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COURAGE boundless optimism and breadth of vision characterized the distinguished career of Sir Charles Tupper. Despite the demands of public office, he maintained an active interest in all matters concerning the medical profession.

Tupper was born at Amherst, N.S., July 2nd, 1821. He studied medicine at Edinburgh University where he received the degrees of M.D. and L.R.C.S. in 1843. Of medium height, erect, and vigorous, Charles Tupper had an abundance of nervous energy which contributed to alertness and ceaseless mental activity. His manner was hearty and genial and he had a broad grasp of most topics.

In 1862 Tupper was appointed a Governor of Dalhousie College, Halifax, where he initiated a medical course which reached full fruition in 1870. It was largely due to his persistence that in 1867 the Victoria General Hospital began its existence in Halifax as a provincial and city institution. When the Canadian Medical Association was formed in 1867 he was elected President.

The year 1855 marked the beginning of Tupper's political career. It is said that history will record the four years of his administration as Premier of the Province of Nova Scotia as the greatest era in Tupper's life—an era in which he achieved the most striking personal success. Against strong opposition he established a system of free schools for Nova Scotia.

Tupper was the apostle of Confederation and played an important part in the passage of the British North America Act. He actively supported efforts to establish a Federal Department of Health which, after much missionary work, became a reality in 1919.

He was made a Baronet in 1888. For two different periods he held the position of High Commissioner for the Dominion in London and, in 1896, was made Prime Minister of Canada.

Sir Charles died at "The Mount", Bexley Heath, England, on October 30th, 1915. The record of his life is a challenge to the medical profession and inspires William R. Warner & Company in their policy of Therapeutic Exactness... Pharmaceutical Excellence.
Thiouracil: Its Present Status in the Treatment of Hyperthyroidism

By W. Bruce Barton, '45

Until recently, thyroidectomy has been the treatment of choice for thyrotoxicosis. X-ray and radium have had their proponents; and some continue to pin their faith upon iodine, either alone or in combination with sedatives. It is true that in quite a number of cases the disease will abate spontaneously; but not infrequently, especially in severe instances, the patient treated medically for too long will become a physical, sometimes a mental wreck, or fall an easy prey to intercurrent infection. The advent of thiouracil bids fair to alter this situation radically. This preparation may be but a milestone in the approach to a problem, the key to which may be a substance acting through the pituitary. At present, to say the least, thiouracil offers a serious challenge to the hitherto undisputed sway of surgery in the treatment of hyperthyroidism, a medical disease.

History

The use of thiouracil in thyrotoxicosis is an example of how seemingly unrelated research may sometimes, almost by accident, be turned to advantage in the treatment of disease.

The research began when the MacKenzies and McCollum (1941), working on the effects of sulphaguanidine in rats, discovered that it had the property of inducing a hypothyroid state and enlargement of the thyroid gland in experimental animals. At about the same time, Richter and Clisby (1941, 1942) who used phenylthiourea, and Kennedy who used allyl urea, which he isolated from rape seed, obtained similar results. Later, the MacKenzies (1943) and Astwood and his colleagues (1943) proved that, besides sulphaguanidine, other sulphanamide derivatives, and to a lesser degree sulphanilamide itself, depressed metabolism and caused hypertrophy of the thyroid gland in rats. In an endeavour to find a metabolic depressant suitable for clinical use, these workers tested a large number of compounds and found that thiourea and thiouracil were the most effective and least toxic. These observations led to the first clinical trial by Astwood¹, who tested the goitrogenous
effects of 2-thiouracil on three thyrotoxic patients with doses of two grams per day. In all cases, the basal metabolic rate was reduced and in one agranulocystosis developed.

**GROSS AND MICROSCOPIC CHANGES IN THE THYROID GLAND**

Early in the course of treatment (up to five weeks) the thyroid gland in nearly all instances becomes enlarged.

_Grossly_: The gland at operation is found to be excessively vascular. Clinically, during the course of treatment, inconsistent changes are noted. Some workers report that after the initial enlargement, the thyroid becomes progressively smaller, eventually returning to its original, normal or even sub-normal size. Other workers feel that there is no change in the size of the gland after the initial enlargement.

_Microscopically_: The microscopic changes observed in the thyroid glands of experimental animals and of man under thiouracil treatment are similar.

In man, biopsies made on the hyperplastic gland before the commencement of treatment have been compared with portions of the gland removed at operation in thiouracil-treated patients. Even though the non-treated thyroid gland shows marked hyperplasia, the gland in patients treated pre-operatively with thiouracil shows intense hyperplasia. The following are the chief histological findings:

1. A marked scarcity of colloid, the tissue consisting of almost solid sheets of hyperplastic cells.
3. Some acini have enlarged lumina with many papillary projections, the cells of which are tall and columnar.
4. An increase in intersititial cells.
5. An increase in the number of subcapsular lymphoid follicles.

Thus far, in spite of the extreme hypertrophy and hyperplasia of the acinar cells, no suggestion of malignancy has been detected as a result of the clinical use of the drug.

**MODE OF ACTION**

Ordinarily, the pituitary, receiving a stimulus _via_ the hypothalamus, secretes thyrotrrophic hormone which, in turn, acts upon the thyroid gland, producing hyperplasia and an increased production of thyroxine. Thyroxine, in turn, has been shown by Rawson, Graham and Riddell² to inactivate the thyrotrrophic hormone and thus prevent excess thyroid stimulation.

The following observations have been made:
THIOURACIL: STATUS IN TREATMENT OF HYPERTHYROIDISM

(1) Concurrent administration of iodine with thiouracil does not prevent the changes described in the thyroid gland.

(2) The administration of thyroxine or desiccated thyroid concomitantly with thiouracil completely prevents the changes in the thyroid gland.

(3) The administration of thyroxine or desiccated thyroid after the changes have been established in the thyroid gland completely reverses them.

(4) The ablation of the pituitary gland prevents the changes described in the thyroid gland, but does not prevent the fall in basal metabolic rate induced by thiouracil.

(5) In treated animals the thyroid gland does not take up iodine in the normal manner.

This fact has been demonstrated by administering radioactive (tracer) iodine (150 gamma of iodine as sodium iodide) 24 to 48 hours pre-operatively to thiouracil-treated patients. The gland removed at operation was almost devoid of iodine, the greater part of which had been excreted in the urine.

It is postulated, therefore, that thiouracil acts by preventing the completion of a physiologically active hormone. Most probably this break in the chain of events occurs at the level of iodinization of tyrosine, because, as has been stated, iodine is not utilized by thiouracil-treated patients.

As a result of the cessation of production of a physiologically active thyroid hormone, the basal metabolic rate falls, this, in consequence, causing the pituitary to respond as it would to thyroidectomy, namely, by the secretion of an excess of thyrotrophic hormone which results in thyroid hyperplasia without causing increased specific hormone production, i.e., the thyroid is now a hyperplastic hypofunctioning gland.

The hypofunction of the thyroid, then, is due to changes within the gland, induced by thiouracil, but the hyperplasia and hypertrophy result from pituitary hypersecretion which is consequent to the initial change of thyroid hypofunction.

ABSORPTION, DISTRIBUTION AND EXCRETION OF THIOURACIL

Thiouracil is rapidly absorbed and rapidly excreted in the urine. The drug, likewise, is capable of being destroyed in fairly large quantities by most body tissues. This tends to dispel any fear of a cumulative action, especially as regards those patients with renal or hepatic insufficiency.

