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KAPSEALS
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Osler, Teacher and Philosopher

By DR. S. A. MACDONALD

My remarks are intended primarily for the undergraduates and for that reason I am going to confine myself to a consideration of Osler as a teacher and philosopher. I am not going to tell you of his scientific accomplishments, great as they were, except to remind you that he wrote, largely from his own experience, one of the greatest of all textbooks of Medicine. This alone would be a life's work for most men, but after its publication he edited a six-volume System of Medicine and later produced several monographs on various subjects. He also wrote a total of 730 original articles; a truly imposing number when one considers all the multifarious activities in which he was always involved.

Despite these productions, which mark him as one of the world’s most prolific medical writers, I do not believe his name will live as much from them as from his clinical teaching and his moral essays.

In order to appreciate this intangible aspect of his character, it is necessary to see the stage on which his early life unfolded. He was born in 1849, in the Province of Ontario, in the tiny settlement of Bond Head. His father was a pioneer minister whom his mother had married contrary to the wishes of her family. She accompanied him to the wilderness of Canada, and there nine children were eventually born to them; of these William was the seventh. As he himself said, later in his life, his outlook at that time, “was not an auspicious one; born seventh in a backwoods family in the wilds of Ontario, with twins ahead.” Important influences, however, were at work in the development of these children despite their humble origin. They grew up in happy, simple, outdoor play of their own devising, and from their parents they acquired a deep religious sense and a fine moral training that were greater than riches. The importance of these influences was reflected in the later marked success of four of the family; but of them all, William, named after William of Orange, was to be the greatest. He was to become the most eminent physician of his time, was to be the pride of four great universities, and was eventually to be honoured by the King.

*An address delivered before the Osler Society of the University of Western Ontario, February 24, 1939.
To the early formative influences of his home there was soon added another, equally powerful, in the person of the Reverend William Arthur Johnson, one of his first teachers. This remarkable man, who was both a priest and a naturalist, started Osler in his first scientific enquiries in the collection and tabulation of fossils and zoological specimens. In the evenings, Father Johnson was in the habit of reading aloud to his pupils and he often selected passages from the "Religio Medici" of Sir Thomas Browne. This book exerted an extreme fascination for young Osler, and at that time he purchased a copy of the 1862 edition, which became his inseparable companion throughout his life and was placed in his coffin at his death. From this beginning, his love of books developed until he became the greatest medical bibliophile of all time.

Another teacher, Dr. James Bovell, a naturalist and a physician, also greatly influenced Osler in this early period of his life. It was he who turned the boy from his intended study of theology to that of Medicine. It was a happy transition, for Osler's love of his fellow-man and his natural scientific tendency, so early developed, made him eminently suited for his chosen profession.

He entered the medical school at Toronto but soon became dissatisfied because of the lack of clinical teaching and opportunity for contact with patients. In his third year he enrolled at McGill because the Montreal General Hospital had taken the unprecedented step of allowing students on the wards. He revelled in this greater freedom and came into contact with a group of extremely capable clinicians, headed by Dr. Palmer Howard. These men were to have as profound an effect on shaping Osler's clinical career as Johnson and Bovell had earlier in stimulating his natural propensity in the study of science.

In 1872 he graduated and went to Europe for two years to complete his studies. On his return to Canada, he did a locum tenens in Hamilton, where he collected his first medical fee of fifty cents for removing a small speck from a patient's cornea. He also substituted, for a short time, as resident physician in the City Hospital in Hamilton, for which service he received the sum of twenty-five dollars and a pair of elastic boots.

He then accepted an appointment as lecturer at McGill in the Institute of Medicine, which department, after the Edinburgh tradition, included Physiology and Pathology as well as Therapeutics. The following year, at the age of twenty-five, he was made a full professor. He remained in Montreal for fifteen years, during which time he was occasionally declared a radical, for he little respected the established order and the accepted methods of the time. He was supported in reorganizing the clinical teaching by the younger group in the university. During this period he spent much of his time in Pathology, doing most of the routine autopsies of the hospital. The profound knowledge he acquired of gross and microscopic pathology greatly enhanced the
value of his teaching and became the basis of the famous text book “Principles and Practice of Medicine” which he later published.

In 1884 he was offered the Professorship of Medicine at Philadelphia. He was approached by a representative of the Philadelphia School while he was sojourning in London. The University of Philadelphia, the oldest medical school in the United States, was a proud and distinguished institution. It insisted that its professorial staff be socially as well as academically qualified. Osler was not found wanting in either score and he received the appointment to follow the renowned Pepper in the Chair of Clinical Medicine.

