below

50% should be considered. Only cases admitted to a hospital for urgent reasons should be tabulated. Statistics that include haemorrhages that originate in diseases other than ulcer must be excluded.

All deaths in ulcer haemorrhage must be included; the tendency to "correct" mortality statistics by excluding deaths due to concurrent disease or cardio-vascular or other fatal incidents is pernicious. If a patient is admitted for gastric haemorrhage and dies of coronary thrombosis or cerebral hemiplegia during the course of the haemorrhage, the case should be included in the series as directly attributable to anoxaemia caused by the bleeding episode. It is probably true that in most cases at autopsy the bleeding vessel has been covered by a firm thrombus and is probably no longer an open locus of exsanguination. It is also established that death is more frequently due to dehydration, to cardio-vascular insult, to cerebral or to coronary thrombosis. And yet, that is no reason for excluding such incidences from fatalities on haemorrhage. "Corrected" statistics are misleading.

The mean medical mortality for massive haemorrhage of ulcer origin is according to statistics collected from the literature by Holman, nine per cent. The more recent statistics for medical mortality of "severe" haemorrhage, after a most critical analysis, show a mortality rate of 5 to 9% in large series of well-controlled groups. (Table 1). If one considers only cases of true "massive" haemorrhage the mortality rate under conservative treatment varies from 0 to 29.0%, the lower figures occurring in smaller groups of particularly fortunate individuals. The gross average is 10.5% (Table 2), as compared with the mean average of 6.8% for moderately severe haemorrhage.

The mortality of haemorrhage from gastric ulcer is considerably higher than that of duodenal ulcers (Table 3), the composite figures showing almost twice the incidence of death for gastric cases.

Sex is an important consideration in the prognosis in grave haemorrhage. The mortality for men is far greater than for women, 10.8% as compared with 8.3% in collected statistics, though my own personal experience is even more marked. In our collected group of 216 cases studied for ten years at the Mount Sinai Hospital<sup>10</sup> (1927-1937) there were included 35 females none of whom succumbed to haemorrhage. This may have been purely fortuitous for the mass statistics in the literature do not bear out this impression.

Age is of course a well known factor in determining mortality from haemorrhage. Below 45 years of age the rate of loss is low; above 45 or 50 years the fatality percentage is materially increased. In the massed statistics the mortality rate below 40 years of age is 4.3%, above 45 years 15.1%, above 50 years 15.4%. This percentage of mortality rises so that between 50-60 years it is 18.4%; between 60-70 years 20.7%; between 70-80 years 25.0% (Ivy). In my own collected series we had no deaths under the age of 35 years.

Haematemesis alone always carries a more significant mortality rate as first pointed out by Meulengracht. Recently Welch pointed out a mortality for haematemesis of 20% as compared with only 4% for melaena alone.

#### *The Feeding of Haemorrhage Cases:*

The introduction by Meulengracht<sup>1</sup> in 1933 of the suggestion of liberal and early feeding of ulcer cases represents one of the advances of recent years. This was regarded by the older school of clinicians as a very radical departure since prolonged starvation and rest of the bleeding stomach and duodenum was the accepted practice of that day. Meulengracht feeds his haemorrhage cases from the onset of bleeding and rapidly increases the dietary allowance until large and liberal meals are given throughout the haemorrhage. He is a bit more cautious in the first three days since he, as have other clinicians, has recognized the first 72 hours as the critical period. The likely mortality of a case is often discernible in the first three days of haemorrhage; deaths may take place later in the course but by the third day one knows fairly well whether one is dealing with a single massive exsanguinating haemorrhage or with repeated recurrences of the haemorrhagic episode. By exercising some dietary caution in the first three days Meulengracht is in agreement with most clinicians, but absolute starvation during this period he opposes heatedly. After the third day it matters little whether one feeds or does not. My own conviction years ago was absolutely against feeding anything in the first 48 to 72 hours. Too many sad experiences warned one against feeding during the episodes of brisk haemorrhage, even in the days before one had intravenous therapy and transfusions. But the mass of statistics, (Table 4), if they are more reliable than clinical experience, would tend to support the program of early and liberal feeding. Yet, the few published statistics of liberally fed patients are not so overwhelmingly better as to be convincing, except for the large group of Meulengracht himself with a mortality rate of 2.5%. This large published group includes haemorrhage of all grades of severity, of all origins, not exclusively ulcer. The free and easy admission of all cases to Scandinavian hospitals under the system of State Medicine possibly favors materially the published figures of Meulengracht. When the more liberal diet is restricted to massive haemorrhage cases alone, the mortality figures are within the range of the overall rates for mortality under the older usage of starvation and conservative measures.

#### *Transfusions and Intravenous Therapy for Haemorrhage:*

The liberal use of intravenous fluids and particularly of blood replacement as fast as it is lost has become an established practice in the profession. If the individual of average weight has about five liters of circulating blood in his body it is not unusual to note haemorrhages of 1000, 1500, or even of 2500 cc. at a single exsanguination as measured

by haematocrit or blood volume estimation. The lag in the haemoglobin reading is understandable since it takes some time before the extra-cellular body fluids enter the circulating channels to replace the blood loss. This extravasation of body fluids into the venous channels results in dehydration, intensifies the shock of haemorrhage, and cries for fluid replacement. The fear that the transfusion will raise blood pressure and force out the clot is not founded in fact. (Marriott and Kekwick).<sup>11</sup> Transfusions at the rate of 480 cc. per hour have been rapidly given and even today transfusions under pressure or into both arms simultaneously are being employed.

Transfusion reactions with chills and rapid rise of temperature are not uncommon but are probably not detrimental to the recipient. However, the increasing incidence of homologous serum jaundice following transfusions of whole blood or of plasma would urge caution against the excessive use of blood in cases of mild haemorrhage where shock is not imminent. Serum hepatitis may be and often is extremely severe and is not infrequently fatal even after a single transfusion. The exact frequency of serum hepatitis is not ascertainable, but sufficient numbers of seriously ill jaundiced patients are seen to warrant some reserve in the too free and easy use of transfusion. According to recent experience it does not seem that irradiated plasma has eliminated the possibility or probability of serum hepatitis. The excessive use of fluids parenterally and of transfusions may embarrass the right heart and induce cardiac failure or generalized oedema.

The question that arises is whether the liberal use of transfusions has actually lowered the mortality rate of ulcer haemorrhage. Our own series of observed cases 1915-1925, before the free use of transfusions, showed a mortality rate of 4.2 per cent. (Manheim)<sup>12</sup>. In the twelve years 1925 to 1937, a similar survey of hospital ward cases, wherein transfusions were freely employed gave a mortality of 6.5 per cent.<sup>10</sup> However, every modern physiological and clinical study calls for fluid and blood replacement to overcome shock and anaemia; if surgery is ever to be contemplated in haemorrhage cases, transfusions must be liberally employed. The free use of transfusions and parenteral fluids in grave haemorrhage has been accepted by the profession. If restraint is used in its cautious employment in only the more grave cases, to overcome shock, to replace excessive blood loss or to prepare for operation, its use is well advocated whether it be reflected directly in lower mortality figures for haemorrhage or not.

A more convincing argument for the use of whole blood is the evidence that anoxaemia has a damaging effect on the myocardium and may induce coronary thrombosis. It is argued that most deaths occur as a result not of continued free haemorrhage from an open vessel but in the later days because of myocardial insufficiency, right heart failure and coronary thrombosis. Ball<sup>13</sup> first pointed out enlargement of the heart

in acute anaemia. Ellis and Faulkner<sup>14</sup> found cardiac enlargement in 20 of 64 cases of anaemia studied with characteristic electrocardiographic findings. Myocardial infarction, coronary thrombosis and fatty degeneration most marked in the papillary muscles of the left ventricle were characteristic lesions. Kinney and Mallory<sup>15</sup> observed four cases of myocardial infarction resulting from ulcer haemorrhage and six cases with clinical cardiac failure following massive bleeding from ulcers. Welch and Yunich<sup>16</sup> performed autopsies on eleven cases that died as a result of massive ulcer haemorrhage. Out of six fatal duodenal ulcers, five were located anatomically on the posterior wall of the duodenal bulb and were bleeding not from an open large vessel but from arterioles. The incidence of cardiovascular deaths was high; in five of the eleven cases coronary sclerosis and various degrees of myocardial failure were present. My own recent experience with a severe haemorrhage case in which the haemorrhage was controlled within a week but the right heart failure required five weeks of digitalization impressed the lesson of anoxaemia and heart damage.

Amphogel intragastric drip as a treatment for haemorrhage has a few proponents. Intubation and gastric emptying and suction is often freely used (Wangensteen) but seems a dangerous procedure. The use of gelfoam and of buffer thrombin has been advocated of late. (Daly).<sup>17</sup> The administration of these substances by mouth during haemorrhage is very simple and is usually followed by cessation of haemorrhage;<sup>18</sup> this was the case in my last few cases, whether merely as a result of a coincidence remains to be established.

#### *Prognosis:*

The prognosis of massive haemorrhage in any individual case is difficult to establish. The first 72 hours mark the critical period. If after the first massive haemorrhage bleeding ceases, the prognosis is excellent. If the first loss of blood ceases, but is followed by recurrent bouts of bleeding, the prognosis becomes increasingly poor. Bok<sup>19</sup> has termed these cases "R.R.H." or rapidly recurring haemorrhages and impresses the gravity of such a type of case.

The reading of blood urea estimations on successive days has been advocated as an index of the gravity of a haemorrhage. Schiff and Stevens<sup>20</sup> advise that the rise in urea nitrogen in the blood is not related to shock nor to the age of the patient but is a direct indication of the mortality. In their experience no rise of B.U.N. occurred in non-fatal cases; when the urea nitrogen was above 60 mgms. per cent, death occurred in 5 out of 9 cases; with blood urea 100 mgms. and over death took place in 4 out of 5 instances. The general hypothesis is that the rise in blood urea is due firstly to pre-renal azotaemia, secondly to rapid break down of body tissues and finally to rapid absorption of digested blood from the upper intestinal tract. By simple experiment Schiff<sup>2</sup> administered beef blood to normal humans; one thousand cc. of



blood given in 12 hours by stomach tube drip caused a rise of blood urea of 30 to 46 mgms. per cent; 2000 cc. so given a rise of from 26 to 54 mgms. per cent. Chinn and Harkins<sup>22</sup> repeated the experiments and gave 250 cc. of beef blood for three successive days with a subsequent rise of B.U.N. to 25 mgms. and a rapid return to normal within 24 hours. On the other hand, shock and the resultant diminution of circulation through the renal bed in itself results in increasing accumulation of urea in the blood, azotaemia; the urea is thus a measure of the circulatory failure. My own experience does not show a correlation between the persistent elevation of blood urea, and the ultimate prognosis. Most of the fatal cases have had definitely elevated urea levels, some of which fell just before fatal exsanguination occurred. Others did show elevated values, which subsequently falling did indicate an improved prognosis as borne out by recovery. If the loss of blood, no matter how extreme, is gradual, urea values will not rise. In a patient who bled for four weeks and who had a persistent haemoglobin of 18% there were no increased blood urea values.

Probably the correct view is that the elevated urea figures are the resultant of more than one factor and are usually due to rapid absorption of blood from the intestinal tract plus the pre-renal azotaemia which accompanies rapid bleeding and shock. The prognostic value of blood urea nitrogen determinations in haemorrhage is very suggestive but obviously not infallible.

#### *Surgery in Massive Ulcer Haemorrhage:*

In spite of the best efforts of conservative therapy a minimum of approximately 10% of the cases succumbed to massive haemorrhage from ulcer. In 1936 and even as early as 1918 Finsterer,<sup>23</sup> a Viennese surgeon, proposed the application of radical surgical measures in an attempt to salvage such residual probable fatalities. Finsterer carried out a direct surgical attack upon the bleeding ulcer, the operation being performed within the first 24 to 48 hours of the onset of haemorrhage, local infiltration anaesthesia being employed. His technical approach varied; the operation of choice was a partial gastrectomy usually with exclusion of the duodenum or pylorus. At times he was limited in his efforts to mere ligation and plication of the bleeding vessel, at times to local excision of the ulcer, at times to tamponage of the ulcer area in the deep duodenum with masses of gauze under pressure. His reported operative mortality for early cases was 5 per cent. It is probably true that in his enthusiasm he operated upon cases that might well have survived under medical conservative treatment, but his attack on older patients with massive haemorrhage and his surgical results were impressive. With succeeding years the surgical profession has become increasingly bolder until today every case of massive haemorrhage, particularly those over 45 or 50 years of age suffering from repeating rapid haemorrh-

age is considered a potential surgical case if seen within the first 24 or 48 hours after the onset of haemorrhage.

Cases of haemorrhage operated upon weeks after exsanguinating bleeding, after the failure of all medical supporting measures, are notoriously bad surgical risks. The mortality of such late calamitous surgery ranges high between 9 and 54%. The same case if operated on in the first hours of haemorrhage can be successfully resected with a considerably lower mortality. The adoption in many hospitals of teams of medical men, surgeons and radiologists, alert and prepared to consider any emergency at an hour's notice, has materially improved the outlook for grave massive haemorrhage. Such teams have published their results in hospitals such as the New York Hospital, The Presbyterian Hospital in New York, University of Michigan Hospital, Peter Bent Brigham Hospital, Buffalo University Hospital and the Veterans' Administration Hospital at Roxbury, Massachusetts.

The usually accepted indications for early surgical intervention are as follows:

1. An established diagnosis of ulcer.
2. Age of the patient, 45 years or over.
3. Recurrent massive haemorrhage while under observation.
4. Possible previous haemorrhages.
5. Type of bleeding, whether haematemesis or melaena.
6. Degree of severity of the haemorrhage.