Blood thiouracil levels have been estimated in an attempt to
determine optimal dosages. Regardless of doses varying from 0.2 to 2.0 gm. daily, a constant blood level was obtained. Likewise, the concentration of the drug in the thyroid gland bore no relation to the dosage employed. Because of the lack of correlation between dosage and blood level, it is obvious that the determination of the blood level is of little, if any, value in thiouracil therapy and that the dosage used will probably be empirical, depending upon the clinical status of the patient.

**CLINICAL APPLICATION AND RESULTS**

The use of thiouracil may be discussed as follows:

(a) Its use as the sole agent in the treatment of hyperthyroidism.

(b) Its use in preparing hyperthyroid patients for operation.

Some workers, mainly surgeons, are prepared to accept thiouracil solely as an agent for preparing thyrotoxic patients for surgery. The greatest use yet attributed to thiouracil, however, is in the continued treatment of hyperthyroid patients—patients who are not suitable for surgery, or who do not wish for surgery. Another great use for thiouracil is that of “tiding over” a hyperthyroid patient, whose toxicity develops at puberty or at the menopause. When these times of stress have passed, the thyroid gland is perfectly normal, causing no upset in physiology or biochemistry. Yet, one must acknowledge the fact that there is the odd isolated case which is absolutely refractory to thiouracil. With regard to this refractoriness, one must differentiate those patients who have been on iodine therapy. Necessarily, there is a considerable amount of physiologically active thyroid hormone stored in the thyroid glands of such patients, and the effect of thiouracil can not possibly be manifest before that thyroid hormone store is spent. Thus there is a delay in response to thiouracil which may be as long as four to six weeks.

**A.—Its Use as the Sole Agent in Treating Hyperthyroidism**

It is difficult to classify this group of patients on a basis which is generally acceptable. One might classify and grade the response according to the duration of the thyrotoxic symptoms; or one might use the degree of thyrotoxicity as a criterion. No such standards for the grading of results appear satisfactory. The duration of the toxic symptoms is unreliable, because in many cases the onset of the complaints is most insidious.

In the majority of cases treated with thiouracil, the response is dramatic. One notes in chronological order the following: Disappearance of skin flushing; disappearance of sweating; disappearance of nervousness; lowering of the basal metabolic rate; relief of emaciation; raising of plasma cholesterol level; lowering of the pulse rate.
THIOURACIL: STATUS IN TREATMENT OF HYPERTHYROIDISM

This order is important because cases have been called thiouracil-resistant, even in the face of falling basal metabolic rate, subjective improvement and gain in weight, because the pulse rate remained elevated.³

Within two days of the commencement of treatment, subjective improvement may be expressed. By the third week, improvement is evident, and by the fourth week, established in the average case. Variations in response from two to three days up to six to eight weeks occur. A slow response is notable in patients who have been receiving iodine. In this latter connection, it is best to withhold iodine for one to two months before commencing treatment with thiouracil.

Changes in the Basal Metabolic Rate: The basal metabolic rate decreased more rapidly in severe cases, but did not become normal, as a rule, until after five weeks; after four weeks in moderate cases, and after three weeks in mild cases. In a few cases the metabolic rate is depressed below normal.

Changes in Protein-Bound Iodine: The protein-bound iodine is usually within normal limits (four to eight per cent gamma) within four weeks.

The protein-bound iodine is usually regarded as a manifestation of the amount of circulating thyroid hormone. It is, therefore, logical that it should not be reduced until all the colloid is depleted from the thyroid and the gland is in the acolloidal state produced by thiouracil. This factor is a good indication of successful therapy.

Changes in the Thyroid Gland: These changes are inconsistent. Throughout the literature, reports are at variance, yet one would assume that all cases should have thyroid enlargement as a result of excess thyrotrophic hormone secretion by the anterior pituitary. Enlargement of the thyroid may regress when the pituitary cells forming the thyrotrophic hormone become exhausted.

It is of note that the thiouracilized thyroid can be made to regress in size by the use of desiccated thyroid used simultaneously with thiouracil in doses of 0.5-1.5 grains daily. This therapy bears rationale because thyroid hormone inhibits production of the thyrotrophic hormone and therefore removes the stimulus to thyroid hyperplasia and hypertrophy.

Ocular Changes: Again, there is variation of opinion as to the effect of thiouracil upon the exophthalmos. Williams and Clute⁴ in their report of 72 cases treated with thiouracil, five of whom showed manifestations of malignant exophthalmos, state that in each case, during the first few weeks of treatment, the manifestations became
accentuated. So desiccated thyroid was used in these cases, after the basal metabolic rate had been normal for 10 days. All patients, however, who exhibited stare and widened palpebral fissures, experienced great relief under thiouracil therapy. Rose and McConnell in their series of 37 cases, report no change or very little change in the eye manifestations of thyrotoxic patients treated with thiouracil. Again, Astwood reports that thiouracil therapy is often followed by an apparent regression of the exophthalmos.

Of the group of patients suitable for medical treatment, the so-called "thyrocardiac" group is of interest. Clute and Williams report on thirteen "thyrocardiacs," four of whom were treated with thiouracil followed by surgery, and nine of whom were treated with thiouracil only. It is encouraging to note that the group treated medically have done equally well.

Patients with auricular fibrillation complicating their thyrotoxicosis usually respond to thiouracil therapy with a complete return of normal rhythm and rate. If thiouracil fails to relieve the auricular fibrillation, quinidine usually effects the desired result.

B.—Its Use in Preparing Hyperthyroid Patients for Operation

In thyrotoxicosis, surgical intervention is indicated with:

(1) Patients having a very large goitre.

(2) Patients who live at a distance and cannot come into hospital for frequent check-ups.

(3) Patients who through ignorance or temperamental difficulties cannot be depended upon to follow medical treatment.

(4) A small number of cases who have undesirable reactions to thiouracil.

(5) Patients who have a discrete adenoma, because such a condition must be considered pre-malignant and be removed. In such patients in whom the thyroid warrants removal, it is of value to prepare the patient for operation with thiouracil.

Clute and Williams report very favourably on 34 patients prepared for operation with thiouracil. Of these patients, 30 had typical uncomplicated exophthalmic goitre and four had toxic adenomatous goitre. These patients were treated pre-operatively for five weeks and concurrently five mgm. of thiamine daily were given. The patients were urged to eat food with much carbohydrate and protein. These patients were admitted two days before operation and discharged six days after operation. In these cases, as in those 34 reported by Moore et al., the post-operative course of all thiouracil-treated patients was extremely smooth. The latter workers stress the fact that patients treated pre-
operatively with thiouracil for 10 to 14 days, rather than five to six weeks, had a more tempestuous course. Rose and McConnell report enthusiastically on three cases of thyrotoxicosis treated pre-operatively with thiouracil for periods of 17, 21 and 38 days, but these patients were in hospital. It is their belief that response is more rapid if the patient be in hospital and at rest. Thiouracil medication can be stopped four to six days after operation.

Clute and Williams further report on 15 cases of persistent or recurrent toxicity after thyroidectomy in which absolutely excellent results were obtained with thiouracil.

Workers at the Mayo Clinic feel hesitant about using thiouracil as the sole therapeutic agent unless some complicating condition has excluded surgery.