At first he was somewhat of a disappointment to the Philadelphia students, who were accustomed to eloquent, didactic lectures. Osler did not approve of this form of teaching and was not at his best in the classroom. However, his instruction at the bedside and in the clinic was a revelation to all. The infectiousness of his enthusiasm soon permeated the whole institution, and it was not long until he was recognized as the greatest teacher in a university which prided itself upon the ability of its professorial staff. One of his colleagues, Professor J. C. Wilson, describes Osler in these words: “Not only by precept but by example has he been an uplifting influence on our professorial life. The source of that influence is to be sought not only in his accomplishments as a physician, not in learning, not in wisdom, not even in his buoyant, well-balanced temperament, but in that basic principle which we all recognize but never can define, which, for want of a better name, we call character.”

After five happy, busy and revolutionary years at Philadelphia he accepted the post of Professor of Medicine at Johns Hopkins Hospital. There he was to have a unique opportunity of applying his theory and principles of teaching. The hospital had just been opened and the heads of departments were young men, keen and enthusiastic like himself; Welch in bacteriology, Kelly in gynaecology and Halstead in surgery. These three, along with Osler, became the luminaries of the institution and, untramelled by tradition, they created the greatest hospital centre on this continent.

Until that time there had never been in America an organized medical clinic devoted not only to the diagnosis but also to the study of disease. Osler secured the appointment of a permanent senior staff and introduced the residency system. Through it the most promising of the students and junior interns were given the privilege of advanced training in order that they might fit themselves for higher positions. The success of this system was soon manifest in the subsequent achievements of the men who passed through the residency.

Seven years elapsed before the university was opened and undergraduate teaching begun. By that time the institution was well organized and every attention could be given the students. Osler introduced the best teaching methods which he had learned first hand from repeated
visits to the great European universities. The students were started from their third year in actual clinical work in the Out-Patient Department, where Osler himself spent much time with them. This was followed in the fourth and fifth years by actual ward experience. The students were privileged to take an active part in examining and diagnosing the cases and, under supervision, prescribed treatment.

He carried his interest in the students beyond the classroom, and every Saturday night over beer and cheese in his home he gathered together his clinical clerks to discuss the interesting cases of the week. At these meetings he invariably enlightened the discussion by bringing from his library original treatises on each subject. In this way he tried to stimulate the students' interest in the history of Medicine. He also attempted to do this on the wards by constantly urging the students to refer to original sources.

During this period of his life Osler is described as a man of small stature, well formed, with an olive complexion and black, piercing eyes. He possessed an overwhelming enthusiasm which infected all those with whom he came into contact. His instruction was full of apt quotations and unexpected interjections which served well to illustrate his point, and he was not reluctant to tell of his own mistakes to further demonstrate a truth.

He always considered himself a student among students, and had the happy faculty of making his charges feel on the same level as himself. In describing the gulf that too frequently separates teacher and student he says:

"A fraternal attitude is not easy to cultivate—the chasm between the chair and the bench is difficult to bridge. The successful teacher is no longer on a height, pumping knowledge at high pressure into passive receptacles. The new methods have changed all this. He is no longer Sir Oracle, perhaps unconsciously by his very manner antagonizing minds to whose level he cannot possibly descend, but he is a senior student anxious to help his juniors. When a simple, earnest spirit animates a college there is no appreciable interval between the teacher and the taught—both are in the same class, the one a little more advanced than the other. So animated, the student feels that he has joined a family whose honour is his honour, whose welfare is his own, and whose interests should be his first consideration."

So successful was Osler's teaching and so widely had his fame spread as a writer and clinician that in 1905 he was offered the chair of Regius Professor of Medicine at Oxford. At that time he was fifty-six and his life in Baltimore had become almost too strenuous. He was beginning to feel the burden, and with sincere regret decided to break the Baltimore association. In his farewell address to America he said:

"I have three personal ideals. One, to do the day's work well and not to bother about the morrow. It has been urged that this is not a
satisfactory ideal. It is; and there is not one which the student can carry into practice with greater effect. To it, more than anything else, I owe whatever success I have had, to this power of sitting down to the day's work and trying to do it well to the best of one's ability and letting the future take care of itself.

"The second ideal has been to act the Golden Rule, as far as in me lay, toward my professional brethren and toward the patients committed to my care.

"And the third has been to cultivate such measure of equanimity as would enable me to bear success with humility, the affection of my friends without pride, and to be ready when the day of sorrow and grief came to meet it with courage befitting a man.