1. The diagnosis of ulcer must have been established either by previous history or by known radiographic studies. While peptic ulcer is the outstanding and most common cause of massive haemorrhage occurring in 65% or more of most series, other causes such as oesophageal varices, portal hypertension, hiatus hernia and gastric carcinoma must be considered as possible diagnoses before operation may be considered. The Hampton technic, as further elaborated by Schatzki,<sup>25</sup> that is, the radiographic examination of a patient during the course of haemorrhage is considered safe today by many observers. The examination is carried out with the patient in the prone and supine positions, little barium being ingested, and brisk manipulations by the hand or leaded glove being avoided. Personally I have seen enough haemorrhages initiated during radiological examinations to make me very wary. The Mount Sinai Hospital even today refuses to employ radiography during haemorrhage except upon the urgent request of the referring physician who assumes the responsibility. Nor are such examinations eminently satisfactory though they may suffice to establish the site of the ulcer.

Cases of repeated massive haemorrhage over a course of years which defy diagnosis and which constitute the undetermined group must eventually be operated upon and resected, even though the exploratory operation fails to demonstrate a positive lesion.<sup>26</sup>

2. The age of the patient. Because the medical mortality under 45

years is minimal, surgery is usually limited to those patients 45 or 50 years or over.

3. Surgical intervention is directed to those cases of massive haemorrhage, or of rapidly recurring grave haemorrhage who enter the hospital within 48 hours of the onset of bleeding. Haemorrhage that does not cease within the first two days, or that tends to recur after apparently ceasing during the first 72 critical hours, may be considered as requiring surgical intervention. The rate of haemorrhage is also important as reiterated by Dunphy and Hoerr<sup>27</sup>: any patient requiring 1500 cc. daily as blood replacement is a surgical candidate.

4. A patient who has had a previous grave haemorrhage and who now suffers a second massive haemorrhage is regarded as a necessitous surgical case. Patients who have once survived a gross haemorrhage under medical treatment have a great tendency to recurrent haemorrhage: (Stewart<sup>28</sup> 9% massive, 25% mild subsequent haemorrhages; Holman<sup>29</sup> in a 5 year follow-up showed that almost 50% again suffer haemorrhage). A second severe recurrent haemorrhage is an indication for surgical intervention.

5. The gravity and higher incidence of mortality in haematemesis is considered an added indication for operative interference.

6. Most important is the degree of severity of the haemorrhage. A red blood count under 3,000,000 red blood cells, haemoglobin values of less than 50%, and cases which require 1500 to 2500 cc. of blood to restore haemoglobin level to normal constitute the usually accepted criteria for surgical intervention.

#### *Types of Operative Procedures as Noted in the Current Literature:*

Subtotal gastrectomy with the excision of the ulcer, gastric or duodenal, is the operation of choice. Unfortunately in the bleeding duodenal ulcers, the ulcer usually occupies the posterior wall of the duodenal bulb, frequently penetrating the head of the pancreas and invading the pancreaticoduodenal artery. At best the excision of the bed of such an ulcer, even when haemorrhage is not present, is a difficult procedure. When the additional factors of exsanguinating haemorrhage and shock are present, the excision of the ulcer base, a procedure which is time consuming and often leads to post-operative leakage, is difficult of accomplishment. Hence we see in the literature that most operations are partial resections with the exclusion of the duodenum and ulcer. This is known to be unsatisfactory and to lead to persistent or recurring symptoms of ulcer and of haemorrhage. Mere ligation of the bleeding vessels at the base of the ulcer, or ligation plus gastro-enterostomy with or without vagotomy, or Devine procedures, are all unsatisfactory. (Gray and Sharpe).<sup>30</sup> Gordon-Taylor<sup>31</sup> has employed various types of procedures: gastrotomy, jejunostomy, resection; Wangenstein,<sup>22</sup> Stewart<sup>28</sup> resect radically. Finsterer,<sup>23</sup> Allen,<sup>6</sup> Warren and Lannon,<sup>33</sup> Claude Welch,<sup>34</sup> practice exclusion operations rather than risk

the life of the patient in a more prolonged procedure, or return to a two-stage operation of the McKittrick type at a subsequent date in order to resect the ulcer proper and the duodenum. In cases of negative findings at emergency operations it is mandatory that a subtotal resection be performed. Merely to open the abdomen and explore, even though a gastrotomy or a duodenotomy be carried out is a futile gesture and is usually followed by repeated haemorrhages. Subtotal resection in these cases is curative though the source of the haemorrhage may never be established.<sup>26</sup>

*Immediate and Late Results of Emergency Surgery:*

It will be interesting to note the mortality rates for surgical intervention applied as an urgent or emergency measure in the first 48 hours of massive haemorrhage from peptic ulcer. This is the more interesting insofar as data are accumulating rapidly and a fair surmise of the risk of such a bold attack may now be ventured. Table 5 represents a compilation from the literature of the last twelve years of the results of emergency surgery for massive ulcer haemorrhage. Six hundred and ninety-four cases have been so operated upon; a careful attempt has been made to check each publication in the literature, to accept only cases explored during the first 24-48 hours after onset and to exclude all later relatively urgent or elective surgical cases. The mortality rate for early or emergency surgery varies from 0 to 33% with a gross average of 10.5%. This is a surprisingly acceptable risk and result for operative interference at such a critical time and under such difficult conditions. Every conservative internist must hereafter take cognizance of the fact that the remarkable improvements in surgical technique, safer anaesthetics, rapid blood replacement during and after operation and the free use of antibiotics, not to mention exquisite team work and timing, entitle the surgeon to assume equal responsibility for the ability to salvage the grave risks that might otherwise have been lost. If operation is delayed until the second or the third week of continued haemorrhage with repeated episodes of shock and a progressive anaemia only partially relieved by blood and fluid replacement, then the late urgent operation is beset with a more grave incidence of mortality. (Table 6). Figures from the literature of late surgery show a mortality rate ranging from 4 to 54%, averaging 25.4%: this in contrast with 10.5% mortality when operative intervention is instituted within the first 48 hours.

When the patient has fully recovered from the effects of the haemorrhage, weeks or months later, surgery can be carried out with the minimum risk associated today with subtotal gastrectomy and with eminently satisfactory results. Recurrent haemorrhage after gastrectomy for previous massive haemorrhage occurred in only 4.5% of resected cases (Hinton and Church),<sup>35</sup> (Holman),<sup>29</sup> though Heuer's<sup>36</sup> figure was higher (19%).

*Comment:*

Quite obviously the massive haemorrhage case is the joint responsibility of internist and surgeon. The medical mortality with conservative treatment of all cases of grave haemorrhage originating in ulcer is 6.8%; if massive haemorrhage alone is tabulated the conservative death rate is 9.15%; cases of massive haemorrhage over the age of 45 show a fatality rate of 15% to 50% in the seventh decade of life.

But these favourable figures for conservative therapy do not tell the whole story, for excluded from these tabulations are those grave unsuccessful cases that in the late course of medical treatment have been subjected to emergency surgery as a last resort. Thus so-called "conservative treatment" is not debited with these surgical mortalities which are really the responsibility of the medical man. On the other hand, the surgeon often is credited with a brilliant result in early haemorrhage that might well have survived under more conservative therapy if the operation had been cancelled.

Prognosis at all times is most difficult; each case is a problem of its own which depends for its final outcome on the judgment and the skill of the physician and the surgeon in attendance. Quite obviously mortality statistics for haemorrhage should be, as has been suggested, the "hospital rate" of both services combined.

The team work as carried out in well organized hospitals would seem to represent the best organization for the care of such grave emergencies. Where a competent surgeon is not in immediate attendance, where a rural or a city hospital is not well equipped to meet all contingencies, surgery had better be deferred. The mortality and survival rate under conservative therapy, while it has not shown striking improvement in recent years in comparison with the past, is still eminently satisfactory. What is vitally needed is more frankness in reporting results of therapy, more critical analysis of the conditions surrounding the patient at the time of haemorrhage, and a more uniform standard of reporting the degree of haemorrhage and the results of treatment in our current medical literature.

TABLE 1  
MORTALITY OF HAEMORRHAGE FROM PEPTIC ULCER  
UNDER CONSERVATIVE MEDICAL THERAPY

	Cases	Deaths	Rate
Holman (collected cases) <sup>29</sup> .....	3,300	297	9 %
Holman (personal cases) 1940-1946	206	11	5 %
Franzen (collected cases) 1942 <sup>45</sup> , from Scandinavian literature, 1916- 1935 .....	3,891	194	5 %
Personal cases .....	563	37	6.6 %
Raffsky and Weingarten <sup>2</sup> —1942 ....	408	36	8.8 %
Brown and Thieme—1950 .....	181	12	7.0 %

Raspberry and Miller—1943 <sup>37</sup> .....	715	42	5.9 %
Miller and Elson—1938 <sup>46</sup> .....	5,843	409	8.7 %
(collected cases)			
Allen and Benedict <sup>47</sup> —1933 .....	200	12	6 %
Crohn and Lerner—1937 <sup>10</sup> .....	216	14	6.5 %
Welch and Yunch—1940 <sup>16</sup> .....	125	11	8.8 %
Porter, Harvey and Schullinger <sup>39</sup> — 1930-1937 .....	213	12	5.6 %
<b>TOTAL</b> .....	<b>15,861</b>	<b>1,087</b>	<b>6.85%</b>

TABLE 2  
MORTALITY OF HAEMORRHAGE FROM PEPTIC ULCER:  
UNDER CONSERVATIVE MEDICAL THERAPY—  
MASSIVE HAEMORRHAGE ONLY

	Cases	Deaths	Rate
Raffsky and Weingarten—1942 <sup>2</sup> .....	104	21	19.4 %
Bok—1944 <sup>19</sup> .....	9	6	66.6 %
Hoerr, Dunphy and Gray—1945 <sup>4</sup> ..	34	4	12 %
Wayburn—1948 .....	36	4	11 %
Thorstat—1942 .....	208	21	10 %
Porter, Harvey and Schullinger— 1930-1937 .....	213	12	5.6 %
Porter, Harvey and Schullinger— 1948 .....	45	0	0 %
Heuer—1946 <sup>36</sup> .....	337	27	8 %
Stewart, Massover, Potter and Schoer <sup>28</sup> —1948 .....	21	6	29 %
Fappworth and Lovtit—1943 .....	30	1	3.3 %
Enthusiastic transfusions			
Frazer and West (duodenal only) —1949 <sup>43</sup> .....	165	7	4.2 %
Welch, Claude—1949 <sup>34</sup> .....	226	22	10 %
<b>TOTAL</b> .....	<b>1,428</b>	<b>131</b>	<b>9.15%</b>

Note: These figures do not include the emergency deaths incurred by early or late surgical intervention.

TABLE 3  
CONSERVATIVE MORTALITY UNDER CONSERVATIVE MEDICAL  
THERAPY OF GASTRIC AND DUODENAL ULCERS

	Gastric Ulcers	Duodenal Ulcers
Welch .....	22 %	10 %
Ivy (composite statistics) .....	16.7%	8.8%
Ivy—since 1915 .....	7.9%	3.3%
Crohn and Lerner .....	10.3%	6.1%
Welch, (Claude) and Yunch .....	29.4%	5.4%

TABLE 4  
MORTALITY RATE — STARVATION VS. LIBERAL FEEDING

	Starvation			Modified Meulengracht Diet		
	Cases	Deaths	Mortality %	Cases	Deaths	Mortality %
Raffsky and Weingarten.....	71	31	11 %	39	4	10.3%
Thorstat .....	138	19	13.7%	70	2	3.0%
Schiff .....			25.6%	160	11	6.8%
Meulengracht 1947 .....				1,031	26	2.5%
Raspberry and Miller <sup>37</sup> .....				75	4	5.9%
Pico-Estrada <sup>38</sup> .....				34	3	8.8%
TOTAL.....				1,409	50	3.55%

TABLE 5  
MORTALITY RATE: EARLY EMERGENCY SURGERY FOR  
MASSIVE HAEMORRHAGE OF ULCER; FIRST 48 HOURS

	Cases	Deaths	Rate %
Bok—1944 .....	11	0	0 %
Hoerr, Dunphy and Gray—1948 .....	9	3	33 %
No surgical deaths in last 4 cases operated			
Finsterer—1936 .....	46	2	3 %
1939 .....	71	3	4 %
1947 .....	150	6	4 %
Holman—1940-1948 .....	19	4	21 %
Worthin, Warren and Wissing—1949 .....	11	1	9 %
Wayburn—1948 .....	7	2	28 %
Gordon-Taylor 1926-1933 .....	10	2	20 %
1933-1937 .....	22	4	19 %
1946 .....	18	1	5 %
Yudin (Moscow) .....	134	17	12.5 %
Heuer—1946 .....	31	9	29 %
Thorstat—1942 .....	7	1	14 %
Porter, Harvey and Schullinger <sup>39</sup> —1948 .....	15	1	6.6 %
Stewart, Massover, Potter and Schoer—1948 .....	33	5	15 %
Matthewson and Pinkham—1946 ..	19	3	15.7 %
Jones, F. Avery—1947 <sup>40</sup> .....	7	1	14 %
Hutchins, L. R.—1946 .....	5	1	20 %
Green—1946 .....	7	1	14 %
Bohmanson—1946 .....	19	1	5.2 %
Amendola—1948 <sup>41</sup> .....	11	1	9 %
Welch, Claude—1949 .....	32	3	10 %
Oliani .....	10	1	10 %
TOTAL .....	694	73	10.5 %

TABLE 6  
URGENT SURGERY PERFORMED IN THE LATER WEEKS  
OF INTRACTABLE MASSIVE HAEMORRHAGE

	Cases	Deaths	Rate
Raffsky and Weingarten—			
11 days to 3 weeks .....	28	5	17.9 %
Wangensteen			
8 to 24 days after haemorrhage ..	7	2	28 %
Finsterer—1936 .....	55	18	32.7 %
1939 .....	63	17	26.9 %
1947 .....	123	28	22.8 %
Gordon-Taylor—1946 .....	11	4	36 %
Frazer and West—1949 <sup>43</sup> .....	12	4	33 %
Hart and Shingleton—1947 <sup>44</sup> .....	12	1	9 %
7-21 days after onset			
Amendola—3-21 days .....	25	3	12 %
Welch—			
repeated recurrent haemorrhage	13	7	54 %
<b>TOTAL</b> .....	<b>349</b>	<b>89</b>	<b>25.4 %</b>

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*"I look back upon my Medical studies as the school which taught me, in a more penetrating and convincing way than any other, the eternal principles of scientific work, principles so simple yet continually forgotten, so clear and yet ever shrouded by a deceptive veil."*  
—Helmholtz.