At the Massachusetts General Hospital, thiouracil is reserved almost exclusively for preparing patients for thyroidectomy, in which case it is more effective than iodine.

**Dosage**

No standard system of dosage prevails throughout the literature. One fact appears definite—that once control of the thyrotoxic manifestations is established, the dose of thiouracil should be reduced as quickly as possible and to as small an amount as possible.

Dosage may be discussed under two headings:

1. **Initial Treatment Period:** Since thiouracil is rapidly absorbed and rapidly excreted, it must be given in divided doses. The current method of dosage, which has come through a series of revisions, is as follows: 0.6 gm. in three divided doses daily, reducing the dose gradually as subjective symptoms improve. It is always possible for one to increase the dose should the reduced dose prove inadequate, for it is known that cases in relapse respond as readily as they did initially, when the dosage is begun anew.

2. **Maintenance Treatment Period:** It is stressed that smaller doses of thiouracil are required for maintenance than to establish control. The decrease of the drug requirement is most striking in the earlier stages, but it extends beyond a simple readjustment of dosage and there are indications that it may be progressive. Doses which at first simply suffice to hold the plasma cholesterol at normal levels later prove too much, so that the plasma cholesterol rises suddenly and symptoms of overdosage appear.

Therefore it is recommended by Himsworth that the dosage be reduced rapidly to 0.1 or 0.05 gm. daily. In none of the cases recorded
by him has a return of symptoms or a fall in weight suggested a too rapid or too severe reduction.

The dosage should be reduced rapidly and continuously until there is evidence that it is insufficient. Then it is adjusted appropriately and maintained at that level for a few weeks, when a further attempt at reduction is made.

For a maintenance dose Nussey recommends 0.2 gm. of thiouracil twice a day for two to four weeks after leaving hospital, with a later maintenance dose of 0.1 or 0.05 gm. daily.

In none of the cases so far reported has any of the patients become drug fast, that is, within the longest follow-up period of any number of cases which is 10 to 12 months.

The consensus of opinion is that thiouracil should not be discontinued completely, for a remission is almost certain to ensue. These remissions, however, are readily controlled by beginning anew the administration of the drug.

A few isolated cases are on record in which thiouracil administration has been stopped for five months, seven weeks and five weeks. Of these three cases, none was severe, and each was weaned gradually onto very small doses before complete cessation.

Rose and McConnell report on 37 thyrotoxic patients, eight of whom remained in remission for three weeks up to seven months following cessation of the drug. Yet, 13 of these patients suffered relapses on reduction of dosage or on withdrawal of the drug. Notwithstanding, administration is prolonged, can eventually be discontinued altogether high hope is held for the possibility that thiouracil, as the period of without relapse.

Nussey reports on 27 patients, six of whom have been without treatment for periods varying from 24 to four weeks. Of these, four presented severe thyrotoxic symptoms and two presented moderate symptoms. The duration of symptoms in these six cases varied from eight years to two months.

During the course of treatment, patients may remain ambulatory indeed, this is one of the advantages of thiouracil treatment. The majority of patients feel fit to resume work, regardless of the severity of the disorder and responsibility attached thereto, in one to three months after the termination of initial treatment.

In the early stages of treatment, one prefers to see the patient at weekly intervals, so that progress may be assessed and white blood cell counts, the basal metabolic rate and blood chemical constituents may be ascertained. At the end of four to six weeks, patients may return
at monthly intervals or immediately should recrudescences or toxic symptoms supervene. The drug, as pointed out later, is a dangerous one, and the fact that patients under treatment with thiouracil must be carefully followed cannot be over-emphasized.

TOXIC EFFECTS

The prevalence of toxic effects, estimated variously at about 10 per cent, is the one concrete objection to thiouracil therapy. New and previously unreported toxic manifestations are appearing in the literature continuously. Among them are included enlargement of the struma, feeling of depression, leukopenia, granulocytopenia, skin rashes, hyperthermia, lymph gland enlargement and sore throat.

Toxic manifestations can be grouped, according to Himsworth, in the following way:

(1) Those Due to Overdosage: By the manifestations of overdosage are meant those symptoms which can be induced in any patient by overdosages. Further, there are two separate groups of manifestations due to overdosage:

(a) That group which is easily recognized and occurs early in treatment from overdosage.

One finds an increase in the size, sometimes painful, of the struma.

The treatment is reduction of the dosage. This manifestation is rare now because of the tendency to give somewhat smaller initial doses.

(b) That group which develops insidiously and then becomes quickly manifest and apparently results from chronic slight overdosage.

The results are mainly subjective, viz., complaints of weariness and depression with a bloated appearance and lack of energy. There is no concomitant depression of the basal metabolic rate nor is there any weight loss. Hence, Himsworth feels that this does not represent a myxoedematous state.

This condition is often associated with and preceded by a rise in plasma cholesterol level. There is no change in the white blood cell count.

This state is probably a manifestation of a rapidly developing hypothyroidism. The treatment consists of: Reducing the dose of thiouracil to the minimum at which weight will be maintained; periodic checks on the blood cholesterol level.

(2) Those Due to Idiosyncrasy: By the manifestations of idiosyn-
crazy are meant those conditions which occur capriciously and inconstantly in a minority of patients.

There are fever, rashes, lymphadenopathy and blood changes, which, as a rule, occur within 14 days of the commencement of administration of the drug.

The most serious manifestations are leukopenia, agranulocytosis and thrombocytopenia. Most of these cases respond to reduced dosage or cessation of the drug.

If the white blood cell count is very low, one may use pentnucleotide until the granulocyte count is adequate, or one may resort to blood transfusions.

The deaths which have occurred during thiouracil therapy have all fallen into this category. The great danger is that the patient will become the victim of an intercurrent infection, against which the requisite neutrophilic response is totally inadequate.

Watson and Wilcox\(^1^0\) and Nussey\(^9\) report on 11 and 27 cases respectively in which there were no toxic reactions recorded. At the other extreme, Lozinski and Siminovitch\(^1^1\) report one fatal case of agranulocytosis out of their series of five cases which dampened their enthusiasm for thiouracil therapy so effectively that the other four cases were submitted to subtotal thyroidectomy. They feel that this fatal case, which developed explosively after five weeks of dramatically successful treatment, represents a reaction which must be feared as a result of prolonged treatment with thiouracil.

Of the toxic reactions then, agranulocytosis is the most formidable and the cause of death in those cases which have terminated fatally. The other toxic manifestations can be controlled satisfactorily by reducing the dosage of thiouracil (which is effective in the majority of such cases) or by discontinuing the drug entirely for a short interval.

There remains the hope that some means of preventing the development of agranulocytosis will present itself. Such a possibility is suggested by the fact that in experimental animals, the development of agranulocytosis may be prevented by the concomitant administration of crude liver extract, the active principle of which may be folic acid.

**SUMMARY**

The medical treatment of hyperthyroidism with thiouracil is the direct result of about three years of work on goitre by pharmacologists, endocrinologists and clinicians, and is an outstanding example of the benefits which can accrue to the medical profession through the combined
efforts of workers in various fields when a common problem is the objective.

The results of treatment in 90 per cent of cases of hyperthyroidism of varying intensity and of varying duration, whether due to diffuse hyperplasia or to toxic adenomatous goitre, have been most encouraging—to the point where hopes are held that thiouracil may make surgery unnecessary in treating this medical disease.