"I have made mistakes but they have been mistakes of the head, not of the heart. I can truly say, and I take it upon myself to witness, that in my sojourn with you

"'I have loved no darkness, Sophisticated no truth, Nursed no delusion, Allowed no fear.'"

His appointment at Oxford was a particular honour because he was the first outsider ever to be given the chair. By an odd coincidence he succeeded Burdon Sanderson, under whom he had studied as a young man on his first trip abroad from McGill thirty-five years before. He had often said that he would like to live within an hour of the British Museum. Oxford was indeed an ideal setting for him; the quiet English town and its ancient university, with its ivied towers, the atmosphere of peace and dignity and, above all, Bodleian's Library, of which he became curator. Amongst its treasured volumes he was to spend many a happy hour, and during his years in Oxford his own library grew apace until at his death it contained 7,600 volumes, for the most part rare books selected because of their value in the study of the history of medicine and science. His home in Oxford became filled with these books, just as it so frequently was with guests from all parts of the world.

The duties of the Regius Professor were not onerous, but here, as in America, he soon became involved in a multiplicity of affairs. The rest he so ardently sought and so badly needed did not materialize. Amongst all the honours which came to him in England there were none that he treasured more, not even his elevation to a baronetcy, than the presidency of the Classical Association, an appointment never before held by a practicing physician. The classical knowledge which made him eligible for this post was acquired through his custom of reading fine literature for half an hour each night after going to bed. This habit indulged in for forty years enabled him to read all that was great
in poetry and prose and filled his mind with a classical lore which is frequently found in his writings.

During his later years in Oxford his health gradually deteriorated. The strain of the increased activity demanded by the war told heavily upon him, and he never quite recovered from the sorrow of his son's death in France. The end came on the twenty-ninth of December, 1919, a few months after his seventieth birthday.

His memory, however, will live for all time, especially in his philosophy and his ideals which he so beautifully expressed in his extra-professional writings. Many of these were intended for and addressed to students like yourselves. They are replete with many counsels of perfection. In one place he says:

"Learn to love the freedom of the student life, only too quickly to pass away; the absence of the coarser cares of after days, the joy in comradeship, the delight in new work, the happiness in knowing that you are making progress. Only once can you enjoy these pleasures."

He goes on to say that

"The hardest conviction to get into the mind of a beginner is that the education upon which he is engaged is not a college course, not a medical course, but a life course, ending only with death, for which the work of a few years under teachers is but a preparation. Whether you will falter or fail in the race or whether you will be faithful to the end depends upon the training before the start, and on your staying powers. You can all become good students, a few may become great students, and now and again one of you will be found who does easily and well what others cannot do at all, which is John Ferrier's excellent description of a genius."

He cautions the student to put his emotions on ice and not to have any "Amaryllis in the shade" and not to become "entangled in Naeara's hair," for thereby, he warns, "lies the worm regret and failure of devotion to the jealous Mistress of Medicine." He also admonishes against too close attention to books by saying:

"The seclusion of the student life is not always good for a man, particularly for those of you who will in after years engage in general practice, since you will miss that facility of intercourse upon which the doctor's success depends. On the other hand, sequestration is essential for those of you with high ambitions proportionate to your capacity. It was for such that St. Chrysostum gave his famous counsel, 'Depart from the highways and transplant thyself into some enclosed ground, for it is hard for a tree that stands by the wayside to keep its fruit till it be ripe.'"

He also asks that the student be not discouraged by critics of the profession. "Some will tell you," he says, "that the profession is underrated, unhonoured, underpaid, its members social drudges—the very last profession they would recommend to a young man to take up. Listen
not to these croakers; there are such in every calling, and the secret of their discontent is not hard to discover. The evils which they depreciate and ascribe—it is difficult to say to whom—in themselves lie; evils, the seed of which are sown when they were as you are now (students); sown in hours of idleness, in inattention to studies, in consequent failure to grasp those principles of their science without which the practice of medicine does indeed become a drudgery, for it degenerates into a business. I would rather tell you of a profession honoured above all others; one which, while calling forth the highest powers of the mind, brings you into such warm, personal contact with your fellow-men that the heart and sympathies of the coldest nature must needs be enlarged thereby."

The young graduate he tells to be prepared for and not to be discouraged by the first lean years of practice when existence is eked out on crumbs from men in the cakes-and-ale stage of their careers. Above all, he hopes that no mercenary attitude be adopted. He says:

“If your heart’s desire is for riches, they may be yours; but you will have bartered away the birthright of a noble heritage, traduced the physician’s well-deserved title of the Friend of Man, and falsified the best tradition of an ancient and honourable guild.”