*"The education of most people ends upon graduation; that of the physician means a lifetime of incessant study."*—Marx.

*"But like a man walking alone in the darkness, I resolved to proceed so slowly and carefully, that, even if I did not get very far, I was certain not to fall."*—Descartes.

# THE USE OF ANTI-SPASMODIC DRUGS\*

*in the Treatment of*

*Functional Spastic Disorders of the Stomach and Intestines*

By J. S. W. ALDIS, M.D., '50

**I**N COMMON with most other organ systems of the body, the stomach and intestines are subject to certain diseases for which it is impossible by present clinical or laboratory methods to discover a basis of morbid anatomy. The only discernable pathology in such diseases appears to concern the various physiological and biochemical mechanisms which comprise the function of the organ or organs. In short, the pathology is, exactly as the word indicates, functional and not what is commonly called organic or structural. It consists of morbid physiology apart from the known existence of morbid anatomy. Such a division of disease into functional and organic creates a problem similar to that of assigning priority to the chicken or the egg—for organic disease would be of little significance if it did not cause disordered function and, of course, functional disease can lead to organic pathological change which in turn creates another more serious and perhaps permanent functional lesion. Nevertheless, there exists a vast amount of disease to which we can aptly apply the term functional. Whatever slight organic disease may be present in such disease quickly disappears with the restoration of normal function. It is worth-while pointing out here that functional is a pathological and not an etiological term and to use it where one really means psychogenic, psycho-somatic or psycho-neurotic is not precise terminology. These latter terms certainly describe the etiology of a great deal of functional disease but that fact scarcely justifies using the term functional in the etiological sense to imply the existence of psychogenesis. When we say that the illness of a certain patient has a "strong functional element" we usually, and unfortunately, mean that it has a "strong psychogenic element" and we are generally understood in this. But would it not be better to use the latter term which is exactly what we mean and reserve the word "functional" for its accurate use in a pathological sense?

The subject of this paper has been somewhat limited by inserting the term "spastic" in the title. Spasm of plain muscle of the gastrointestinal tract is a common accompaniment of true organic disease of the tract; it is often the forerunner, perhaps in an etiological sense, of such organic lesions as gastric and duodenal ulcers, and it certainly is one of the commonest forms of functional disease in this organ system. The commonest use of the term "spasm" implies a pathologically increased tonus, i.e., a pathologically increased resistance to a distending force. It differs from a "motile" contraction both quantitatively and qualitatively. However, gastro-intestinal muscle commonly exhibits what is called "excessive peristalsis" which is only a quantitative exag-

\*The First Charles R. Will & Company, Limited. Prize essay in Pharmacology, 1950.

geration of the normal "motile" and inter-segmental contractions. Both "true spasm" and "excessive peristalsis" are painful and common and may appear separately or together in the same patient. Both pathological conditions will be discussed in this paper as "Functional Spastic Disorders of the Stomach and Intestines".

#### *Incidence of Functional Gastro-Intestinal Disease:*

It is not hard to be assured that functional gastro-intestinal disease includes some of the most popular ailments among the doctoring public today. These ailments masquerade under a host of aliases, both lay and medical, including: "functional dyspepsia," "nervous indigestion," "abdominal distress," "gastro-intestinal upset," "gastric neurosis" and many others. All of these include at least some element of spasm and a good many are purely spastic. Hobbs<sup>1</sup> investigated 33,199 visits to the Medical Officers in M.D. 1 during a seven month period in 1943 and found 5.3% of these visits were for gastric complaints. Five hundred and twenty-four of the soldiers making these visits were followed for a period of from five to nine months and of these only 4% were ultimately diagnosed as peptic ulcer, the latter being the only truly organic gastro-intestinal diagnosis made among the group. These figures indicate that about one in every twenty visits to Medical Officers during the period studied, involved gastric symptoms for which it was difficult, to say the least, to find a basis in organic pathology. Another army study<sup>2</sup>, this time the British Army, showed that of 2,851 cases presenting with an "ulcer syndrome" 16% had gastric ulcer, 42% had duodenal ulcer and 42% had non-ulcer dyspepsia.

Regarding the incidence of gastro-intestinal symptoms in civilian life, the following are typical figures from large studies: in a study of 9,000 white families in 18 states for one year<sup>3</sup>, the gastro-intestinal morbidity rate was the second highest, exceeded only by respiratory and stood at 328.5 per thousand population. Gastro-intestinal illnesses constituted almost exactly 10% of all illness. The very latest study from Saskatchewan, as yet unpublished<sup>4</sup>, shows gastro-intestinal illnesses as using 11.4% of all physicians' services for a period of six months in 1947. An extreme figure is a report of 269 patients at an outpatient department of whom 41.5% gave gastro-intestinal symptoms as their chief complaint<sup>5</sup>. I think we should be in no doubt that people with "stomach ache" are multitudinous. What is just as important is that a goodly proportion of this multitude suffer from "psychogenic functional stomach ache". One study of 3,000 cases presenting gastro-duodenal symptoms found only 15% with gross gastric or duodenal lesions<sup>6</sup>. A Mayo study of 15,000 chronic dyspeptics<sup>7</sup> found only 15.5% with ulcer and 2.6% with carcinoma. The accuracy of this last study was checked by following 354 of the functional cases over a period of seven years<sup>8</sup> at the end of which time 303 still had no organic pathology. No more need be said to indicate that men and women with functional disorders of the stomach and

intestines will be very common occupants of the patients' chairs in our offices — and very commonly too the man in the doctor's chair will have a similar complaint — both being important reasons for learning the art of healing these patients.

*Etiology of Functional Disease of the Stomach and Intestines:*

The following classification of functional gastro-intestinal disease is a modification of one used by Rivers and Ferreira of the Mayo Clinic<sup>9</sup> to classify chronic dyspepsias and, in the altered form, as I have used it, is adequate for this discussion. There are, on this basis, three main types of functional gastro-intestinal disease:

1. *Reflex*: wherein the gastric or intestinal symptoms are based on local functional pathology but are the result of reflex irritation from organic disease in such neighbouring organs as the gall bladder, bile ducts, pancreas, etc.
2. *Systemic*: where the local pathology is still functional but where it is caused by co-existing systemic disease which may be of a neurological, metabolic, toxic, deficiency or endocrine type. Many infections, especially in children, also produce severe disturbances of gastro-intestinal function.
3. *Psychogenic*: where the disturbed emotions of the patient have wrought, by a mechanism as yet uncertain, a disturbed function of the stomach and/or intestines. This is the largest group, the group we should be able to do the most for, and the group we shall discuss.

I shall not waste any time in the discussion of the Reflex and Systemic Types. Obviously, if there be co-existing disease elsewhere, the therapeutic aim must be to treat this disease. If a purely symptomatic treatment of the patient's gastro-intestinal symptoms be desired in order to bring comfort to the patient temporarily (and any patient in pain will tell you that this is extremely desirable treatment) then the methods which I shall later discuss can be used effectively in such treatment. However, it is worth-while discussing the etiology of the Psychogenic Type because it has much to do with the treatment.

Folk-lore has, from the beginning of the spoken word, regarded the stomach and intestines as being closely connected with emotion, if not as the actual seat of emotion at least as the sounding-board of emotion. Men have always "felt in their bowels"; men have always "had guts"; and, strangely enough, men with "lots of guts" are frequently the ones to get spastic disorders in their "guts". However, despite shrewd clinical observations and abundant empirical evidence which certainly indicated that the gastro-intestinal tract was, in fact, a sounding board of emotion, this was not fully confirmed scientifically until the classical work of Wolf and Wolff<sup>10</sup> reported in 1942. These men were, like Beaumont, fortunate enough to have a male human subject with a ready-made gastric fistula created because of a childhood occlusion of the oesophagus.

They noted the effects of emotion on the stomach over long periods and two types of emotional effect were recorded. The first consisted of blanching of the mucosa, inhibition of both acid secretion and contraction. This type resulted from "withdrawal" emotions such as fear and sadness. The second effect consisted of accelerated acid secretion, hypermotility, hypersecretion and engorgement of the mucosa all brought on by the "conflict" emotions of anxiety, hostility and resentment. Both effects were increased by greater intensity and greater duration of the emotion and one type of pathogenesis of peptic ulcer was demonstrated. The particular reaction we are interested in for this discussion is, of course, the increased muscular activity. Since the work of Wolf and Wolff the whole gastro-intestinal tract has been psycho-somatically investigated by balloon-kymograph, sigmoidoscope, X-Ray and fistula. In fact, some recent work<sup>11</sup> has shown that spasm of the sigmoid colon occurs in healthy persons when they are under stress produced by experimental stimuli. The appearance of this reaction depends not only upon the stimulus but also upon the subject's interpretation of the stimulus. By further experiment on this hypothesis it has been shown that the fundamental abnormality in patients with spastic constipation lies not in the behaviour of their colons but in their susceptibility to stress-producing life situations.

In this connection it is also interesting to note that the only workers<sup>12</sup> fortunate enough to find a woman with a gastric fistula got somewhat different results from those who studied men. For instance, they found that where men show hyperaemia, hyperacidity and hypermotility in response to emotions of resentment, anger, etc., the woman showed precisely the opposite — blanching, decreased acidity and motility. This raises the question of sex differences in response to emotion and offers some explanation of the lower ulcer rate in women. It also points to the probability of different responses in the same sex as being the explanation of why ulcer occurs in one individual and not in another under what appear to be the same conditions.

We must remember, however, that while we know that disordered emotion causes disordered gastro-intestinal function, we are still highly uncertain as to just how this is accomplished. The exact pathogenesis still eludes us. We have always considered the parasympathetic system as being motor to gastric and intestinal muscle but inhibitory to sphincters and the sympathetic system, conversely, being motor to sphincters and inhibitory to muscle. Yet, we use atropine, a parasympatholytic drug, to relieve pylorospasm which, so far as we know, is probably a sympathetic effect. The so-called "adrenalin-releasing" emotions do not necessarily produce the sympathetic effects we would expect. In fact, recent work<sup>13</sup> has shown that while adrenalin acts initially as an intestinal sedative its administration in the cat is followed by an after-effect of greatly increased muscle activity. Similar observations have been made

following stimulation of the splanchnic nerves. The suggested explanation of such phenomena is that adrenalin produces a state of increased muscle excitability such that greater response in tonus and motility is obtained for a lesser stimulus.

Gastro-intestinal muscle activity is generally considered to be of three types<sup>14</sup>: first is tonus; second are propulsive peristaltic contractions; third are what have been called "intersegmental relationships" since they involve the co-ordination or inco-ordination of one functioning segment with another and thus comprise the actual mechanism which passes a mass of solid material from the upper to the lower end of the gut. These functional activities are all produced by the contractions of the circular and longitudinal muscle coat known as the *muscularis*. It has now been shown<sup>15</sup> that mucosal movements are independent of this gross muscle activity and that parasympatholytic drugs which will reduce this activity of the *muscularis* have no effect on mucosal patterns. The latter are produced by the contractile activities of the *muscularis mucosae* which, it has now been suggested<sup>15</sup>, are under motor control of the sympathetic. The only drug which has successfully eliminated both general and mucosal movements is tetraethylammonium chloride which, of course, blocks both sympathetic and parasympathetic ganglia.

These etiological factors in gastro-intestinal functional disease have been mentioned specifically to point out that the problem of spasm in the tract is a complicated one. It may involve the *muscularis*, the *muscularis mucosae* or both. The neuro-muscular mechanisms are uncertain and the ways in which emotions affect these mechanisms are still more uncertain. It is, therefore, not surprising that the hunt for a good gastro-intestinal anti-spasmodic is still in full cry.

#### *Spastic Syndromes:*

Most functional gastro-intestinal disorders involve some element of spasm. Cardiospasm and pylorospasm are prominent examples of what are purely spastic disorders. The first will not be discussed at all, since it is not amenable to drugs and since it is a clear-cut picture which does not fit into the "dyspeptic" group which is our concern here. Pylorospasm is also a disorder of the sphincter but is much less common in adults than in babies. The commonest spastic disorder of the upper tract, however, is one which presents with some variant of the "ulcer syndrome" — the patient may even appear with a set of symptoms which make a text-book picture of ulcer. Since upper tract disorders are, like ulcer, much commoner in men, the patient will commonly, but not necessarily typically, be intelligent, ambitious, and probably hold a position of some responsibility. Outwardly he may appear calm, very considerate of other people, but with a lot of what is popularly called "nervous energy". Inwardly you will find he is often uncertain, extremely demanding of himself, tending to perfectionism so far as his own activities are concerned, but carrying around a surprising number of resentments

and dislikes which he is completely unable to get rid of because of the high ethical standard of conduct which he requires of himself. He has probably been in pain for about two years and finally has come to the doctor because his wife made him. He will probably show what the psycho-somaticists call "positive indications" of psycho-somatic disease. For example: his distress may become worse with meals rather than better as we expect with ulcer; he may relate that his symptoms disappear when he is distracted by playing golf, gardening, etc; he may report that he can escape the pain simply by going to bed and going to sleep; he may say that he feels better when he has had a few drinks. All of these are examples of positive indications, which rarely if ever occur in organic disease such as ulcer, and, if they or similar indications do appear, do much to assure one that it is functional and not organic disease even before the negative indications are sought for by diagnostically eliminating organic disease. If the disorder be largely spastic his only complaint will probably be epigastric pain and the only X-Ray finding will be of a contracted pyloric antrum and/or duodenal cap. While this is a description of a common clinical type we must remember that as we move away from this picture of almost pure spasm into disorders which involve less spasm but also nausea, vomiting, heartburn, flatulence, etc., we meet a wider variety of personality types, varying degrees of somatic component and a much more complicated clinical picture — usually with a poorer prognosis.