It has been emphasized that thiouracil is a potentially dangerous drug which, in inadequately supervised cases, may cause death. With the advent of smaller dosage systems, toxic reactions are becoming less frequent. When one is alive to the dangers of thiouracil therapy, toxic reactions are bound to occur less frequently. Perhaps measures which will eliminate toxic reactions are in the offing.

The subject is really too new to permit of any definite and factual conclusions. One must await the results of therapy continued over a period of years.

The following questions remain to be answered:

(1) What late toxic effects may follow the prolonged use of thiouracil? Is it possible, for example, that depression or exhaustion of the bone marrow might follow prolonged ingestion of the drug in some cases?

(2) What undesirable dislocations of endocrine relationships may be induced by chronic inhibition of the thyroid hormone production and the consequent disturbance in thyroid-pituitary balance? Is there, thus, a possibility that pituitary exhaustion might ensue or that irreversible thyroid gland changes supervene?

(3) What types of thyrotoxicosis will respond best to thiouracil and how long must such cases remain under treatment before permanent cure is effected?

Only further experience and time can provide the answers to these vital queries. If the progress which, up until this time, has been so outstanding, continues at the same tempo, one cannot be but optimistic regarding the end results of thiouracil therapy in treating hyperthyroidism.

BIBLIOGRAPHY


Early Ambulation of the Post-Operative Patient --- A Review of Current Literature

By BRUCE COLWELL, '45

FOR almost half a century there has been an active interest in the subject of early ambulation of the patient following section of the anterior abdominal wall. In the early days of modern surgery, patients were kept in bed after clean laparotomies and herniorrhaphies for periods of three weeks or more. (Newburger\(^1\)) Even today, such prolonged periods of enforced bed rest are not uncommon.

**HISTORY**

Ries\(^2\), in 1899, was the first to record his opinion, based on his experience with his own patients, “that the period for which it was advisable to confine such cases (surgical patients) to bed could be counted by hours instead of days.” He first used this on vaginal celiotomy cases, but soon extended it to include ventral celiotomy cases. He noticed that the patients felt better, looked better, ate better, bowels worked regularly and easily, were stronger, etc., than the same category of patients treated in the conventional way. He got his patients up 24 to 48 hours post-operatively. He attributed his courage to Abel, who had shown that the avoidance of ventral hernia depends upon accurate layer suture of the anterior abdominal wall and the absence of infection, while all other factors are of secondary importance. For a rational explanation of the early healing of wounds, even though movement is present, he cited the operations on neck, tongue, chest, bladder, bowel, veins, etc., after which you cannot keep the part completely still, and yet these heal by primary union if you keep infection out.

Rehn, cited by Newburger\(^1\), in 1902 sensed the danger to the patient as a whole in contra-distinction to the wound itself in this regimen of immobilization, and he proposed respiratory and muscular activity as well as a sitting position for the patient while still confined to bed.

In a letter, cited in the article by Boldt\(^3\) in 1907, Dr. William J. Mayo said, “We now bend every effort to get our patients about early and encourage movement of the limbs, especially with patients who lie in bed a longer time.” Mayo also quoted figures to show benefits of such treatment as follows:

- 1904—1,788 abdominal operations—1.0 per cent phlebitis.
- 1905—2,157 abdominal operations—0.3 per cent phlebitis.

Boldt\(^3\), himself, in his article in 1907, says that for 15 years he had been allowing his patients to move about in bed as much as they pleased.
after abdominal operations, and had noticed no harm from the practice. He refers to 384 of his personal cases.

Kümmell, of Hamburg, in 1908 cited by Newburger\(^1\), was practising and strongly advocating early post-operative walking. Kelly, cited by Newburger\(^1\), reported in 1911 in America that Ries’ example had been followed by “others too numerous to mention.” In 1912 a favorable report on the subject was published with contributions by such famous surgeons as Bier, Koenig, Döderlein, etc. In 1923 it received favorable notice in the surgical text of Bier, Braum and Kümmell. The use of the method spread throughout all Europe, and reports came from South America and Africa of good results.

Andre Chalier, cited by Newburger\(^1\), of Lyon, did much to popularize the method in Latin countries by his profuse writings between 1929 and 1934. He, however, considers early ambulation as meaning getting patients out of bed from the second to the fifth day post-operatively.

Havlícek, Mermingas and Paschoud, cited by Newburger\(^1\), were very radical in their views, and by their example and publications between 1935 and 1939, advocated what is called “immediate rising,” that is, walking from the operating room back to the ward, and there continuing activity out of bed until discharge.

Campaneau, as reported by Zava and cited by Ochsner and DeBakey\(^1\), reported in 1940, 1,300 cases, many of which were severe, in which the method of immediate rising was used, and even the taking of gymnastic exercises.

In America, Newburger\(^1\), Leithauser and Bergo\(^4\), in 1941, and Nelson and Collins\(^6\) in 1942, and others (see Bibliography) have given leadership in this field.

**DEFINITION**

Early post-operative ambulation is defined by modern surgeons interested in the subject, as walking within 24 hours post-operatively. The daily post-operative continuation of bodily activity, including walking, self-care in the matters of toilet, dressing and feeding, and even actual gymnastics (advised by a few extremists), is considered an integral part of a regimen directed toward an uncomplicated and rapid convalescence. In cases where early post-operative walking is contraindicated, then respiratory and leg exercises in bed are substituted for it by most writers on the subject.

**RATIONALE**

The rationale of the whole procedure is based upon several facts and observations as follows:
EARLY AMBULATION OF POST-OPERATIVE PATIENT

(1) Henle, in 1900, demonstrated that pulmonary complications are most likely to occur within 48 hours after operation.

(2) It is believed that other complications appear within a few hours after operation.

(3) The excellent healing of wounds and the low incidence of post-operative complications in children despite the fact that they are never restrained after operation and that their movements from the moment of their recovery from anaesthesia sometimes approach violence. This has been shown to be experimentally true in animals submitted to abdominal section for various experimental procedures. (Ries\textsuperscript{2}; Kimbarovsky, as cited by Leithauser\textsuperscript{5}; Localio\textsuperscript{7}; Newburger\textsuperscript{12}.)

(4) The assurance of Abel, as cited by Ries\textsuperscript{2}, that the occurrence of ventral hernia is dependent upon failure to suture the anterior abdominal wall in layers and upon the presence of infection, and that all other factors, including the wearing of a binder, are of secondary importance.

(5) The observed excellent healing by primary union of operations on neck, tongue, chest, bladder, bowel, vein, etc., that you cannot keep absolutely at rest. (Ries\textsuperscript{2}.) Healing is by primary union if infection is kept out. Why should abdominal wounds not be treated similarly?

PURPOSES

(1) Prevention of post-operative complications—because these cause the majority of deaths following surgical operations. (Nelson\textsuperscript{13}.)

(2) To free the patient of many irksome and disagreeable features of the after-care as usually carried out. (Ries\textsuperscript{2}.)

(3) To shorten the period of convalescence. (Clairmont as cited by Newburger\textsuperscript{1}.)

INDICATIONS

It is of importance mainly in laparotomies and herniorrhaphies because of the ensuing high incidence of the so-called post-operative syndrome of vascular and/or pulmonary complications. It is used for aseptic operations with firm closure of the incision where strict adherence to rules of surgery have been followed (see later), and where no contraindications exist. (Jeanneney, as cited by Newburger\textsuperscript{1}.)