He goes on to say that “Five years, at least, of trial await the man after parting from his teachers and entering upon an independent course—years upon which his future depends, and from which his horoscope can be cast with certainty. It is all the same whether he settles in a country village or goes on with hospital or laboratory work; whether he takes a prolonged trip abroad; or whether he settles down to practice with a father or a friend—these five waiting years fix his fate so far as the student life is concerned. Without any strong natural propensity to study, he may feel such a relief after graduation that the effort to take to books is beyond his mental strength. Ten years later he is dead mentally, past any possible hope of galvanizing into life as a student, fit to do a routine practice, often a capable, resourceful man, but without any deep convictions, and probably more interested in stocks or horses than in diagnosis or therapeutics.”

To ward off such stagnation he recommends a quinquenial brain dusting. He asks that you “Deny yourselves all luxuries for it—harken not to the voice of old Dr. Hayseed, who tells you it will ruin your prospects and that he never heard of such a thing as a young man, not yet five years in practice, taking three months’ holiday. To him it seems preposterous. Watch him wince when you say it is a speculation in the only gold mine in which the physician should invest—GREY CORTEX! What about the wife and babies, if you have them? Leave them! Heavy as are your responsibilities to those nearest and dearest, they are out-weighed by the heavier responsibilities to yourself, to the profession and to the public.”
His remarks concerning general practice are particularly appropriate today. In speaking to a gathering of students, he said:

"May this be the destiny of a large majority of you! Have no higher ambition! You cannot reach any better position in a community; the family doctor is the man behind the gun who does our effective work. That his life is hard and exacting; that he is underpaid and overworked; that he has but little time for study and less for recreation—these are the blows that may give finer temper to his steel, and bring out the nobler elements in his character. . . . The practice of medicine is an art, not a trade; a calling, not a business; a calling in which your heart will be exercised equally with your head. Often the best part of your work will have nothing to do with potions or powders, but with the exercise of an influence of the strong upon the weak, of the righteous upon the wicked, of the wise upon the foolish. To you, as the trusted family counsellor, the father will come with his anxieties, the mother with her hidden grief, the daughter with her trials, and the son with his follies. Fully one-third of the work you will do will be entered in other books than yours. Courage and cheerfulness will not only carry you over the rough places in life, but will enable you to bring comfort and help to the weak-hearted and will console you in the sad hours when, like Uncle Toby, you have 'to whistle that you may not weep.' . . . There are country practitioners among my friends with whom I would rather change places than with any in our ranks, men whose stability of character and devotion to duty make one proud of the profession. As I have said before, have no higher ambition than to become an all-round family doctor whose business in life is to know disease and to know how to treat it."

In bringing this paper to a close, I would like to give you this last quotation:

"Remember what we are—useful supernumeraries in the battle, simply stage accessories in the drama, playing minor but essential parts at the exits and entrances or picking up here and there a strutter who may have tripped upon the stage."

I would like you to carry away with you this precept, one which Osler held always before him, "That we in medicine are here to add what we can TO, not to get what we can FROM life."
Primary or Bronchogenic Carcinoma of the Lung
By HAROLD LIPOWITZ, M.D. (Tor. '39)
St. Joseph's Hospital, London, Ontario

In studying the literature one is impressed by the rapidly growing interest in primary or bronchogenic carcinoma of the lung. The importance of this disease may be appreciated by the general statement that its incidence has supposedly increased from roughly 1.5 per cent of all carcinomas to approximately 5-10 per cent. It has been said that it is important to think of pulmonary neoplasm when a patient in the cancer age group, showing no symptoms of cardiac, renal or arterial disease, begins to cough and is short-winded. It is a generally accepted idea that the condition is now more common than formerly. The increase is evidently due to early diagnosis, which may be explained by: (1) improved clinical and pathological methods of diagnosis, (2) increased attention to the malady and (3) the increased span of human life.

The age incidence varies from 13 to 73 years, but the disease occurs most often between 40 and 60 years of age. It is three times as common in men as in women. This is explained on the basis that persons of the male sex are more exposed to pulmonary disease, and the preponderance of the male population. Rosedale, in his analysis of 57 cases with respect to occupation found that 48 to 75 per cent of cases were exposed to atmospheric hazards. The ratio of the incidence in the right lung as compared to the left is 5 to 3. This is attributed to the shorter, wider and more vertical right bronchus, which is thus more subject to irritation.