Spastic disorders of the lower tract involve women more commonly than men. Spasm of the caecum, spastic constipation and mucous colitis are the commonest syndromes with the element of spasm becoming less important in about that order. Each is diagnosable as psycho-somatic on the basis of certain well-known positive and negative indications. Each is a legitimate object of the use of anti-spasmodic drugs.

#### *Pharmacological Activity of Some Anti-Spasmodic Drugs:*

There are a good many drugs which possess the property of inhibiting or relaxing smooth muscle. Only a few of these possess characteristics which make them useful as gastro-intestinal anti-spasmodics. For instance, Demerol is a fairly powerful anti-spasmodic but its sedative effect is too great and its habit-forming potentialities too prominent to make it of any value in treating a patient who has to hold down a job or manage a household while he or she is being treated. The tetraethyl ammonium compounds are very effective blocking agents at autonomic ganglia and will relieve spasm very effectively only to substitute a paralytic ileus in its place. A number of smooth muscle inhibitors have too great an effect on smooth muscle outside the gut to be practical for gastro-intestinal therapy. In short, a good gastro-intestinal anti-spasmodic must act in reasonable doses definitively and solely on that tract; toxic side-effects must be minimal and the means of administration and length of activity

such that the drug can be taken easily and effectively by a patient carrying on with his daily work.

These last-mentioned criteria lead us to a group of drugs, members of which have been used and developed almost entirely as gastro-intestinal anti-spasmodics. This group is headed by atropine and papaverine and includes a number of drugs which are frequently designated as "atropine substitutes" but which are both tropine-like and papaverine-like. As an introduction, therefore, the general characteristics of both atropine and papaverine will be briefly discussed.

*Atropine:* This drug, a mixture of d- and l-hyoscyamine, is a belladonna derivative. It is generally accepted that atropine, at least experimentally, is capable of inhibiting tone and motility in the gastro-intestinal tract. According to Goodman and Gilman<sup>16</sup>, atropine acts directly on the surface of the effector cell either to prevent attachment of acetylcholine or to prevent its response to acetylcholine attachment. It has also been discovered that there is no interference with local or intracellular release of acetylcholine so that parasympathetic stimulation will still excite a piece of gut under the influence of atropine<sup>17</sup>. There is an almost general agreement that atropine will inhibit both abnormally violent and normal contractions of the human gastro-intestinal tract following parenteral or oral administration.<sup>18</sup>

However, so far as therapeutic value of atropine is concerned, Bastedo<sup>19</sup> in his textbook concludes: "In the small doses usually employed or permissible for any length of time, atropine and belladonna are practically without effect on the secretory and motor functions of the stomach." He also feels it is little better in the intestines.

Atropine is known as a neurotropic drug. This is because *in vitro* it acts most spectacularly to inhibit spasm caused by acetylcholine. Such spasm is neurotropic because acetylcholine acts on muscle by way of its neuronal connections. Therefore, when an anti-spasmodic drug is said to be tropine-like it means that it acts neurotropically to block the acetylcholine mechanism. Such drugs are, therefore, parasympatholytic, at least so far as the gut is concerned. Recent clinical investigation<sup>18</sup> using the balloon-kymograph on patients with ileal and colonic stomata, atropine, in doses of from 0.65 to 1.3 mg. by mouth, after latent periods up to 42 minutes, either completely abolished or diminished intestinal motility for periods up to 27 minutes. There was no effect on tone. The addition of 32.5 mg. of phenobarbital did not increase the effects. However, a dose of 1.3 mg. of atropine combined with 25 mg. of ephedrine not only succeeded in reducing tone but in extending the inhibitory activity to a point where it was still acting at the end of 45 minutes. Atropine, of course, has side effects which are well-known and which frequently make their unpleasant and undesired appearance in therapeutic doses.

*Papaverine:* Papaverine is the most important member of the benzyloisoquinoline group of opium alkaloids. It is not a narcotic. It is



a direct depressant to all forms of smooth muscle. It is more effective than atropine in reducing spasm caused by barium chloride on a strip of isolated intestinal muscle. Since barium stimulates smooth muscle directly, and does not act by way of any neuronal connections, it is said to be musculotropic or myotropic. Papaverine is, therefore, known as a musculotropic or myotropic anti-spasmodic drug and the term "papaverine-like" is used to indicate that the activity of a drug is largely myotropic. Papaverine itself is not an important gastro-intestinal anti-spasmodic.

Atropine and papaverine have become "type" drugs in the search for an effective gastro-intestinal anti-spasmodic. Generally speaking the search has been for a myotropic or "papaverine-like" drug. This is because it appeared probable that a drug which acted directly on gastro-intestinal muscle would have fewer toxic side-effects and less effect on smooth muscle outside the gastro-intestinal tract. In addition the idea has been held by many that, since we are not at all sure that gastro-intestinal spasm is either a sympathetic or parasympathetic effect, a drug which acted directly on muscle might be more effective in more cases. There is a weighty list of such drugs and a few of them will be briefly discussed here.

*Novatropine:*<sup>18</sup> This is sometimes called novatrin. It is homatropine methyl-bromide. It has been found to have an atropine-like effect on the isolated intestinal strip. Its intravenous injection has inhibited the tone and motility of the unstimulated gastro-intestinal tract of dogs and the hyper-motility of the human stomach induced by insulin. The activity of the human gastro-intestinal tract has been inhibited for 5 to 60 minutes after the intramuscular injection of 2.5 mg. Recent investigation, using the balloon-kymograph, and following oral administration of the drug to four patients with stomata, one ileal and three colonic, has shown no effect in three cases and a slight increase in tone in one case. Motility was not altered. No reactions were experienced.

*Trasentine:*<sup>18</sup> This drug is about mid-way between the neurotropic atropine and the myotropic papaverine. It is diphenyl-acetyl-diethyl-amino-ethanol-hydrochloride. Experimentally it relieves spasm, induced by acetyl-choline and barium chloride, in an isolated intestinal strip. It is said to have a selective action for gastro-intestinal tract and uterus. Its intravenous administration into human beings has been found to inhibit the activity of the unstimulated gastro-intestinal tract. On intramuscular or oral administration, it has inhibited the action of the unstimulated intestinal tract in 14 percent of instances. Intersegmental coordination is said to be improved by the drug. Recent investigations with the balloon-kymograph in which the drug was administered orally to five patients with stomata found no observed effects in four. The fifth experienced a slight increase in tone which persisted for at least 26 minutes. No side-effects were apparent.

*Pavatrine*:<sup>18</sup> This is diethylaminoethyl fluorine - 9 - carboxylate hydrochloride. It is a strikingly myotropic drug which has been found more active than papaverine in combatting barium spasm but less active than atropine in combatting acetyl-choline spasm—both, of course, in the isolated intestinal strip. It has also been found to inhibit tone and motility of the unstimulated intestinal strip. However, when used orally 10 times on 12 patients with stomata, absolutely no effects were recorded on the balloon-kymograph. Other recent work on pavatrine<sup>20</sup>, and two other diethylaminoethyl esters of fluorine - 9 carboxylic acid designated as "D" and "X", attacked the problem from a different angle by injecting the drugs directly intragastrically, intraduodenally and intravenously in doses large enough that they produced side-effects equivalent to those of therapeutic doses of atropine. They concluded, in brief, that none of these drugs was so effective as atropine intravenously. However, intragastrically or intraduodenally the synthetic drugs produced a greater and longer-lasting reduction in gastric and duodenal motility than did atropine. They suggest that the response of gastric motility to these drugs is via the duodenal mucosa and may be mediated by a duodeno-gastric reflex.

The three drugs described above are used as samples. Each represents a different proportion of neurotropic and myotropic activity as measured on the isolated strip of gut, novatropine being largely neurotropic, trasentine both neurotropic and myotropic, and pavatrine largely myotropic. Other drugs described both in advertising and medical literature are: eumydrine, syntropan, perparin, amethone, octin and several, recently synthesized, known only as NU-72-4D and "D" and "E" mentioned above. The newest on which scientific literature is available is dibutoline. Despite glowing clinical reports<sup>21</sup>, its measured effects when administered orally were equivocal to say the least.<sup>22</sup> Like most of the others, however, it shows prompt but very short-lasting effects when administered intravenously or intramuscularly.

The following is an attempt to summarize the present status of gastro-intestinal anti-spasmodics from a pharmacological point of view:

1. There are a good many drugs which have striking effects in reducing tone and motility in the isolated intestinal strip. Their actions may be neurotropic, myotropic or both.
2. Most of these drugs will produce similar effects when administered parenterally, and especially intravenously or intramuscularly, in the living human.
3. In doses as recommended by the manufacturers, none of the drugs, with the possible exception of atropine, can be scientifically shown to be effective orally.
4. There is evidence that some of the synthetic drugs, used in doses large enough to produce side-effects equivalent to those of atropine,

will, when applied directly to the duodenal mucosa, produce long-lasting reductions in motility.

5. Such drugs as reduce motility *in vivo* rarely at the same time reduce tone. There may have to be positive sympathetic stimulation in addition to parasympathetic inhibition, such as using ephedrine with atropine, in order consistently to reduce both tone and motility. A loss of parasympathetic activity does not necessarily mean, as we have long supposed, that there is a compensatory increase in sympathetic activity. The ephedrine-atropine combination is, unfortunately, not therapeutically practical because of the undesirable side-effects of both drugs.

Finally, it is obvious that we have not got what we need: an effective anti-spasmodic drug which acts locally in the gastro-intestinal tract to reduce tone and motility for reasonably long periods without, of course, substituting a paralytic ileus and without toxic side-effects.

#### *The Therapeutic Use of So-Called Anti-Spasmodic Drugs:*

We have come a long way only to learn that there is not an anti-spasmodic drug. Nevertheless, in the laboratory negative results are as valuable as positive, and there is no reason why the same dictum should not apply here. Despite the fact that scientific investigation has shown that these drugs are ineffective when used orally in therapeutic doses in clinical experiments, the literature is full of clinical reports of their great value as therapeutic agents. Are we, therefore, to assume that they are effective only as placebos and that their power comes only from the authority and prestige of the physician who prescribes them? The answer to the latter question, despite scientific findings, is not necessarily "yes". Most patients investigated scientifically had organic pathology in the form of ulcer, ileal stoma, or colonic stoma. It is quite possible that the drugs may be pharmacologically much more effective in purely functional disorders. We must also remember that both physiology and pharmacology can be easily upset by emotion-arousing experimental situations, particularly when they involve such complicated apparatus as balloon-kymographs. Then too we must bear in mind that even if they be placebos they are, at least, placebos with "good intentions" and that in therapeutics a placebo which works in a reasonable number of cases is, if used with intelligent artistry, a device worth using and honouring.

Since we are dealing with psychogenic disease, it must at once be obvious that there can be no substitute for psychotherapy in producing a cure. Indeed, the use of drugs of any kind in these disorders without attention to psychotherapy is very likely to produce more harm than good. This single fact, therefore, enables us to formulate a set of basic rules for the use of all anti-spasmodic drugs:

1. The patient must be told that the only purpose of the drug is to reduce his distress by reducing his symptoms and that it will not

have the slightest effect by itself in curing his disease. Your exact instructions might not be so blunt but you would make sure that there was no doubt in the patient's mind that the drug was not his salvation.

2. If the drug be not effective within a week one might make one or two trial increases in the dose, or make one attempt with another drug, but if it be still ineffective the drug should be promptly withdrawn with proper explanation. There is no point in keeping the patient in hope that there might be a drug which will help him.
3. The drug should not be taken for more than a few days after a symptomatic "cure" has been obtained. Since many forms of emotional stress will bring on an "attack", it might happen that the patient will get a second attack while he is still under treatment for the first and will promptly lose all confidence that the drug can help him even symptomatically.
4. If the patient keeps returning with successive attacks it is often wise to abandon anti-spasmodic drugs even though they appear to help the individual attack. It must be remembered that these drugs are, in the last analysis, only a "prop" and if used too often the patient will lose all ability to "stand by himself" and complete cure will go beyond reach.

These are very general rules. There may be some exceptions but they are indeed few. For instance, an intelligent patient with good insight might use an anti-spasmodic drug for a few days at the beginning of successive attacks to relieve his pain and thus assist him to "get over the hump" as it were. However, what must be remembered is that the most desirable progress comes only when he can cure his attacks by himself and final cure only when the attacks do not occur at all.

Before describing more specific rules of therapy it must be re-emphasized that they can concern only the truly functional case where there is still no evidence of organic pathology. Once disease such as ulcer enters the scene, many other therapeutic factors must be taken into consideration and the same rules regarding the use of drugs do not apply. However, having made a diagnosis of a functional disorder, one must to some extent assay the parts that spasm, hypersecretion and inflammation (the proportions of these factors vary according to the individual and the part of the tract concerned) are playing in making up the total symptom complex.

With the common and varied "dyspepsias" of the upper tract it is always possible that there is a fairly important element of gastric hyperacidity—at least it is common enough, and dangerous enough so far as the pathogenesis of ulcer is concerned, that it seems wise to take prophylactic measures against it, even though a goodly proportion of those patients with extremely chronic functional dyspepsias go through life without developing a sign of an ulcer. The use of prophylactic anti-acid

medication, aluminum hydroxide, magnesium trisilicate or one of the newer resins is, therefore, a sound therapeutic effort. Sedation likewise is valuable in reducing both the psychic and muscle tension which so frequently accompanies the disorder both as cause and effect. The barbiturates in sedative doses are, for this reason, also worthwhile therapeutic adjuncts.