CONTRA-INDICATIONS

General—
Cardiac insufficiency.
Shock.
Severe anaemia.
Cachexia.
Haemorrhage or fear of haemorrhage.
Presence of thrombi or emboli.
Prolonged pre-operative bed confinement.
Pregnancy in which abortion is feared.

Local—
Suppurative conditions such as peritonitis, cholangitis, pancreatitis, liver infections, etc.
Potentially infected incisions.
Insecure gastro-enteric anastomoses.
Copious tamponade.

Such complications as post-spinal anaesthesia headache, unexpected wound infections, etc., may force the return to bed of patients who have been up and walking. (Newburger\textsuperscript{1}, Nelson\textsuperscript{13}.)

CONDITIONING CIRCUMSTANCES

(1) No contraindications present.
(2) Aseptic technic strictly adhered to.
(3) Type of Incision. Boldt\textsuperscript{3} says that the abdominal incision should be made sufficiently big to permit of easily accessible work on the seat of the pathological condition present. An extra 1" or 2" is of no significance so far as healing of the abdominal wound is concerned or so far as concerns the probability of the subsequent occurrence of ventral hernia if the incision is properly closed according to the Abel method. In fact, you are more likely to secure primary union of such a wound more readily than of one that has been abused by traumatism during manipulation as is necessary in too small an incision.

Rees and Coller\textsuperscript{8} point out the advisability of adoption of transverse abdominal incisions because of several benefits: Minimal tension in the wound; less danger to the nerve supply; less damage to the muscle masses; ease in getting to the site of trouble; adaptability for various operations; ease of closure, etc.

(4) Absolute haemostasis is imperative.
(5) Minimum of local tissue trauma is essential.
(6) Suture Material. Nelson and Collins\textsuperscript{6} have made a careful study of the various materials used as sutures, and have come to the conclusion that non-absorbable sutures are to be preferred, and of these, cotton is probably the best. They also advise early ambulation in absence of any distinct contraindication. Their results have been quite satisfactory.

Localio\textsuperscript{7} demonstrated that wounds sutured with non-absorbable suture became normal with respect to tensile strength at an earlier
date than was the case with catgut. There was also found to be a high correlation between the lag period (period of delay in increase in tensile strength) and healing period. The longer the lag period the longer the healing period. He also showed that there was less tissue reaction produced by the presence of non-absorbable sutures than by catgut.

Leithauser, however, used chronic catgut reinforced by alloy steel wire for all cases except appendix and hernia. Hernial repairs were done entirely with No. 32 alloy steel wire.

(7) Closure of Incision—Must be done by accurate suturing in layers and prevention of infection and with a minimum of drainage. (Newburger.)

(8) Anaesthetic—A local anaesthetic permits of immediate or very early post-operative walking at any elected time. All other anaesthetics require longer times, but none more than 24 hours before walking may be commenced. (Newburger.) Local anaesthetics are largely favored by European men. Spinal anaesthesia seem to be the choice in America.

**Benefits of Early Rising Post-Operatively.**

(1) Asthenia is avoided. This is generally agreed to be one of the most important points from the patient’s standpoint. Ries, in 1899, noticed in his patients that they did not present the picture of listlessness and muscular weakness which the same category of patients presented after the performance of the same type of operations, but with the conventional method of after treatment.

(2) Improvement in the patient’s morale is a psychological advantage which must not be overlooked, for they feel that they are progressing. They are freed from many of the irksome and disagreeable features of the conventional post-operative period.

(3) Economy is a definite factor. The period of hospitalization is cut down to a minimum, which is about one-half of the usual time. In addition, the patient on leaving hospital is able to return to life feeling well and not half sick, as is the case with the usual type of treatment. (Ries; Leithauser, Leithauser, Nelson and Collins; Nelson.) For instance, Leithauser in a series of 900 cases treated by early post-operative ambulation, reports the average length of stay in hospital for various operations as follows:

- Acute appendicitis ........................................ 2.3 days
- Ruptured appendix ..................................... 9.4 days
- Cholecystectomy ........................................ 7.8 days
- Gastrectomy ............................................. 10.7 days
Herniorrhaphy ........................................... 7.0 days
Pelvic operations (hysterectomy, etc.) ....... 7.4 days
Thyroidectomy ........................................... 5.6 days
Renal operations (stones, etc.) ................. 10.6 days

(4) Simplification of the post-operative care of the patient is attained.
This naturally follows for the ambulatory patient can look after
the details of feeding, toilet, excretory functions, etc., himself.
This feature is reported in most of the articles.

(5) Reduction of the incidence of pulmonary complications. The
question of aetiology of pulmonary complications has been thor­
oughly investigated.
Powers, cited by Newburger\(^1\) and Leithauser\(^5\), report that post­
operative hypo-ventilation varies from 50 per cent in inguinal
herniorrhaphies and McBurney incisions up to as high as 66 per
cent in upper abdominal operations.
MacLeod, cited by Newburger\(^1\), has shown that recumbency itself
decreases the vital capacity 15 per cent.
Churchill and McNeil, cited by Leithauser\(^5\), at the Massachusetts
General Hospital, have established that there is a pronounced
diminution in vital capacity most evident on the first post-operative
day, after which the vital capacity gradually improves. The extent
and duration of reduction in vital capacity bears a direct relation
to the extent of the surgical procedure. They also emphasized that
pulmonary complications increase in direct proportion to the
reduction and duration of reduction of the vital capacity.
Cutler and Hoerr, as cited by Leithauser\(^5\), state that 50 per cent of
all primary post-operative pulmonary complications are established
by the end of 24 hours, and that 90 per cent make their appearance
before the end of the fourth day. It usually requires seven to 14
days for the vital capacity to return to normal under conventional
post-operative treatment.
Churchill and McNeil, as cited by Leithauser\(^5\), have found that in
patients treated by early ambulation post-operatively, the time
required for the return of vital capacity to normal was one-half
the usual time.
Khromov, cited by Newburger\(^1\), gives similar figures. Thus we
should expect a marked reduction in pulmonary complications.
Barman and his associates\(^10\), in corroboration of the hypothesis
of Gesell, Haldane and Henderson, found that muscular exertion
results in an alteration in the blood which clinically has been found
to stimulate the respiratory centres.
Salischew, cited by Newburger\(^1\) states that by early ambulation
post-operatively, the pulmonary complications are reduced four to five-fold.

Kimbarovsky, cited by several, including Leithauser, in a comparative series, found a reduction of incidence of pulmonary complications, from both gynaecological and gastric operations, to about one-tenth by early rising. This marked diminution is credible since this same prophylactic course has been suggested by conservative surgeons (Pack, as cited by Newburger) for years in both elderly patients and after gastric resections where the danger of pulmonary complications is high. The remarkably low incidence of pulmonary complications in the series mentioned above, and also by Nelson, furnishes adequate clinical evidence of the value of early rising in the prevention of these complications. It is all the more surprising that this knowledge has not been applied more generally.


(7) Rapid, good healing of incisions. Fear that the wound will fail to heal properly is the chief objection advanced to early amputation. It is easy to understand why it exists since the dependence of the healing of a wound on immobilization has been taught since ancient times.