Ætiology

Many factors have been incriminated in the ætiology of bronchogenic carcinoma of the lung. Of these, the three most important factors are discussed:

Tuberculosis: Friedlander and Perrone describe a squamous cell carcinoma developing in the wall of a tuberculous cavity. However, many believe in the existence of an antagonism between cancer and tuberculosis. Also there seems to be an antagonism between cancer and the granulomata of syphilis and leprosy. This might indicate that the antagonism is not specific but common to the granulomata.

Influenza: One finds at autopsy in influenza patients a metaplasia of the bronchial mucosa. Since in other viscera this type of regeneration results in the formation of cancer, in 30 per cent of instances it was thought to be true of the lungs. However, in Iceland, where the influenza epidemic was severe, not one case of carcinoma was found.
Also, metaplasia of the bronchial epithelium occurs in fatal cases of whooping cough, measles, diphtheria and in some cases of non-influenzal pneumonia.

IRRITATION THEORY: In the Schneeberg cobalt mines there occur acutely developing cancers which are attributed to the inhalation of irritants to which the workers are exposed. A survey showed that no cases occurred in persons of the same district who were not working in the mines. In these mines, cobalt, bismuth and arsenic are obtained. In other mines where bismuth and cobalt alone are produced this disease does not occur. Twenty miles from Schneeberg are the radium mines of Joachimsthal, where the workmen also commonly develop pulmonary cancers. Thus it would appear that arsenic and radio-active substances are probable etiological factors. A similar example is the osteo-sarcoma of the radium dial workers, referred to by Maritand.

Moller painted the backs of young rats with tar and did not produce carcinoma of the skin, but rather carcinoma of the lungs. Similar results were obtained with mice. It was believed that tar acts as a factor in lowering the resistance of mice, while the cancer is caused by the inhalation of irritants. The irritation in this case was due to the fact that the mice lived in burrows under sawdust and hay. Today, the irritation theory of Virchow is regarded as an essential factor in the etiology of carcinoma of the lung.

The study of the etiology of cancer thus comprises three distinct phases:

1. An extrinsic factor, that causes tissue injury,
2. An intrinsic factor, which is the general susceptibility of the individual,
3. The transformation of the cell to a malignant status.

PATHOLOGY

Practically all primary pulmonary carcinomas originate in a bronchus. The cells lining the respiratory tree and forming its glands are all derived from the epithelial bud. The air sacs in the lungs are not "lined" by epithelial cells but by macrophages scattered in groups along the alveolar walls. Since these are mesenchymal in origin, they cannot give rise to epithelial tumours. The lining of the bronchi and their divisions is made up of three different types of cells, ciliated columnar, goblet cells and basal cells. The basal cells, only, have the property of regeneration. One might conclude that the basal cells are concerned in the histogenesis of malignancy of the lungs. These cells, being undifferentiated, can therefore undergo metaplasia to form the squamous cell, adeno- and small cell carcinomas.

There is no tumour which is so pleomorphic as cancer of the lung. The cells vary from the most fully differentiated to very anaplastic types.
HISTOLOGICAL CLASSIFICATION
(Mattick and Burke)

A — CELL DIFFERENTIATION

1. Adenocarcinoma:
   (1) Not mucus-producing, with columnar cells lining the acini.
   (2) Mucus-producing.
   (3) Cuboidal cells lining the acini.

2. Squamous-Cell:
   (1) Squamous-cell tendencies:
      (a) Keratinizing,
      (b) Non-keratinizing.
   (2) Basal-cell tendencies.

3. Anaplastic:
   (1) Round-cell.
   (2) Spindle-cell (oat-cell).

B — CELL UNDIFFERENTIATION

1. Adenocarcinoma: This is diagnosed by the presence of acini lined with cuboidal or columnar cells resembling the columnar cells lining the bronchial mucosa. The acini vary in size and shape, having one or many layers of cells. There may be evidence of mucinous secretion and cell debris in the lumina of the acini. Some show invasion of the blood vessels with the formation of tumour thrombi in the lumina. This type of tumour is, in most cases, remote from the hilus.

2. Squamous-Cell Carcinoma: This tumour is acute pleomorphic and grows without any definite arrangement. Nests and groups of cells are scattered through it, surrounded by thick bands of dense fibrous tissue. The cells are of the large, flat, squamous type, with scant, pale-staining cytoplasm and hyperchromatic, vesicular nuclei. The cells present the appearance of cornified epithelium with keratinization and pearl formation.