But what about anti-spasmodics? We have our tongues in our cheeks when we use them at all—shall we use them completely as placebos—or shall we include at least an element of pious hope? I have suggested that the scientific evidence does not necessarily encompass the final and complete answer. I suggest that in using one of the newer synthetic drugs such as pavatrine or dibutoline one is losing nothing so far as placebos are concerned and is gaining a possibility, albeit distant, of achieving an effective pharmacological result. I suggest that it be used in the same manner in which belladonna is used—that is, to increase the dose until toxic effects appear and then reduce the dose slightly from that point. This method means several things: first that one cannot use an anti-spasmodic in the same mixture as an anti-acid and a sedative—it must be administered separately so the dose can be altered at will; second, that, since most of these drugs come in tablet form, they be used in the smallest tablet available so the dose can be altered more easily or else, and this is to be preferred, administered in liquid form, if available, for the same reason.

Disorders of the lower tract present different problems. Patients frequently present with symptoms of excessive peristalsis in the entire lower bowel with no complaint other than bouts of severe crampy pain. The medication in this type of case might well be identical in content and method to that for the upper tract syndromes, except, of course, that anti-acid medication is unnecessary. Mucous colitis, however, is one of the most difficult psycho-somatic problems in all medicine. So far as anti-spasmodic drugs are concerned, it is obvious that one which will also reduce secretory activity is certainly to be desired. We, therefore, must come to the neurotropic and parasympatholytic atropine which is generally recognized to reduce colonic secretions<sup>17</sup>. It may be given either as atropine sulphate or belladonna and in doses which cause slight toxic effects. Spastic constipation, according to most authorities, is better treated without anti-spasmodic drugs of any kind. The problem here appears to be one of restoring normal inter-segmental relationships and, while it is claimed that some of the synthetic agents will accomplish this, there is no supporting clinical or scientific evidence.

Let us for a final minute return to the patient described earlier. We have diagnosed his complaint as functional and largely spastic. We have discussed his problem with him and outlined its nature. We have taken great care that he does not get the idea he is neurotic else he will interpret this as a sign of personal weakness, something he cannot permit in

himself, clap his hat on his head and leave the office to begin a typical campaign of renewed self-discipline. Since this aspect of his personality had much to do with his being in the office in the first place, such action can only compound his anxiety, his tension, his pain and our difficulties in treating him. We have made a start at psychotherapy by trying to lead him to a personal realization of his characteristic emotional patterns and habits which have helped bring him to this state; we have perhaps pointed out the value of reasonable eating and drinking habits without actually giving him a diet which will continue to draw attention to his illness—for dietary regimens, like medicine, can, if improperly used, do more harm than good in these disorders. Finally we have handed him a four or five day supply of combined sedative and anti-acid drugs, a separate supply of an anti-spasmodic drug and fully instructed him in their use, their purpose and their limitations. We can then ask ourselves what exactly we hope to accomplish by giving him medicine at all. I think the answer lies in an understanding of the dynamics of the pathogenesis of his illness—he has proceeded from anxiety to tension to spasm to pain and back to more anxiety. The answer to our question, therefore, is that the intelligent use of anti-spasmodic drugs helps us break into that vicious cycle at a second point—it enables us to perform a therapeutic "pincers movement". By psychotherapy we are already trying to break in at a point between anxiety and tension where lies our main objective. But the cycle may be most vulnerable at a point between pain and anxiety and to break in here by the use of drugs may considerably expedite a final cure. If anti-spasmodic drugs accomplish this, and the evidence is that they frequently do, it is worth-while to use them, to experiment with them and probably always to use the latest in the expectation that, sooner or later, there will be one which is scientifically effective.

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*"Where there is love for humanity, there is also love for the art of medicine."—Hippocrates.*

*"Even in populous districts, the practice of medicine is a lonely road which winds uphill all the way and a man may easily go astray and never reach the Delectable Mountains unless he early finds those shepherd guides of whom Bunyan tells, Knowledge, Experience, Watchfull and Sincere."—Osler.*

## OSLER AT JOHNS HOPKINS\*

By C. B. FARRAR, M.D.

WILLIAM OSLER was one of the four giants of medicine who built the Johns Hopkins Medical School. It was an experiment in the teaching of medicine, calculated to do what nowhere else in America had been attempted. The school founded by these four men and the group of great teachers they gathered about them revolutionized medical education on this continent.

Immortalized in the record of what they did, the memory of the original four is also perpetuated in Sargent's splendid painting, "The Four Doctors," which hangs in the Welch Memorial Library in Baltimore. These four, in the order of their appointment, were Welch (1884) professor of pathology; Osler (1888), professor of medicine and physician-in-chief to the Johns Hopkins Hospital; Halsted and Kelly (1889), heads respectively of surgery and gynaecology.

It would be difficult to bring together to launch a new and pioneer undertaking four men of more widely differing personalities; but they worked together in "unity, peace and concord" and evolved a medical curriculum that set the pattern throughout the country.

To appreciate the labours of this quartette, and of Osler in particular, in inaugurating an unique educational movement, it is necessary to look for a moment at the background and the setting in which they did their work. For if it is true that they created an exceptional medical school it is also true that the conditions under which they laboured were exceptional and challenged and brought out the best that was in them. It was a case of individual and environment perfectly adapted to each other for achieving great results.

In the background were two remarkable personalities, the Baltimore merchant and philanthropist, Johns Hopkins, and the first president of Johns Hopkins University, Daniel Coit Gilman.

The munificence of Johns Hopkins which provided for a new kind of university and a new kind of medical school may be regarded as a consequence of a disappointment in love. He and his cousin, Elizabeth Hopkins, were anxious to marry, but the young woman was overruled by her parents' objection and neither ever married. Having no children of his own, Johns Hopkins dedicated the bulk of his fortune, some seven million dollars, to the education of the youth of the nation and to medicine.

A most significant feature of this double bequest was that no strings were attached. The trustees of the two institutions were to have *carte blanche* to act according to their best wisdoms. Yes, there were two conditions, but of a most salutary kind. In a letter to the trustees of the hospital in the year of his death (1873) Mr. Hopkins instructed that they were to secure "surgeons and physicians of the highest character and of the greatest skill." This admonition is understandable when one con-

\*Read at the Osler Society Banquet, U.W.O., March 8th, 1950.



siders the general standards of medical education in the United States at that time. The other condition was that the conduct of the hospital was to be "undisturbed by sectarian influence, discipline or control." Moreover, the institution "should ultimately form a part of the medical school of the university."

These unique conditions made possible the launching of the Johns Hopkins Medical School upon an entirely new plan and so made possible also the splendid accomplishments of the men who were selected to do the launching.

President Gilman came to Baltimore and opened the university in 1876; the hospital was not opened until 1889, and the medical school not until 1893. These dates and intervals are important.

It was Gilman's purpose to build a university according to a new pattern, one that should be dedicated as a major objective to graduate studies, to prepare mature students for careers as teachers and investigators. The same idea was to prevail in organizing the future medical school; but the president knew that the standards of medical education throughout the country were far below what they should be, and also that young men were entering medical schools without suitable preparation. The first step therefore was to provide this requisite premedical program, the main features of which were physics, chemistry, and biology, together with French and German; and such a course was promptly instituted. All Hopkins undergraduates who intended to study medicine were required to take this course. Remember this was in the early eighteen-eighties. It was a discipline in medical training such as existed nowhere else in America.

The first of the "Four Doctors," William H. Welch, was appointed professor of pathology in 1884. By that time the general plan of the medical curriculum had been outlined, and from then on Welch was to exercise a directing influence in its organization.

The opening of the medical school had to await the completion of the hospital, which was not ready until 1889, but as events turned out it had to wait four years longer.

These delays were discouraging at the time, but had they not occurred it might not now be possible to look back to the "Heroic Age" of medicine in America. President Gilman was projecting plans for the medical school coincidentally with the organization of the arts faculty, but in that year, 1876, Osler was but 26 years old, had graduated in medicine from McGill University only four years earlier and had just been appointed pathologist to the Montreal General Hospital. The other three of the immortal Four were all younger than Osler, and none was ready in 1876 for the important post he was to fill later. It seems providential, therefore, that the hospital was so long abuilding and that the university's depleted funds delayed the opening of the medical school until 1893.

Osler was in his fortieth year when, as Number Two of the immortal Four, he joined Welch on the medical faculty. His fortieth year! Seventeen years later he was to remark that "all the great advances have come from men under forty," — his own record calling to question his own saying. The year following his arrival in Baltimore the hospital opened its doors and Osler assumed the duties of physician-in-chief. There were still four years to go before medical students would be claiming a major portion of his time. The financial misfortunes that caused this delay may be regarded as providential in another respect; they gave the Chief time to write his famous textbook which appeared in 1892, just a year before the medical school opened.

Just here it is appropriate to mention the debt medical education in America owes to the women of Baltimore. One-half the endowment the university received by the will of Johns Hopkins consisted of shares of Baltimore and Ohio Railroad stock. In 1887 this railroad suspended dividends, and the consequent loss of income to the university delayed completion of the hospital and made prospects for the medical school precarious indeed. At this juncture a group of young women, daughters of trustees of the university, set to work. They formed a committee both to contribute and to raise money and caused other committees to be organized across the continent. The objective was half a million dollars, a sizeable sum in those days. It was only provided eventually through a substantial contribution by one of the Baltimore committee, Miss Mary E. Garrett. But this act of grace was not without stipulation. The ladies made conditions. No student should be admitted to the medical school who had not completed a full preparatory university course such as the Hopkins had already set up; and women were to be admitted on the same terms as men. There were no women in medical schools at that time. Welch and Osler had their misgivings, but there was no alternative. The conditions and the gift were accepted and the medical school became a reality. Osler remarked to Welch that they were fortunate in coming in as professors for they would not have been accepted as students.

When the Johns Hopkins Medical School opened in the autumn of 1893 the original Four had grown into a faculty of fifteen exceptional teachers. The entering class comprised fifteen men and three women.

The closing years of the 19th century and the opening years of the 20th have been referred to as the Heroic Age in American medicine. With equal fitness they may be called the Golden Age. It may be doubted if ever before or since such a galaxy of first magnitude personalities in medicine has ever been assembled at one time and in one place.

But our present concern is with one man, and I must try to tell you what Osler meant to a Johns Hopkins medical student at the turn of the century.

He first took notice of us in our third year and kept us under his eye throughout the final two years of the course. During these two years the medical student of our time at Johns Hopkins had the priceless boon

of fully 200 hours of instruction from Dr. Osler — a generous allowance by any reckoning. It is not difficult to understand that so ample and rich a relationship could not fail to make on the mind of the student an indelible impression of the quality of the Chief both as a teacher and as a human being — an impression that years have not dimmed and that lives in memory as one of the peaks of experience.

But there was one feature of the instruction that demands special attention, namely, the ward visits with students during the fourth year. This innovation introduced in medical education by Osler was of inestimable value. Cushing dedicates his "Life" to medical students "in the hope that something of Osler's spirit may be conveyed to those of a generation that has not known him; . . . lest it be forgotten who it was that made it possible for them to work at the bedside in the wards." And in his address to his students, colleagues, and friends in Baltimore on leaving America in 1905 Osler said: "I desire no other *epitaph* . . . than the statement that I taught medical students in the wards, as I regard this by far as the most useful and important work I have been called upon to do."

The fourth-year class was divided into four sections, each section serving for two months in the wards as clinical clerks, and it was during this period that we accompanied the Chief on ward rounds three mornings a week at nine.

May I take you to one of those ward visits? It is necessary to be punctual. Tardiness is not looked upon indulgently. We make it a point of honour to assemble in the passage outside the ward a little before 9 o'clock. In the brief interval there is almost the hushed expectance of a theatre audience awaiting the appearance of the great actor. But Osler is no actor; he is at all times his own natural self, displaying that fine blend of easy informality and native poise and dignity that betokens greatness. The Chief appears, humming a tune, probably improvised. The group divides to let him pass through and lead the way; as he does so he will perhaps link his arm in that of one of the students and march with him at the head of the column into the ward. The student who enjoyed the distinction of walking arm in arm with Osler that day would later tell his children about it, yes, and his grandchildren.

In those days Johns Hopkins was the only medical school with the college degree qualification for entrance, and classes were naturally small. I think there were forty-four in our year. The class being divided into four sections for these ward clinics, each one in the group would be assured a bedside position as we passed from patient to patient. What we learned on those ward visits was in two parts. First, the direct instruction and demonstration. The second part was something that could not be put into words. It was the Oslerian manner with patients. To each he comes with a word and a look, almost like the greeting of an old friend, that puts the patient at ease at once. He stands at the head of the bed, his stethoscope hooked in the armhole of his vest (a trick we all

imitate), his head cocked a little to one side, the fine scrutiny in his downward glance so veiled by the look of friendly interest and sympathy as to be imperceptible. He has a jocular or reassuring word for the patient as often as a word of guidance for the student. About each bed we are just a little family party, and it is often apparent that the one who happens to be in bed has the satisfaction of feeling that he is a pretty important member of that party. (You will note that I am putting all this in the present tense. It seems the right way to say it.)

The ward visit by an instructor followed by a troop of students is not always the most pleasant thing for anxious and sensitive patients. To lie there and have one's heart murmur or tumour exploited may not be exactly conducive to comfort and well-being, and it is not unheard of that even casual and presumably harmless remarks of the physician in the patient's hearing have been ill-advised or misunderstood and have contributed to the sick person's complaints. These are the "iatrogenic" symptoms which, unhappily, have been common enough to earn a place in the dictionary. It is difficult to conceive of such symptoms resulting from Osler's ward teaching. On the contrary, there was evidence that patients looked forward to his visits and were buoyed up by them. To be talked to and about by Osler was an experience and a distinction as well as a subtle influence for good.