Improvement in suture material has shown that non-absorbable sutures, especially cotton, give best results and most comfort to the patient as well as a more rapid convalescence as compared with catgut. (Nelson.)

Localio has shown experimentally that the period of delay in increase in tensile strength (lag period), was longest when catgut suture was used. He also showed that the tensile strength of the wound became normal at an earlier date with a non-absorbable suture than with catgut, and found that there was a high correlation between the lag period, tensile strength and healing period.

Kimbarovsky, cited by Leithauser, in 1936 found experimentally in restricted animals, as opposed to freely ambulatory ones, that there was a delay in formation of connective tissue in artificially produced wounds. Shaus, Pozharskiy and Abrikosv agreed with this conclusion.

Nelson reports no instances of wound disruption in a series of 160 cases treated by early ambulation.

Newburger has shown experimentally in rats, in a study of standard laparotomy incisions, that it took one-half the time for exercised animals' wounds to reach maximum tensile strength (which is a good indication of rapidity of wound healing). The
explanation is probably that a shortened lag period is found in exercised animals or, conversely, a more rapid initiation of the period of fibroplasia.

(8) Reduction of incidence of thrombosis and embolism. One of the objections raised by those opposed to early ambulation is the danger of thrombosis and embolism. But these dangers are very much present even by the usual method of post-operative care.

Virchow and Aschoff were the original exponents of the contention that retardation of the venous circulation is the basic cause of thrombus formation. This is now generally conceded by all. After operation, a high degree of slowing venous return is known to occur. (Smith, as cited by Newburger; Ochsner and DeBakey.) This deceleration is a direct result of decreased muscular activity of legs and respiratory system and of general loss of tone of the vascular system as a consequence of recumbency.

Boldt in 1907 stated that there is no better way of keeping up a good circulation than by taking rational exercise.

Potts gives incidence of:
Thrombosis—1.0 per cent to 7.5 per cent of all surgical patients.
Embolism—0.1 per cent to 7.5 per cent of all surgical patients.
In 1908, Dr. William J. Mayo reported that they were bending every effort to get their patients about early, and encouraged movement of the limbs, especially with patients who lie in bed a longer time. He reported that by so doing, they had reduced the incidence of post-operative phlebitis from one per cent in 1,788 operations done in 1904, to 0.3 per cent in 2,157 operations done in 1905, and treated by the above described new system.

Potts in 1940 points out that whereas thrombosis and embolism are common in patients with fractures who are confined to bed and in plaster, they are rare in ambulatory patients with arm, leg, shoulder or spine fractures in plaster.

At the Essinger University Clinic, cited by Ochsner and DeBakey, the incidence of thrombosis and embolism was reduced from:
2.63 per cent thrombosis and 1.40 per cent fatal emboli in 1,504 cases from 1906 to 1912, to:
1.75 per cent thrombosis and 0.60 per cent fatal emboli in 2,053 cases from 1912 to 1918,
and the improvement is explained as being due largely to the fact that in the last group they were all treated by early ambulation post-operatively.

Nehrkora, cited by Newburger, in 1927 reduced the incidence of
Early Ambulation of Post-Operative Patient

thrombosis and embolism by one-third in a series of 4,600 laparotomies.

Von Jaschke, cited by Ochsner and DeBakey,\textsuperscript{11} presents essentially similar results in a report in 1937.

Potts\textsuperscript{9} in 1940 reports a series of 518 cases of general surgery without a single case of embolism or thrombophlebitis.

Leithauser\textsuperscript{5} in 1943, in reviewing the literature, found that there was ample evidence that early ambulation was responsible for this marked improvement in the incidence of thrombosis and embolism. Final judgment in the matter will rest on future well-controlled clinical observations duplicating and extending those of Schumaker, cited by Newburger.\textsuperscript{1}

The low incidence of post-operative complications in patients ambulated early is the obvious answer to possible charges of malpractice. This question was first raised by Boldt\textsuperscript{3} in 1907, and was answered very satisfactorily by him then. "To prove that this practice is responsible for such post-operative complications as occur (he spoke particularly of thrombosis and embolism), it would be necessary to prove that these complications do not occur in patients kept in bed for conventional periods of time."

The same author's devastating observation that those who oppose the plan of early post-operative ambulation are generally those who have had no experience with it is also still valid.

As soon as the patient has fully recovered from the effects of anaesthesia (in Nelson's opinion, the particular anaesthetic agent used is not significant), the bed is sharply tilted, so that the head is elevated. After this position has been maintained for a time, the bed is leveled and the patient assumes a sitting position on the side of the bed, with the feet resting on a chair. In this position, he breathes deeply and coughs frequently. He then lies down, and the head of the bed is again sharply elevated. After a second period of rest he is assisted to stand and is conducted to the bathroom, where the bladder is practically always emptied without difficulty. If his condition is good, and if he wishes, he sits up in a chair for a time before returning to bed. The rapidity with which these different steps are carried out varies with the individual case, but ordinarily there is no great delay between them.

After the pain of the initial ambulation, patients seldom complain again of even significant discomfort. Those who are oversensitive to the pain of the first rising, or who are unduly apprehensive, are made to practice sitting at the edge of the bed, with intervals of rest between each attempt, until they are strong enough and willing to walk to the bathroom. After the initial ambulation, all patients
are allowed to rise as often as they please, to go to the bathroom, which they invariably prefer to the use of the bedpan, to fetch drinks and to sit on the sun porch.

Greatly debilitated patients may find it necessary to confine their first out-of-bed activities to the use of a wheelchair and a commode, but even these persons exhibit a more rapid return of strength than do other patients in the ward who, although perhaps originally stronger, lose strength by continued confinement to bed. It is important, however, that the initial activities of all patients be supervised by the nursing staff, and that excessive fatigue be prevented by frequent intervals of rest in bed, for many, in their enthusiasm, are inclined to overdo. It should also be emphasized that periodic breathing exercises and coughing are part of the regimen of post-operative activity.

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Fluid Requirements of the Surgical Patient

By L. Stewart Wells, '45

The administration of parenteral fluids in patients undergoing surgical procedures has all too frequently been used in an empirical manner, without due regard to the amount or type of fluid indicated. The purpose of this paper is to call attention to some simple fundamental principles which should be kept in mind when using parenteral fluids. That the importance of maintaining the fluid balance cannot be stressed too highly has been forcefully demonstrated by Rubner, whose studies in metabolism reveal that an animal can lose all its glycogen and fat, half of its body protein and 40 per cent of its total body weight and still live; whereas the loss of 10 per cent of its water content will cause serious disorder, and the loss of 20 to 22 per cent of its water content will result in death.

Water Availability and Secretion

In health and in sickness where there is no condition which prevents or contra-indicates the administration of food and fluid by mouth, there are two ways by which water is made available to the body, and three ways in which it is excreted.

Available Water:
1. Water drunk.
2. Food, i.e., diet or body substances.
   A.—Water content.
   B.—Water of oxidation.

Excreted Water:
1. Water in urine.
2. Water in stool.
   A.—Perspiration.
   B.—Lungs.