   The Basal-Cell is the non-keratinizing type, consisting of polyhedral cells which have large cytoplasm and voluminous, vesicular nuclei. The cells are arranged in columns from two to three cells in width which show anastomosis and branching. There is no pearl formation, the stroma is of loose oedematous tissue infiltrated with small round cells. The tumour does not metastasize even to the tributary lymph nodes and has no tendency to degenerate.

3. The Anaplastic Group (Synonyms: “oat,” spindle, round cell) is found chiefly at the hilus. In the round-cell type, the tumour is made up of cells resembling lymphocytes with scant cytoplasm and hyperchromatic nuclei. There is a tendency to invade the lymphatics and venous system. Hence this type is characterized by widespread and distant metastases. The oat-cell type have cells which are small and oval with scant cytoplasm, which have been likened to oat grains. The tumour
forms a large mass which replaces the lymph glands of the posterior and lateral mediastinum, and infiltrates the pericardium.

**GROSS PATHOLOGY**

1. *Hilar Type* (90 per cent): The majority of the hilar type of tumours originate in the primary bronchi; others arise in the main lobar divisions of the latter. Through a bronchoscope the tumour is seen as a slight roughening of the mucous membrane. In this area the bronchial wall is thickened as a result of neoplastic cell infiltration. One may also see a polypoid mass projecting into and narrowing the lumen. The tumour presents a greyish, translucent surface often studded with pigment, thrombosed vessels and an occasional infarct. The consistence will vary with the cell type. A tumour arising from the main bronchus may produce inflammation and obstruction of the bronchus, leading to collapse distal to the obstruction, bronchopneumonia, abscess formation and empyema. Infection and weakening of the wall plus repeated coughing lead to bronchiectasis. Ball-valve occlusion results in emphysema. In some cases unilateral or bilateral hydrothorax or hæmothorax occurs.

2. *Peripheral Type* (10 per cent): This type is similar to the first but the origin is the bronchial epithelium at any point as far distally as the respiratory bronchiole. Here the carcinoma cannot be seen with the bronchoscope, but may be detected with X-ray. It is recognized as a circular nodule with infiltrating strands extending from its surface. Again, the consistence depends on the cell type.

In either case, the tumour, as it advances, becomes a large mass with involvement of the tracheo-bronchial lymph glands and distant metastases. The pleura becomes diffusely infiltrated, forming an adhesive pleuritis. One can conclude that bronchogenic cancer is a single, unilateral lesion near the hilus in contrast with bilateral, multiple, metastatic tumours near the periphery.

**METASTASES**

1. *Direct Extension*—Through the lung, mediastinum, pericardium, diaphragm, liver and pleura, *e.g.*, squamous-cell cancer.

2. *Lymphatics*—(a) Through the lung by perivascular and peribronchial lymphatics; (b) To neighbouring lymph nodes—which is a constant finding, at first to the regional (tracheobronchial and mediastinal) and, later, to distal glands (supraclavicular, cervical and retroperitoneal), *e.g.*, small cell cancer.

3. *Hæmatogenous*—Liver, brain, bone, kidney and adrenals are affected most frequently; metastases to pancreas, thyroid and other organs are not commonly found. If, at autopsy, tumours consisting of small round cells are found in the brain, lung and adrenals, the primary tumour is quite possibly cancer of the lung. The frequency of cerebral metastasis is favoured by the absence of a barrier between the lungs and the brain.
4. *Aerogenous*—Tumour cells may be coughed into the opposite lung and set up secondary foci.

**CLINICAL INVESTIGATION**

1. **History:** Clinically pulmonary cancer presents two groups of patients. One is a typical group which includes patients whose chief complaints point to thoracic organs, and the other, a group whose symptoms are referable to metastatic involvement. In the typical group the onset is insidious but occasionally it is acute with hæmoptysis and pain. The sudden appearance of these symptoms without evident cause in a man of cancer age should suggest the inclusion of cancer of the lung in the differential diagnosis.