Was it psychotherapy that he used? It was, and of the best kind, although he never called it by that name. Psychotherapy as such was not a subject of instruction during Osler's American period. Today it has in many quarters become a very complicated performance, and one almost gets the impression that it is regarded as the one all-important method of treatment. That it is of great importance in medicine generally there is of course no question, but in the hands of not a few operators it has been developed into a highly artificial technique and as complicated as the Ptolemaic system. Contemporary literature on psychotherapy too often suggests that the therapist is more concerned with elaborating his psychological manoeuvres than in dealing in a common-sense way with the patient — in making the patient fit his preconceived theories than in adapting the most suitable and simplest treatment measures to the patient. Osler's psychotherapy was not a studied and learned procedure; it was an emanation of a sensitive and fine personality that understood how to handle people. He had a remarkable gift of empathy. There was healing in his voice. The vocal tone, the facial expression, the chosen word, all united to enhance the effect of the treatment measures he might use or the advice he might give. That anomalous thing, psychosomatic medicine, which Stanley Cobb has characterized as "a glaring example of loose talking and loose thinking," had not been invented in Osler's day in Baltimore; but his own therapeutic philosophy was consistently holistic and can be summed up in one of his sayings: "The good physician treats the disease, but the great physician treats the patient who has the disease."

To improve his students' powers of observation for accurate diagnosis Osler would urge that we follow the "method of Zadig." Few of us, perhaps, had ever heard of Zadig, but most of us, probably, attended promptly to a needful extension of our education by reading Voltaire's delightful tale of Zadig, the young man of Babylon, who by the acuity of his observation achieved a discernment that seemed miraculous and was as wise as it was possible for a man to be.

Another item in Osler's teaching was the practice of living in what he called "day-tight compartments." When he was 23 years old he had come upon this comment of Thomas Carlyle: "Our main business is not to see what lies dimly at a distance but to do what lies clearly at hand." This thought became a keynote in Osler's philosophy — not to cross bridges, not to borrow trouble, also not to count chickens — to live in day-tight compartments, sufficient unto the day. This habit he recommended in his lecture, "A Way of Life," to students of Yale University in 1913.

The word "charm" has often been used in describing Osler's personality. It is a most appropriate term, with all that it implies; and it goes far to explain his influence upon his patients (and indeed upon all who came in contact with him) and why he was so well beloved by those in many parts of the world who had known him. His students were acutely conscious of this quality in him. Along with the vivid impression of his teaching he communicated the warmth of his spirit, which made the lesson a lively experience and a lasting memory. In every clinical demonstration he exemplified and inculcated both the art and the science of medicine.

Our most intimate association with the Chief was during our clinical clerkship in the fourth year when, each Friday evening, we were guests at his house — the famous 1 West Franklin Street. Our small group of 10 or 12 sat around his dining table and talked about the clinical events of the week. For historical background Osler would bring out some of the rare volumes from his medical library. These were memorable evenings and not less pleasant by reason of the biscuits and beer that were provided.

William Osler was a true humanist. He wanted his students to become something more than good clinicians, researchers, or teachers. He sought ever to inspire a love for the history of medicine and of science, indeed for the cultural history of man. His own writings reflected his wide acquaintance with great literature, especially the classics.

The first book he purchased to start his library was a Shakespeare; but this book was lost. "Some son-of-Belial stole it!" he reported. The second book, which thus became the first in his permanent collection, was the "*Religio Medici*" of Sir Thomas Browne. And this little volume in red leather, purchased in 1868, journeyed and sojourned with him

through the remaining 51 years of his life. It remained, as Dr. William Francis records, "his favorite copy of his favorite work of his favorite author." It had its influence on his literary style. The "*Religio*" was not cremated with him, as was rumoured, but rests under glass in the *Bibliotheca Osleriana* at McGill University, where I am sure Dr. Francis will gladly show it to any of you who may pass that way. On the fly-leaf Osler wrote in pencil, on his death bed, "I doubt if any man can more truly say of this book, *Comes viae vitaeque*."

Appreciation of Osler's devotion to humane letters was expressed by a high honour that came to him in 1918. He was elected President of the Classical Association and the following year, a few months before his death, he delivered the presidential address. What this recognition meant will be clear when we recall that he followed the great Hellenist Gilbert Murray in the president's chair and had in fact been nominated by him as his successor. In his nominating speech Gilbert Murray spoke of Sir William as "not only one of the most eminent physicians in the world, but [one who] represents in a peculiar way the learned physician who was one of the marked characters of the seventeenth and eighteenth centuries and stands for a type of culture which the Classical Association does not wish to see die out of the world." Osler richly exemplified that "type of culture" and promoted its cultivation in his students and associates.

In his many-sided nature there was one prominent feature, without mention of which no story of Osler would be complete, and that was his sense of humour. He was an incurable joker. The Peter Pan of his youthful days and prankish ways was never quite outgrown. Many of his jests and pleasantries have been told and retold and have become part of the Osler legend. There was the polymastia case. As the patient's chest was bared for examination there were disclosed two normal breasts and below these two additional pairs, the six nipples neatly aligned in two rows. The Chief quietly inquired: "And how many children have you, madam?" "Two, Doctor Osler." "What a pity! And the table all set for six."

Known among his friends as a hoaxer, some of Osler's true stories of extraordinary medical experiences were liable to discount. In the days of the *Canada Medical and Surgical Journal*, which became the Canadian Medical Association Journal, he was a regular contributor of brief medical items — case reports, historical and literary notes, etc. In the January, 1888 number, page 376, will be found this entry signed by Dr. Osler:

"Dr. Parvin's paper on injuries to the foetus (Med. News, Nov. 1887) reminds me of an interesting experience which I had in the North-West in 1886, which is worth placing on record. Mr. Fred Brydges had kindly met our party at the Portage to take us over the Manitoba and North-Western Road, and he mentioned that two days before, a woman, while in the water-closet on the train, had given birth to a child, which had dropped to the track and had been found alive some time after. I

was so incredulous that he ordered the conductor to stop the train at the station to which the woman had been taken that I might see her and corroborate the story. I found mother and child in the care of the station-master's wife, and obtained the following history: She was aged about 28, well developed, of medium size, and had had two previous labors, which were not difficult. She had expected her confinement in a week or ten days, and had got on the train to go to see her husband who was working 'down the track'. Having a slight diarrhoea she went to the water-closet, and while on the seat labor pains came on and the child dropped from her. Hearing a noise and groaning, the conductor forced open the door and found the woman on the floor in an exhausted condition, with just strength enough to tell him that the baby was somewhere on the track, and to ask him to stop the train, which was running at the rate of about 20 miles an hour. The baby was found alive on the side of the track a mile or more away, and with the mother was left at the station where I saw her. She lost a good deal of blood, and the placenta was not delivered for some hours. I saw no reason to doubt the truthfulness of the woman's story, and the baby presented its own evidences in the form of a large bruise on the side of the head, another on the shoulder, and a third on the right knee. It had probably fallen between the ties on the sand, and clear of the rail, which I found, on examination of the position of the hole in the closet, was quite possible."

In the issue of June, 1888, page 734, we find the following note by Osler:

"The highly improbable obstetric tale which I told in the January number has been too much for the credulity of many of your contemporaries, and to their criticisms I meekly submit, knowing well that in obstetrics and gynecology I cannot lose a reputation for veracity; but I am glad to see that Mr. Brydges has come to my rescue and that much fuller details of this truly remarkable case have been published in one of the Manitoba papers and have been copied into a recent number of the New York Medical Journal. With the doctor who delivered the placenta and the conductor who found the child on the track I now leave the skeptics."

As an interesting corollary, my friend Dr. Norman Gwyn told me of a conversation with his uncle Sir Edmund Osler in which he had expressed some doubt as to the railway train confinement; whereupon Sir Edmund assured him that the report was quite true, that he himself was of the party on that northern trip long ago and had personal knowledge of the events as reported by his brother William.

Osler could relish a joke as well as perpetrate one. May I relate one amusing incident from the Baltimore period. As an old story it has often been repeated and has even found its way into print. My only excuse for reviving it now is that it is one of the personal reminiscences upon which these present remarks are based:

The scene is the hospital amphitheatre on Wednesday morning just before noon; the occasion, Osler's famed weekly clinic. The subject is *diabetes mellitus*. The circles of seats are already filled. Down on the floor are a table and beside it a chair for the Chief. The residents are standing about, waiting to assist with the clinic. It is the old familiar scene. But today there is something different. One of the girls in the class — our year was well-supplied with the feminine element, (one to every two men, as I remember, although that created no special problem) — has seen to it that this particular clinic shall be properly presented. On the table in a vase is a gorgeous bunch of sweet peas. Also, each student is wearing a spray of the same flower. The amphitheatre from top row of seats to pit is as gay as any flower garden. The Chief enters, glances about, a split-second perhaps of wonderment, then he gives way to his hearty, contagious laughter, the echoes of which ripple around the rows of seats. The tension thus eased, the clinic on *diabetes mellitus* proceeds according to protocol. Is it surprising that the little spray of flowers which each wore that day was carefully pressed and mounted on a page in our medical bible, Osler's "*Principles and Practice of Medicine*," where the subject of that Wednesday clinic is described?

And there on page 430 of my copy of the famous textbook that mounted botanical specimen still remains, and a sentiment clings to it that makes the book more precious. The flowers are faded a little — they cannot be blamed for that, having bloomed so long ago. But they bring a glow to the memory that they were within the range of Osler's vision on that far-off day and beamed their brightest in response to the notes of his good-natured laughter.

May I close with another reference to the ancient *Canada Medical and Surgical Journal*. In December, 1887, page 319, Osler wrote:

"Rarely has a more graceful — and truthful — estimate of our profession been put on record than in the opening sentences of the dedication of Robert Louis Stevenson's recent volume of poems, *Underwoods*. 'There are men and classes of men that stand above the common herd: the soldier, the sailor and the shepherd not unfrequently; the artist rarely; rarelier still, the clergyman; the physician almost as a rule. He is the flower (such as it is) of our civilization; and when that stage of man is done with, and only to be marvelled at in history, he will be thought to have shared as little as any in the defects of the period, and most notably exhibited the virtues of the race. Generosity he has, such as is possible to those who practise an art, never to those who drive a trade; discretion, tested by a hundred secrets; tact, tried in a thousand embarrassments; and what are more important, Heraclean cheerfulness and courage. So that he brings air and cheer into the sick room, and often enough, though not so often as he wishes, brings healing.'"

What better picture of Osler himself and of the ideals for which he stood!



## FRACASTORIUS — MEDICAL POET\*

1483-1553

By JOHN TWELVES, B.A., '53

IN THE TOWN OF VERONA, Italy, in the year 1483, the ancient family of Fracastoria was blessed by the birth of a son destined to fame the name of town and family with his writings. Typical of the romantic Italian soul of that era, there are told of the early days of Fracastorius two wondrous tales—that he was born with his lips so unparted that a surgeon was called to separate them; and that, while yet an infant, he remained unscathed in his mother's arms when she was killed by a bolt of lightning. It would seem, therefore, by all standards of that day, not too incredible that the youth should show early signs of unusual ability and be sent to Padua, that great centre of learning. He left the school to enter the army and after seeing his commander and friend, Livianus, defeated and captured, he returned to his home in Verona.

It is not known where Fracastorius received his training in medicine. However, it is on record that he was extremely successful as a physician, possibly the more so because he practised for the love of his profession and not for the worldly rewards. Medicine did not claim the whole of his energies. He was an ardent poet, astronomer, cosmographer and natural philosopher.

Fracastorius lived his 71 years in Verona but was in constant touch with the world by way of an extensive correspondence with many distinguished men in science and in letters. He died of apoplexy in 1553 and immediately monuments to his memory were built at Padua by his friends and fellow citizens.

It is recorded by one of his biographers that, 'A lively air was spread over his countenance, that displayed the serenity and ingenuity of his mind; he was of low stature, but of good bulk, his shoulders broad, his hair black, his nose short and turning upwards by his continual contemplation of the stars.' It seems that, if nothing else, the author has provided us with the etiology of 'button-noses'!

The scientific renown of Fracastorius rests upon his composition, *De Contagione* and his poem on syphilis.

*De Contagione* presents among other things three items of prime importance — a clear statement of the problems of contagion and infection, a recognition of typhus fever, and a remarkable pronouncement on the contagiousness of phthisis.

Fracastorius in his active professional life had lived through an era when the spread of syphilis was rapid, and when there were repeated

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\* Read at a meeting of the University of Western Ontario's "Osler Society" on October 4th, 1950.

outbreaks of the plague and exanthematic typhus, so that he had ample opportunity to study them. He says that there are three fundamental classes of infections — diseases infecting by contact alone; those rendered infectious by means of an intermediate agent, the fomites, such as garments, eating utensils, and so on; and those which infect at a distance through the air, as the pestilent fevers. The first he compares with the putrefaction that spreads from a mouldy grape to a peach lying in contact with it. The second he differs from the first simply in that the seeds of contagion, *seminaria contagionum*, while remaining whole and unchanging, may travel by way of the fomites through a period of two to three years before infecting the second victim. His discussion of fomites was with an understanding new to the Medicine of his day. In fact he may have been the originator of the term. He seems to find those infections of the third class, those which act at a distance, even more curious and astonishing. The germs appear to be more powerful and have a greater faculty for penetrating the body. Besides this, they differ among themselves in that some attack trees and grains, others animals; some attack the old, some the young; some males, others females; and some the eyes, others the deeper organs, such as the lungs.

In 1505 and 1528 Italy experienced for the first time a disease, the symptoms of which were a high fever, early loss of consciousness and an extensive petechial and lenticular rash. Fracastorius describes the disease extremely well and points out that it differs from the plague and other such pestilent fevers, with which it had till that time been confounded. From his description we have no trouble in recognizing it as epidemic or exanthematic typhus.

With regard to phthisis he points out that habitual residence with a consumptive is one of the most common sources of the disease, the germs being able to remain in a room for a year or more.