Water Balance in the Normal Individual (Daily)

Available:

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water drunk</td>
<td>1200 cc.</td>
</tr>
<tr>
<td>Food (1)</td>
<td>1000 cc.</td>
</tr>
<tr>
<td>(2)</td>
<td>300 cc.</td>
</tr>
<tr>
<td>Total</td>
<td>2500 cc.</td>
</tr>
</tbody>
</table>
Excreted:

<table>
<thead>
<tr>
<th>Excreted</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>1200 cc</td>
</tr>
<tr>
<td>Stool</td>
<td>100 cc</td>
</tr>
<tr>
<td>Vaporization</td>
<td>1200 cc</td>
</tr>
</tbody>
</table>

Total: 2500 cc.

The exact balance as given here may be incredible, and actually such a balance does not exist for any given day, but, taken over a period of time, the normal individual intake and output will balance exactly.

**DAILY REQUIREMENTS OF THE SURGICAL PATIENT**

**A.**—The Uncomplicated Case:

- Water of vaporization: 1000 to 1500 cc.
- Water for urine: 1000 to 1000 cc.

**Total:** 2000 to 2500 cc.

**B.**—The Complicated Case, i.e., complicated by fever, hyperthyroidism or the hot humid atmosphere prevailing in a hospital in summer:

- Water for urine: 1000 to 1500 cc.

**Total:** 3000 to 3500 cc.

A more exact evaluation of the fluid requirements of the patient on parenteral feeding is offered by Wolff and Bauer:

1. Daily requirements for urine and vaporization plus
2. 250 cc. \( \text{H}_2\text{O} \) per degree of Fahrenheit above normal, per day, plus
3. 3 to 5 grms. of \( \text{NaCl} \) per day.

These requirements are basic and must be given in addition to the doses indicated for correction of dehydration, acidosis, etc. We know that
1. Regular Hospital Diet contains 1200 cc. of water per day;
2. Soft Hospital Diet contains or affords 500 cc. of water per day. Then the uncomplicated case must be given from 800 to 2000 cc. of water per day in addition to his food, while the complicated case will require 1800 to 3000 cc., depending on the diet. A general clinical rule is to give sufficient fluid to guarantee 1000 cc. of urine in the uncomplicated and 1500 cc. of urine in the complicated surgical patient as the daily output.

**RESTORATION OF FLUID BALANCE IN THE DEHYDRATED PATIENT WITH EMPHASIS ON HYPOCHLORAEMIA**

Clinically, according to Coller and Maddock, dehydration is not manifested until the patient has lost an amount of water equivalent to
FLUID REQUIREMENTS OF THE SURGICAL PATIENT

six per cent of his body weight; e.g., in a patient whose normal body weight is 132 pounds, the amount of water already lost when dehydration becomes apparent is 3600 cc. This amount must be given in addition to daily basic requirements. Wolff and Bauer are in accord with Coller, but recommend their “2-4-6” rule, depending on the degree of dehydration, as follows:

(1) 2% for slight dehydration as manifested clinically by:
   1. Marked thirst.
   2. Some dryness of mucous membranes.
   3. Urine with Specific Gravity of 1.028 to 1.030; Volume of 500 to 600 cc. daily.

(2) 4% for moderate dehydration with:
   1. Pronounced dryness of mucous membranes.
   2. Dry skin.
   3. Urinary volume of 200 to 300 cc. daily.

(3) 6% for severe dehydration with:
   1. Reduced intra-ocular pressure.
   2. Very dry skin which stands up when pinched into a fold.
   3. Little or no urine.

Coma may or may not be present in this stage.

Dehydration is seldom, however, an uncomplicated entity. Almost always there is a reduction in blood chlorides. There may be alkalosis, acidosis, hypoproteinaemia or anemia, all of which require treatment.

Chlorides are depleted by:
1. Sweating—2 to 5 gms. NaCl per litre.
2. Vomiting—3.3 gms. NaCl per litre.
3. Wangensteen Drainage—5.7 gms. NaCl per litre.
5. Enterostomy—5.1 gms. NaCl per litre.

In the treatment of hypochloraemia, the well-proven Coller-Maddock rule may be followed, i.e., 0.5 per cent NaCl per kilo of normal body weight for every 100 mg. chloride below a normal value of 560 mg. per 100 cc. of blood.

e.g.—Blood chloride value—460 mg. per 100 cc. (100 mg. per cent below normal.)

Body weight—60 kilo.

Therefore 60 x 0.5 = 30 gms. of NaCl, which will be the amount necessary to restore the blood chloride level to normal.

Now, when we assume that the patient is severely dehydrated (vide supra), then 30 grams of NaCl for correction of the hypochloraemia must
be given together with 3500 cc. of water for the correction of dehydration, and these combined will be readily seen to be approximated by 3500 cc. of Ringer's Solution. As previously stated, fluids and electrolytes for correction of deficiency must be given in addition to basic daily requirements.

\[
\text{e.g.—Daily requirement} \quad \begin{align*}
1000 \text{ cc. for urine} \\
1500 \text{ cc. for vaporization}
\end{align*}
\]

For correction of dehydration \quad 3500 \text{ cc.}

\[
\text{Total} \quad 6000 \text{ cc.}
\]

The daily requirement is given in the form of five per cent glucose in distilled water; the excess as Ringer's Solution. Coller and Maddock suggest that this amount be given over a 24-hour period at a rate of 250 cc. per hour.

Having corrected the dehydration of the patient, then the fluid balance of the patient must be maintained by the administration of sufficient fluid for basic requirements plus the addition of volume for volume of loss by:

1. Wangensteen Drainage
2. Miller-Abbot Drainage
3. Enterostomy
4. Vomiting

using Ringer's Solution plus five per cent glucose.

ACIDOSIS

This condition may occur in dehydration, starvation or diabetes. Existence of acidosis is determined by the value of the carbon dioxide combining power (CO$_2$ C.P.) of the blood. Normal value for CO$_2$ C.P.:

\[
\begin{align*}
\text{Adults} & \quad 53 \text{ to } 75 \text{ per cent.} \\
\text{Infants} & \quad 40 \text{ to } 55 \text{ per cent.}
\end{align*}
\]

Interpretation of values:

1. Value below 50 per cent—acidosis.
2. Value below 30 per cent—severe acidosis.
3. Value above 80 per cent—alkalosis.
4. Value of 90 per cent or over—severe alkalosis with Tetany.

Treatment:

1. Value of 45 per cent requires 1000 cc. five per cent glucose in saline.
2. Value of 35 per cent requires 2000 cc. five per cent glucose in saline.
3. Value below 35 per cent requires Sodium bicarbonate or Sodium lactate in addition to glucose in saline. Approximately 7.5 grams
of Sodium bicarbonate must be given for every point below 35 per cent. If the CO₂ C.P. is normal within 12 hours, then repeat the dose. With regard to Sodium lactate, 72 cc. of 1/6M. Sodium lactate may be substituted for each gram of Sodium bicarbonate.

GASTRIC DRAINAGE

The loss of gastric juice may be caused by:
1. Pernicious vomiting.
2. High intestinal obstruction with vomiting.
3. Gastric drainage, i.e., Wangensteen.

As a result, the blood chlorides are depleted, particularly the acid radicle. The end result is:
1. Dehydration—"2-4-6 Rule" of Bauer and Wolff.
2. Alkalosis—CO₂ C.P. = 80 per cent or more.
3. Hypochloraemia—Blood chlorides may go as low as 300 mg. per 100 cc. of blood.

Treatment:
The treatment must correct all three conditions as described in previous sections.