2. **Chief Symptoms** (in order of their frequency):
   (1) *Cough:* Productive or dry. At first it is an irritative, non-productive cough, which is later accompanied by expectoration of mucoid, muco-purulent, or frankly purulent sputum, often troublesome at night. Cough is present in about 90 per cent of the patients. A superficial dry cough or grunt may be, often, unnoticed by the patient.
   (2) *Sputum:* Mucoid, muco-purulent material. Blood-tinged or rusty sputum is early and is evidence of mucosal ulceration. Frank hæmoptysis occurs later.
   (3) *Pain:* Thoracic pain is a persistent, sharp, stabbing or dull, substernal, deep, aching, continuous pain, very persistent in nature and failing to respond to treatment. Thoracic pain, persistent and boring, and not accompanied by rales, is almost diagnostic of cancer.
   (4) *Dyspnoea* in the absence of cardiovascular disease is suggestive of carcinoma. It may be caused by the tumour growing around the bronchi and blood vessels and constricting them in a ring-like manner, thus interfering with respiration and circulation. Wheezing in the chest suggesting asthma may be due to a papillomatous nodule in a large bronchus.
   (5) *Low Fever and Night Sweats* are probably due to superimposed pulmonary infection.
   (6) *Cachexia:* Loss of weight, appetite and strength occurs from six to eighteen months before death.
   (7) **Symptoms of Metastasis:** 1, Abdominal pain; 2, nausea and vomiting; 3, dysphagia in 25 per cent of cases; 4, slow speech, hoarseness and dysphonia; 5, spontaneous rib fracture; 6, Horner’s syndrome; 7, bronchial palsies; 8, symptoms of brain tumour, *e.g.*, Jacksonian epilepsy, etc.

3. **Physical Findings:** Physical examination frequently reveals nothing as the tumour is covered by lung tissue.
   (1) *Asymmetry of the chest* may be seen, as bronchogenic cancer is an unilateral lesion. The asymmetry is usually due to bronchial
obstruction with collapse of the lung. The respiratory excursion of the affected side will be rather shallow, and the intercostal spaces narrowed.

(2) Cyanosis: It is necessary for the whole lung to be shut off from aeration before cyanosis occurs. This is probably due to the slow development of the tumour, during which time the patient adapts himself to the condition.

(3) Oedema: Occurs when the tumour interferes with the circulation either from within by a thrombus or from without. Oedema may be confined to one arm or to the entire chest. In such instances there is also dilatation of the superficial veins.

(4) Adenopathy: The finding of a sentinel gland (left subclavian lymph node) is uncommon in cancer of the lung, and characteristic of gastric cancer.

(5) Inequality of the pupils: Due to sympathetic paralysis.


(7) Deviation of the trachea or mediastinum.

(8) Increased area of mediastinal dullness.

(9) Club-fingers: This is secondary to some primary disease elsewhere and is not pathognomonic of bronchogenic cancer.

When infection is superimposed one may get a clinical picture of bronchiectasis, lung abscess, pneumonia or empyema. Diminished breath sounds, dullness or flatness on percussion, rales, rhonchi, etc., are the usual findings.

SUMMARY: Clinically it is difficult to make a prompt diagnosis of bronchogenic cancer due to the similarities existing between this disease and a number of other chronic pulmonary diseases. There is not a single symptom which is not common to tuberculosis, lung abscess and bronchogenic cancer. Of particular interest, however, is the frequent diagnosis of brain tumour, which is due to metastasis to the brain.

4. SPECIAL EXAMINATIONS:

(1) Sputum: Occasionally microscopic fragments of tumour have been found in sputum. In 1935 Dudgeon described the “wet film” method of examination for malignant cells, which is positive in 60 per cent of the cases.

(2) Bronchoscopic Examination: Negative in 20 per cent of cases (where the growth is more peripheral), and positive in 80 per cent. Thus the sputum and bronchoscopic examinations will give a positive diagnosis in approximately 90 per cent of cases. One may see narrowing of the lumen, due to the tumour growing into it or causing pressure from without. The mucosa may show roughening or thickening. Any broadening of the carina between the two main bronchi is suggestive of glandular involvement below the tracheal bifurcation and would contra-indicate operation.
Bronchoscopic Biopsy is highly recommended and diagnostic.

Pleural Exudate: Haemorrhagic fluid of a sterile type is suggestive of malignancy. The fluid is centrifuged and the sediment is fixed in a 10 per cent solution of formaldehyde or Zenker's fluid and paraffin sections are cut. The diagnosis rests on the demonstration of cells indicative of the tumour. In the small-cell tumour the cells resemble blood cells and the nuclear structure may be obscured by hyperchromicity.

Radiology: Is of considerable value and it has been possible to detect the outlines of growths in the main bronchi, using radio-opaque oil.

In the more peripheral neoplasms which have become necrotic and resemble abscesses, the gross thickness of the cavity wall, due to the presence of neoplastic tissue, is demonstrated. X-ray of the chest may be essentially normal but quite frequently reveals pulmonary collapse, lung abscess, bronchiectasis or enlarged mediastinal glands.