By far, however, his consideration of syphilis is his greatest work, and, indeed, it gained for him the recognition of the world. It is in the poetic form; the original edition was a small *quarto*, issued from a Verona press, and not a very good example of the printing of the period. As was the vogue, Fracastorius dedicated his works to a dignitary of the Church, his friend, Bembo, Secretary to Pope Leo X. As the disease at this time was not considered completely of venereal origin, a dedication of this sort was not held in bad taste.

Not only was his description of the disease admirably observant and precise but he was the first to use the term, syphilis. After expounding the usual semi-superstitious cures Fracastorius writes,

“The greater part, and with success more sure,  
By mercury perform the happy cure;  
A wondrous virtue in that mineral lies.”

Its healing power was revealed to one Ilceus, a huntsman, who was afflicted with the disease in Syria. Callirrhoe, a goddess, directed him to get the precious metal from the 'spacious voids and subterranean roads', and after bathing in the lakes of liquid silver he was healed.

So Fracastorius tells us that as early as the 15th century the mercurics were in use, and his reference to the goddess is in accord with other sources which lead one to believe that their value was known for some centuries.

Osler, in his *Biographical Essays*, says of Fracastorius: 'He occupies a distinguished position in our annals as the author of the most successful medical poem ever written, and as the man from whom we date our first accurate knowledge of the processes of infection and contagion.'

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*A physician in a great city seems to be the mere plaything of fortune; his degree of reputation is for the most part casual; they that employ him know not his excellence; they that reject him know not his deficiency. — SAMUEL JOHNSON.*

*There is one kind of specialism which to some men is ruinous, and is mischievous to all; namely to cultivate apart either intellect or imagination. Specialize each as you please, but do not sunder them, nor neglect either of them. — ALLBUTT.*

## MEDICINE AND PHILOSOPHY

By EDWIN SEABORN, M.D., F.A.C.S., LL.D., '93

THE FIRST ORGANISMS to succeed the plants which invaded the earth from the sea were the herbage-eating reptilians, monsters with relatively enormous heads and mouths, adapted to the gathering and grinding of the great quantities of sedges necessary to maintain them, slow moving and rendered unsociable by the great area of pasture surrounding of necessity such slow-moving creatures.

Following them in time came the flesh-eating reptilians with small heads and long necks, adapted to their function of penetrating deeply into the body cavities of their victims.

All of these were egg-laying animals without thought or affection for their offspring. Cold-blooded, they took no comfort from the temperatures of their surroundings. Their only satisfactions were a full stomach and the sense of security given them by their enormous size or thick armour.

Following the reptilians in time came the small, agile mammalians, feeding on such concentrated foods as seeds and nuts. They were able to gather into groups. Among these, the child depended entirely on the mother, while the mother in turn depended on the child for the suckling which relieved the fullness of her breasts. These animals depended on quickness, ruse, or the protection afforded by trees. Warm-blooded, they huddled together for comfort and warmth. They learned that the warmest nooks faced the sun, that great ball of red which rose a mile or two in one direction and set a mile or two in the other. They noticed strange figures on the ground — shadows of themselves. How strange that these shadows should shorten and lengthen as the day passed! And the shadows of the trees! How strange that these moved to the "east" as the sun moved to the "west"! What great hands drew clouds across the sky? What angry hand hurled flaming brands to the earth? How more than brave was the creature who first drew flaming brands together! How more than wise was he who first carried fire to his cave! What must have been his reflections as he dimly realized that he had subjected the demon of the lightnings to his will! He barricaded his cave, he shouted in derision to other animals or warned his companions by imitations of their cries. So he originated a language. As the mother crooned to her baby she added soft words to the rude language of her husband.

To guard the creeping child the fire was raised on stones and these stones became an altar. The attendant became a priest, sustained by such as came to petition for some coals of fire. As he had been the instrument in the domination of the demon of fire so he became the interpreter to men of the wishes of the gods. As the mother, watching over her dying child, instituted the ART of medicine so the Priest-Physician, wondering

how he might circumvent the death of the child, instituted the SCIENCE of medicine. As he interpreted the forces of nature as magical so the remedies to be employed against death were magical. In his wondering was the beginning of philosophy.

As will be seen as this paper develops the greatest philosophical movements have been motivated by a few individuals. So we may suppose that he who subjugated fire instituted other advancements. He may have first broken the sticks across his knee, then broken them with a great club, which became an axe. So he chipped stones into knives and arrow heads. This was the Stone Age. In this period of time the ARTS advanced much more rapidly than the SCIENCES. Practice outstripped Theory.

The country which had advanced the farthest in Philosophy but which still pertained to the Stone Age was Egypt. The individual who made the greatest contribution to that advancement was named IMHOTEP.

He flourished some 3000 years B.C. As Grand Vizer to King Zoser he instituted the storing of grain and freed Egypt from the continual menace of Famine.

As the Architect of the Kingdom he built the Pyramid of Sakkarah, the Tomb of King Zoser, the first large pyramid to be built in the world. Its sides were not a continuous slope but rose in steps. Its base covered an area almost as large as the average block of land in any city. Its interior halls and chambers were lined with glazed tile of highest artistic merit.

As the Lector Priest of the Kingdom he saved by magic the bodies of the dead from the belly of the crocodile. By magic words he insured that the souls of the dead would continue to advance from stage to stage of perfection in the lower world.

As a Physician he built temples and instituted schools of medicine which were attached to them, notably that at Memphis. Here the people flocked and were cured and wrote tablets in praise of the Physician indicating their symptoms and the manner of their cures.

After the death of Imhotep poor people still flocked to the Temple and it was their continual devotion which resulted in his apotheosis and worship for 2,500 years or until all semblance of refinement in Egypt was destroyed by the many invasions of the barbarians.

While Imhotep failed to disassociate magic from medicine he commands the continued gratitude of humanity for formulating the axiom that the symptoms of disease are invariable and the action of medicine invariable also.

Following the death of Imhotep, 25 centuries elapsed before the institution of the next great epoch of advancement. The Greek, ARIS-

TOTLE, was its greatest protagonist. The subjects which most advanced Philosophy in this era were the stars in the heavens and the bodies of men.

Aristotle added much to both of these subjects. Of his additions to Astronomy I am incompetent to speak. In Physiology he wrote on Respiration, Memory and Recollection, Sleep and Waking, Youth and Age, Life and Death. His enemies charged him with practicing medicine. This may have been so, for although he was not a physician his father and associates were.

Aristotle created the whole of the Science of Logic; he also created the sciences of embryology and comparative anatomy. In these subjects he had no predecessor and no worth-while successor until the discovery of the microscope.

He formulated biological laws which obtain until this day: that the division of labour is physiologically advantageous: that development is from a general to a special form: that in some forms of life increase is by parthenogenesis: that development in the embryo is from the homogenous to the heterogenous form. Aristotle created the models on which almost all modern philosophy has been formed.

Other great figures of the Greek period were AESCULAPIUS, HIPPOCRATES who preceded him, and GALEN who followed. It is from Aesculapius that the Army Medical Corps of all nations derive their motif — a serpent twined around a staff. During an epidemic of plague at Rome a pilgrimage was made to Cos to secure the services of Aesculapius. As he boarded the ship a snake is said to have crept to the ship from the temple. The late Professor A. B. MacCallum showed the writer of this article a picture of the grape vine and arbor of Aesculapius at Cos secured when he made a visit in person to the Island.

HIPPOCRATES, a Physician born of a line of priest-physicians, was the first to cast superstition aside and to apply the principles of inductive philosophy to medicine. His treatise on epilepsy, the "sacred disease", is rightly named — "The Charter of Science." He says: "As regards the disease called sacred, it appears to me this is no more divine than other diseases. They who refer to such conditions as of the gods are as charlatans and conjurers and mountebanks, who claim to be excessively religious, and to know what is hidden from others. . . ."

GALEN was separated from Aristotle by 450 years. Galen wrote several hundred treatises on Philosophy, Hygiene, Dietetics, Materia Medica, Therapeutics, Physiology and Anatomy. At an early age he had been physician to gladiators and I wonder if he had not surreptitiously dissected the bodies of some of these. He was so faithfully accepted that his influence restrained advancement in medicine for some 1,300 years.

The next great period of advancement began only some 400 years

ago and was at first conditioned by the study of the heavenly bodies and later by the study of medical subjects.

COPERNICUS, by substituting the heliocentric for the geocentric system of astronomy, initiated the world's greatest scientific revolution. He graduated from the University of Cracow with the degree of Doctor of Medicine; later he studied law and later again entered Holy Orders. Following his astronomical discovery he spent a good period of every day in giving medical advice gratuitously to the poor.

GALILEO, who had been sent to Pisa to study medicine, while contemplating the swing of the cathedral candelabra and thinking of an instrument for the measuring of the pulse, had his interest in mathematics so aroused that he left medicine to study Astronomy. In watching the candelabra he noticed that no matter how far or how little a pendulum swung it always returned to its point of departure in equal times. While he did not discover the telescope he adapted it and made possible the viewing of the satellites of Jupiter, a demonstration of smaller bodies revolving around a larger, just as the earth and other planets revolve around the sun.

KEPLER, by his great skill in mathematics corrected the error of the Copernican system by demonstrating that the paths of heavenly bodies are not in circles but in ellipses. He thus removed the church's quite logical opposition to the new system. He formulated the laws that heavenly bodies move in ellipses with the sun as one of the foci: that the radius vector of an ellipse passes through equal areas in equal times: that the square of the periodic time of the revolution of a body around the sun is always equal to the cube of the mean distance of that body from the sun.

These seem small circumstances but never since Kepler's time has there been any sustained criticism of Philosophy in general.

As already said the first advancement was conditioned by the study of the heavenly bodies, the next was by the study of the body's diseases, and the name above all others attached to this period is that of PASTEUR.

As regards Pasteur. This great luminary in medicine worked under inadequate and discouraging conditions but his work has resulted in the delivery of Man from many of the plagues which had continually devastated the earth, and has given us hope that all infectious diseases will ultimately be banished forever from all the world. His work has profoundly modified surgery as well as medicine. And more still it has altered our religious belief—and last of all has changed our philosophy of life.

In the first part of Philosophy here described it was shown that practice preceded theory. In this the third great period, especially as it

applies to medicine, theory preceded and precedes practice inasmuch as imagination is the basis for experiments yet to be made.

All the remarks I have made are intended to demonstrate the part medicine has played in the advancement of Philosophy. Medicine reflects to what extent Man has mastered his surroundings; how great an influence he has had in the extension of his own life; that he has done this through his own efforts; that it was intended (at the Creation) that Man work out his own salvation; that (at the Beginning) inspiration came from the Almighty, and so still it does. Inspiration at one time or another comes to all of us. The attempt at the fulfilment of an idea may land us in error and disappointment but the sense of satisfaction which comes to those who succeed removes fear from this life and largely removes also the fear of death, and may perhaps be a sufficient oblation for wrongs committed.

It is altogether a false statement that Science is antagonistic to Religion. Rather it has resulted in the feeling that Man is co-partner with the Almighty. It has resulted in an immense elevation of mankind. I feel this spiritual elevation each time I hear that part of the Communion service of the Anglican Church — to my mind the sublimest words ever written by man: "Therefore with angels and archangels and with all the company of Heaven, we laud and magnify thy glorious Name."

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*"There is a time in every man's education when he arrives at the conviction that envy is ignorance; that imitation is suicide; that he must take himself for better, for worse, as his portion; that though the wide universe is full of good, no kernel of nourishing corn can come to him but through his toil bestowed on that plot of ground which is given to him to till."—Ralph Waldo Emerson.*

*It is with medicine as with mathematics; we should occupy our mind only with what we continue to know; what we once knew is of little consequence."—Saint-Bleuve.*



## THE MEDICO-HISTORICAL COLLECTION IN THE MEDICAL LIBRARY

By LLOYD G. STEVENSON, M.D., PH.D., '44

IT WOULD REQUIRE too much space to list all the acquisitions to the medical history collection during the last three or four years. The University had previously lacked many of the greatest classics of medicine, and large gaps still remain; but a beginning has been made toward a working selection of the chief writings of the great medical authors of the past. This, and not the purchase of bibliographic rarities, has been the aim. Consequently the best collected editions have been sought. Avicenna, Malpighi, Willis and Whytt, to choose names at random from various periods, are represented by their *Opera Omnia*, van Helmont by his *Ortus Medicinae*, Haller by his eight-volume *Elementa Physiologiae*. For Morgagni, we possess not only his *Opera* and *Adversaria Anatomica* but also, by a stroke of luck, the rare 1769 English translation of *De Sedibus*. An earlier classic of pathology, the *Sepulchretum* of Bonetus has also been acquired. Where an important book is beyond our present means, we have contented ourselves with second best: Hooke's *Micrographia*, for instance, is replaced for the time being by the *Micrographia Restaurata* of 1745, which has almost all of the original plates. The eighteenth century is particularly well represented because of a fortunate opportunity to purchase at low cost a large number of duplicates from the University of Bristol. Included among these are not only standard works of the Enlightenment but such special classics as Caleb Hillier Parry's *An Inquiry into the Symptoms and Causes of the Syncope Anginosa, Commonly Called Angina Pectoris*, Bath, 1799. An "association item" of particular interest is a presentation copy of Edward Jenner's *A Letter to Charles Henry Parry . . . On The Influence of Artificial Eruptions*, London, 1822.

Of comparable value for the study of medical history are several great bibliographic works, such as the compilations of Haller and the three-volume *Venerische Krankhuten* of Proksch. The medical historians from Sprengel to Sudhoff, Edelstein, etc., have not been neglected, but our holdings of modern works on the history of medicine are still unfortunately meagre.

Pride of place in the collection must be given to a fine copy of the second edition of the *Fabrica* of Vesalius, cornerstone of modern anatomical medicine. The title-page is not a brilliant impression but the famous plates are all present and in good condition. This book was purchased in part through the generosity of London doctors, whose names will be inscribed on a flyleaf.

It is to be hoped that students, alumni and local physicians will make full use of the growing historical collection. Its continued growth in extent and usefulness will depend on the support it receives from all who are interested in the history of medicine and in the Library of the Medical Faculty.