DIARRHOEA

Treatment is the same as for dehydration.

BURNS

In burns the fluid imbalance is related to the loss of plasma protein. In a third degree burn involving 30 to 40 per cent of the body area, 50 per cent of the total plasma protein will be lost in eight to twelve hours following injury. Hematocrit values rise while plasma protein values fall. It is essential to maintain cell volume value below 55 per cent and the total plasma protein value above six grams per 100 cc.

Plasma requirements vary from 25 to 100 cc. per hour, and the continuous drip is better than single or repeated doses. Dosage is calculated from repeated tests. Acidosis, hypochloraemia and dehydration, which also accompany burns, are treated as has previously been mentioned.

PERITONITIS

Peritonitis is associated with:
1. Hypoproteinaemia.
2. Dehydration.
3. Acidosis.

The treatment of these conditions is as outlined above.
PULMONARY DRAINAGE

Drainage of the pleural cavity, as required in treatment of lung abscess, empyema, pneumonectomy and lobectomy, entails a definite loss of plasma protein which must be compensated for. As a rule, 100 to 200 cc. of plasma given bi-weekly with due regard to hematocrit and plasma protein values is the amount required.

SHOCK AND HEMORRHAGE

Generally speaking, in the treatment of shock and hemorrhage, 500 to 1000 cc. of plasma or blood must be given in the first half hour, followed by 100 cc. of plasma or blood per hour until the peripheral pulse is normal. It is to be noted that 1000 cc. of blood will raise the red cell count by 1,000,000. However, the blood volume is more important than the red cell count in shock therapy.

CONCLUSION

A few general rules for the administration of intravenous fluids, as set forth by Coller and Maddock, who are the first and foremost workers in this field, may be considered of value:

1. When volumes of fluid less than 3500 cc. are to be given, they may be given at the rate of 300 to 500 cc. per hour.

2. Volumes of fluid over 3500 cc. are given on a 24-hour basis at 200 cc. per hour.

3. When 10 per cent glucose is given at 150 to 200 cc. per hour, it has been shown that 95 per cent of sugar is retained and that glucosuria is minimal.

4. Fluids and sodium chloride are to be given by mouth whenever it is at all possible.

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THE ARCHES OF THE YEARS
By HALLIDAY SUTHERLAND


This is a thrilling autobiography guaranteed to hold the interest of the reader from beginning to end. From the very first sentence which reads, "Wanted, a detective—to arrest the flight of time," until the echo has faded from the last wave to beat on the shores of Ultima Thule, you are taken on a wide and varied tour of the Western Hemisphere.

On the pages of this book there is not, as might be expected, an uninteresting chronology of a crotchety, old scientist or a dull practitioner. Here you will find the story of a man whose life was full of colour, one who knew how to accept his own mistakes and benefit by them and by those of others. Sutherland is an interesting personality and will introduce you to others just as alive and exciting as he.

Listed on the table of contents you will find such tempting chapter titles as Northern Seas, Senoritas, A Castle in Spain, the White Plague. You will read about the teachers and students of Scottish medical schools, the excitement of the whale hunt, the "blood and sand" of the Spanish bull fight and the "German" invasion of England in the first Great War.

Truly, for anyone who wants to live a few invigorating hours and travel over this world without losing sight of his chosen profession, this is a wonderful book.

—A. Woolever.

FREUD'S CONTRIBUTION TO PSYCHIATRY
By A. A. BRILL, Ph.B., M.D.


This book has grown out of Dr. Brill's close application to psychiatry during four decades. It is made interesting by his association with well-known personalities—Kraepelin, Bleuler and Freud himself.
The author shows how Freud aided in transmuting the descriptive psychiatry of the past into the dynamic science of today. Where others had described mental diseases, Freud, by his psychoanalytic methods of study, provided a microscope for the examination of both abnormal and normal mental mechanisms. The development of psychoanalysis is traced from its early beginnings and Freud's explanation of the mechanisms involved in neurotic and psychotic behaviour is interestingly outlined.

Dr. Brill says of Freud, "... he has wiped out the line of demarcation between normal and abnormal mentation."

—Ken Ward.

NOTABLE NAMES IN MEDICINE AND SURGERY
By Hamilton Bailey, F.R.C.S., and W. J. Bishop, F.L.A.

All medical students and practitioners are familiar with the countless proper names by which such things as anatomical landmarks, syndromes, surgical procedures, etc., are designated, and yet in most cases are quite ignorant of the lives of the men whose names they perpetuate by everyday usage.

Bailey and Bishop have assembled historical facts concerning the lives and work of some 80 men whose names are most commonly used, embracing medicine from Hippocrates to William Gallie and Lorenz Boeler of our own day. A short biographical note is presented for each man, accompanied by illustrations of the individual, the hospital where he worked, or if a surgeon, a sketch of the operation or particular apparatus named in his honour. There is also a complete index which makes information regarding any name, structure or condition quite easy to find.

The biographies presented are short yet full of information—a characteristic common to most British texts. The particular style and human interest which Hamilton Bailey seems to instill into all his books makes this one as interesting as it is instructive. Judging by the amount of interest shown in this book already, it is evident that it will soon form a part of many medical libraries.

—J. S. Lott.

VENTURES IN SCIENCE OF A COUNTRY SURGEON
By Arthur E. Hertzler, M.D.

Arthur E. Hertzler is a remarkable man. He is a keen anatomist, a well-recognized pathologist, a diligent, precise research worker as well as a surgeon of about fifty years' experience.
In his book, "Ventures in Science of a Country Surgeon," he draws upon the knowledge gained through years of work on the peritoneum under the guidance of Professor Virchow to present a very enlightening and authoritative chapter on the anatomy and physiology of this structure. His treatise of wound healing, based on wide research, is very instructive, practical and, though relatively brief, is complete. The essential principles of local anaesthesia, together with the chief indications for its use, are presented in a fascinating manner. His excellent work on goitres and inflammation of bursae is described. Other interesting chapters are written on chronic appendicitis, surgical pathology, conservative operations on the uterus and ovaries, operations on the perineal region, sciatica and other neuralgias as well as a few chapters on non-medical aspects of medical practice. The final chapter is called "Ventures in Therapeutics." Much good advice on how to learn therapeutics as well as some practical therapeutic measures are presented here.

The excellent features of this book are, first, that the short, practical subjects are chosen so that each may be dealt with fairly adequately and, second, that he writes in a light, easy-to-read, fascinating manner, interposing personal experiences that give an unusually genuine atmosphere to such a scientific text. Many photographs and sketches give added clarity.

I found this a very practical, yet fascinating book.

—J. D. O'Neill.

THE "CONTINENTAL" BREAKFAST

is not suitable for a growing child.

In far too many homes, a breakfast of a roll and a cup of coffee is the fare for children as well as adults. Woefully deficient in vitamins and minerals, such a meal furnishes little more than a small amount of calories. A dish of Pablum and milk, however, is just as easily prepared as a "continental breakfast," but furnishes a variety of minerals and the vitamin B complex, not found so abundantly in any other cereal or breadstuff. The addition of a glass of orange juice and one Mead's Capsule of Oleum Percomorphum can easily build up this simple breakfast into a nourishing meal for the children of the family as well as the adult members. It is within the physician's province to inquire into and advise upon such nutritional problems, especially since Mead Products are never advertised to the Public.
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