## Case Report



### AN UNUSUAL ACCIDENT

On August 6, 1950, Mrs. B., a farmer's wife of 56, was in her yard picking raspberries. She stumbled and fell, and felt some sharp object strike her on the lateral side of the right knee. She noted a small puncture wound just above the knee but did not think it needed attention. The next day there was soreness, swelling and redness around and above the wound, but she went to market, as usual, to sell eggs. On August 8, she consulted her physician who probed the wound, and found a foreign object in its depths. She was admitted to hospital for wound exploration.

On physical examination at the time of admission a puncture wound, the size of a dime, was noted three inches above the lateral condyle of the right femur. The lower half of the lateral aspect of the thigh was inflamed, warm, swollen, tense, and tender. There was a very slight sanguinous discharge from the wound. The lymph glands were not remarked on as enlarged. Her pulse was 110, she had a fever of 102°, but her white blood count was only 6,700, with neutrophils 86%, lymphocytes 14%. Sedimentation rate was 36 mm. in one hour. There were no other physical findings of importance. Pre-operative diagnosis was puncture wound, with retained foreign body.

On the day of admission, under general anaesthesia, an eight inch incision was made from just below the wound, upwards and the wound edges were debrided. At a depth of 3.5 cms. a segment of raspberry cane measuring 15 x 1 cms. was discovered. Surrounding its upper extremity was a considerable amount of sero-sanguinous fluid which was under pressure. The upper end of the raspberry cane appeared digested. The excised tissue and the cane were sent for bacteriological examination. Streptomycin 1.0 Gm., and penicillin 400,000 units were injected into the incision. The wound was packed open with vaseline gauze, wrapped in sterile bandages, and encased in light plaster. No sutures were used. A direct smear from the end of the cane was made at once, and showed polymorphonuclear leucocytes, and a moderate number of gram-positive rods.

On the evening of operation the patient received 3,000 units of antitetanus serum. Antibiotic therapy was begun with Streptomycin, 0.25 Gm., every six hours, and Procaine Penicillin, 400,000 units every twelve hours.

On August 9th, cultures showed a heavy growth of *Clostridium welchii*, a moderate growth of *Micrococcus pyogenes* (*Staph. aureus*), *E.*

coli, *Bacillus cereus*, and a white micrococcus. Following this report the patient was immediately given 40,000 units of anti-gas gangrene serum intramuscularly and then 10,000 units every six hours for the rest of the day.

On August 10th, one injection of 10,000 units was given. Cultures taken at this time showed no growth on direct plating; however, culture on fluid medium showed non-pathogenic *Clostridium cochlearium*.

By August 12th, the patient had a normal temperature; on the 14th the antibiotics were discontinued, the cast was removed, and the wound closed by secondary suturing. She was discharged as completely recovered on August 24th.

*Summary:*

On August 8th, a patient was admitted to hospital with a painful swelling above a puncture wound on the lateral side of the right knee. At operation a 15 cm. length of raspberry cane was removed, and the wound was packed open with vaseline gauze and encased in a padded plaster cast. The wound was infected with *Clostridium welchii* and *Micrococcus pyogenes*. The response to treatment with Penicillin, Streptomycin, anti-tetanus serum, and anti-gas gangrene serum was good. The patient was discharged as well on the 16th day.

—K. R. FERGUSON, '52.

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*"Learn to see, learn to hear, learn to feel, learn to smell and know by practice alone can you become an expert. Medicine is learned by the bedside and not in the classroom. Let not your conceptions of the manifestations of disease come from words heard in the lecture room or read from the book. See and then reason and compare and control. But see first."*

*"Do not waste the hours of daylight in listening to that which you may read by night. But when you have seen, read. And when you can read the original descriptions of the masters who with crude methods of study, saw so clearly."*

*"To study medicine without books is to sail an uncharted sea, while to study medicine only from books is not to go to sea at all."*

—Sir William Osler.



## TUBERCULOSIS

### A Global Study in Social Pathology

J. B. McDougall, 442 pp. E. & S. LIVINGSTONE LTD., EDINBURGH, 1949.

Dr. McDougall is on the section of tuberculosis of the World Health Organization. His book uses statistics from all countries, connecting them with readable discussions and explanations, comparing and rating methods of detection and control. For example, in an interesting account of B.C.G., its use in different countries is evaluated for various social groups, in techniques and in the use of control groups.

The book generally discusses the status of various methods of diagnosis and control of tuberculosis, including trends in mortality and morbidity. The author incidentally indicates the necessity of cooperation among health organizations, and also of standardizing the classification of results.

—H. THOMPSON, '52.

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## CLINICAL AUSCULTATION OF THE HEART

S. A. LEVINE AND W. P. HARVEY. 327 pp.

W. B. SAUNDERS COMPANY, PHILADELPHIA, 1949.

Impressed by the fact that not only general practitioners but specialists in cardiology were not applying all the information obtainable with such an inexpensive and expedient tool as the stethoscope, the authors discuss in detail the simple data pertaining to bedside auscultation that can be grasped and applied by any physician.

The sounds have been reproduced by phonocardiographs which are recorded in conjunction with electrocardiograms. First the normal heart with its many variations is described. Following this, the cardiac irregularities and murmurs of various pathological states are discussed as "heard" by the phonocardiograms.

In addition to the auscultatory findings, the book has been made more useful by comments concerning the related clinical conditions and therapeutic implications involved. Occasional specific experiences and case reports are presented for completion of this very excellent text.

—J. STEPHENSON, '52.

**ANKYLOSING SPONDYLITIS**

F. HERNAMAN-JOHNSON AND W. A. LAW. 200 pp., Illus. 41.

BUTTERWORTH & CO. (PUBLISHERS) LTD., LONDON, 1949.

This book is intended as a practical guide to the treatment of the disease in all its stages. The authors want to dispel the unjustified attitude of extreme pessimism towards this disease and show that the therapeutic approach to these cases should be one of hope and confidence. The points to be emphasized in treating this condition are:

- (1) that the earliest symptoms of spondylitis are not necessarily referred to the spine,
- (2) that changes in the sacro-iliac joints occur years before any crippling occurs and
- (3) that X-Ray treatment in the early stages of the disease will in most cases avert any serious consequences.

The first part of the book deals with the recognition of the disease and its treatment by all means short of surgery. Here the author stresses the beneficial effect of X-Ray therapy. However, the radiological plates in the book are not convincing, possibly because of inferior reproduction.

The second part deals with the recent orthopaedic procedures which have given new hope to cases formerly labelled as hopeless and discusses methods to prevent or overcome the deformities of the earlier and more acute stages of the illness.

On the whole, the book is well organized and very readable. The presentation of case histories adds to the interest.

—G. CALVERT, '52.

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**THE CRY AND THE COVENANT**

M. THOMPSON. 469 pp. DOUBLEDAY & COMPANY, INC., NEW YORK, 1949.

Here is a story told with passion and conviction of a man who all his life struggled on the side of truth. The man is Phillip Ignaz Semmelweis, the discoverer of the cause, and the method of prevention of puerperal fever. After tirelessly and relentlessly proving his discovery by experiment and statistical observation, the medical profession refused to acknowledge his brilliant work.

The book portrays vividly the emotions of this great man who never faltered in his attempt to convince medical men of the significance of his work. It is not only stirring and interesting, but also informative.

—J. BERGER, '53.



## THE MANAGEMENT OF OBESITY

D. E. RODGER, J. G. MCFETRIDGE,  
EILEEN PRICE,  
Canad. M.A.J. 63, 3, 1950.

Obesity can be defined as that condition in which there is an excess of fat in the tissues resulting in an increase of from ten to twenty percent above normal weight. The authors agree that the diagnosis of obesity can be made on clinical impressions. Differential diagnosis is rarely a clinical problem, but obesity must be clearly distinguished from such conditions as myxoedema, chronic induration from congestive heart failure and lipodystrophies.

A review of the literature reveals increasing evidence that excess calorie intake is the primary cause of obesity and that endocrine dysfunction has been astonishingly overestimated. Studies by Hochman, Bruck and Bronstein and his group showed that psychological factors were involved in obesity from excess calorie intake. Newbury concludes that obesity is caused by overeating and states several causes of overeating.

A low calorie diet with coincident psychotherapy is now being emphasized. This treatment has been successful in obtaining weight loss only when the patient co-operates faithfully. The authors advise that the dietary standards approved by the Canadian Council on Nutrition be explained to patients and that poor food habits be corrected.

The food allowance of a low calorie diet must be adapted to the patient's occupation and income. The patient should return for weekly checks regarding the diet and at all times be encouraged to continue the diet faithfully.

## Abstracts

Out of six hundred cases of obesity of all ages the largest number were found in the age group twenty to forty years. Of the six hundred, ninety-three per cent were female. As sufficient time had not elapsed to determine the success of the entire group, the results from sixty-four patients each of whom had visited the dietitian at least ten times are recorded. These patients were on a 1500 calorie diet with psychotherapy for an average of 21.96 weeks per patient, representing an average loss of 1.05 pounds per patient per week.

Since most cases of obesity were found in females, one wonders whether or not the female is more inclined to relieve frustrations and tensions by food. The male may have other outlets.

The authors have used a scheme of a relatively higher calorie value diet than other diets, and a slower weight loss. This has been intentional, since they believe that too rapid a weight loss results in mobilization of depot fat which can lead to a high blood cholesterol, which in turn may increase the likelihood of vascular accidents.

—N. L. MARSHALL, '52

## THE TREATMENT OF VARIOUS INFECTIONS WITH SINGLE DOSES OF 300,000 UNITS OF PROCAINE PENICILLIN IN OIL PLUS ALUMINUM STEARATE.

HIRCH, H. E.; AND KURLAND, W.

Am. Pract. 1:923-5, 1950.

This article illustrates the results of treatment of various mild to moderate infections, (lobar pneumonia, scarlet fever, otitis media, Vincent's angina and cellulitis) with 1 cc. of 300,000 units of procaine penicillin in oil with aluminum monostearate. In the hands

of the authors, this method of treatment of clinically established infections gave satisfactory results. The success of this single injection as compared to multiple injections may be an important consideration in its use.

In a series of ninety-two patients with lobar pneumonia, only two failed to respond to a single injection. Seven patients with serious complications died. In a series of forty-one patients with scarlet fever, all but three had negative throat cultures within forty-eight hours of a single injection of this drug and these became negative after seventy-two hours. Complications were readily cleared in all instances.

In otitis media, pharyngitis and cellulitis series, complete and prompt recovery resulted from single injections of 300,000 units of procaine penicillin in oil with aluminum stearate.

Reported failures with this preparation are considered to be the result of improper administration.

—C. C. L. BUCK, '52

#### GROUP PRACTICE AND MEDICAL EDUCATION

P. H. T. THORLAKSON,  
Canad. M.A.J. 63:336, 1950.

The science and practice of medicine is in a state of constant evolution. No longer is it possible for the individual doctor to acquaint himself with all aspects of medicine. Similarly, methods of training medical students have evolved from the apprenticeship stage to the long course of study in well-equipped medical schools and hospitals. The student, however, finishes his internship with some experience in treating patients encountered in hospital, but little contact with the larger group of patients not hospitalized, who form the bulk of medical practice.

Group practice could be the ideal solution to this problem since the doctor who specializes remains in constant contact with those in other branches of the profession and is allowed the availability of consultation with them.

A properly organized clinic, composed of men of high professional standing can be utilized as an import-

ant training ground for men in general practice and for those who wish to specialize. The patient receives specialized attention at a reduced cost, due to group sharing of the maintenance of the costly facilities necessary for proper diagnosis and treatment.

The problems encountered in group practice are mainly financial. In the case of the Winnipeg Clinic, the ownership of buildings, property and equipment, and the distribution of income were dealt with in the following ways:

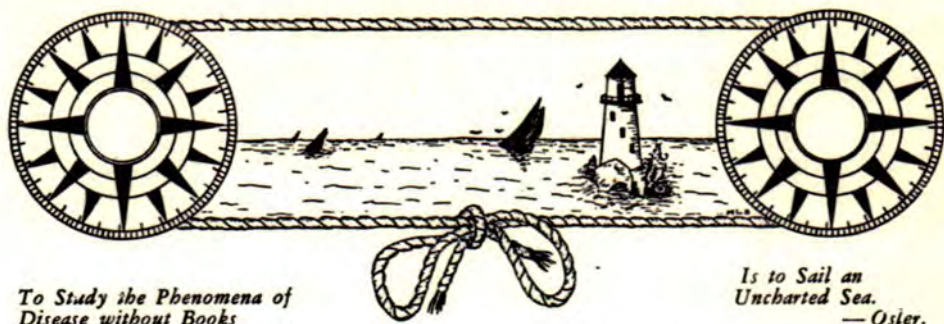
1. The physical assets of the clinic are not owned by the medical members themselves, but by a larger community group — including business and professional men. The indebtedness and expenses of the clinic are paid to this group in the form of rent. As the mortgage is reduced, more money will become available towards providing facilities for medical research and education, which is one of the objects of the clinic.

2. The clinic was organized as a corporation, so that the powers of the members could be defined satisfactorily. Every member named in this Corporation Act has a right to determine the policy of the clinic and no individual or small group can in future take over complete control of the clinic. But each department, which consists of three or more doctors with their nurses and secretaries, is an independent unit. The doctor retains his own clientele and has as much freedom in dealing with them as in private practice.

3. The factors which determine an individual's income depend upon the net income of the group and his contribution to this income.

This clinic hopes to aid graduate studies of doctors in several ways. Those who plan on entering general practice will spend two years rotating among the different departments of the clinic—at the same time being paid a substantial living wage. Those who wish to specialize will spend two years in the department of their "specialty", after which it is hoped to secure appointments for them in America or England to continue studies for fellowship examinations.

—ALEC GRAY, '52



*To Study the Phenomena of  
Disease without Books*

*Is to Sail an  
Uncharted Sea.  
— Osler.*

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