DURATION AND PROGNOSIS

Clinical reports have shown that pulmonary cancer runs a rapid course, from about three months to three years. However, the disease probably runs a chronic course, lasting for several years, the short histories reported being due, in all probability, to late recognition. The prognosis will depend on metastases, secondary infection, haemorrhage, necrosis collapse, pneumothorax and pleural involvement.

THE RELATION OF SYMPTOMS TO LESIONS

(1) The silent tumour is in the parenchyma of the lung and discovered only by X-ray or the development of distant metastases.

(2) Pleurisy, friction rub and pleural effusion are due to a tumour in close proximity to the visceral pleura.

(3) Bronchial obstruction by the tumour gives rise to atelectasis of the corresponding area of lung. Bronchiectasis and abscess formation may be complicating factors. Fever and leucocytosis are due to secondary infection. The signs of bronchial obstruction resemble closely those of localized pleural effusion. However, a knowledge of physical symptoms helps one to differentiate between them. Signs of an occluded bronchus are usually an indication for bronchoscopic examination.

(4) Superior Sulcus Syndrome, described by Pancoast, is due to apical involvement by the tumour.

(a) Horner's Syndrome—due to sympathetic trunk paralysis.

(b) Pain, referred to the arm and partial paralysis of the ulnar and median nerves due to first dorsal root invasion.

(c) Erosion of the ribs—seen by X-ray.

(5) Hoarseness and dysphonia due to involvement of the recurrent laryngeal nerves.

(6) Oedema and distended veins of the upper chest are the results
of obstruction of the superior vena cava by the tumour in the mediastinum.

(7) Cough and haemoptysis caused by the irritation of a bronchus, with ulceration of the mucous membrane, by the growth. Recurrent, blood-stained sputum may lead to the erroneous diagnosis of pulmonary tuberculosis.

(8) Shoulder pain may be due to irritation of the central part of the diaphragmatic pleura supplied by the phrenic nerves.

(9) Foul, copious, purulent sputum is the result of necrosis of the tumour with cavitation and abscess formation.

(10) Dysphagia—is due to oesophageal obstruction by pressure of the tumour.

(11) Pain in the back may be due to erosion of the vertebral bodies by the tumour, or bone metastases.

CORRELATION OF THE TUMOURS WITH REGARD TO GROWTH, DISSEMINATION, CLINICAL COURSE AND PROGNOSIS (Koletsky)

(a) Small-Cell Carcinoma: Highly malignant, metastasizes chiefly through the lymphatics, and offers a poor prognosis. It is primary at the hilus, affects younger persons and there is a rapid clinical course without notable remissions. It is surgically inaccessible at the onset.

(b) Squamous-Cell Carcinoma: Slow-growing, locally invasive, and relatively non-metastasizing; accompanied by infection, necrosis and cavity formation. Involvement of the lymph nodes, other than regional, is infrequent. It offers the most favourable prognosis for complete resection. Pneumonecctomy in the early stages is possible.

(c) Adenocarcinoma: Surgical intervention is less favourable since the tumour, while locally invasive, shows more frequent and more extensive lymph node involvement and metastasizes by way of the blood stream.

SUMMARY

Bronchogenic carcinoma is frequent enough to be included in the differential diagnosis of chest diseases, in patients over 30 years of age. A rather abrupt onset of symptoms and signs due to a more or less rapidly developing intra-cranial lesion in a person of middle age should suggest brain metastasis and examinations of the lungs for a primary tumour should be performed.

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A Case of Undulent Fever

By ODON VON WERSSOWETZ
A.B. (Cop. Col.); B.A. (Tor.); M.B. (Prague); M.D. (Tor.)
St. Joseph's Hospital, London, Ontario

MRS. R. F., a housemaid, aged 22 years, was admitted to St. Joseph's Hospital on December 15, 1938, with the chief complaints of nausea and vomiting, feverishness, headache, generalized aches and pains, malaise and insomnia. According to the patient, the condition began last winter (1937) when she started to experience insomnia and nightmares. She was very much upset about this and became extremely nervous, irritable and excitable, crying on the least provocation. At about the same time she felt very weak and had malaise and lassitude. About the end of January, 1938, she began to have generalized aches and pains, mostly in the upper abdomen, radiating to the back. Her bowel function seemed to be very irregular, having alternating constipation and diarrhoea. In June, she had a suspension operation for retroversion and prolapse of the uterus. Recovery was uneventful. Her symptoms appeared to be relieved only for a short time because during the summer she again had attacks of diarrhoea and constipation. The pain in her upper left abdomen, as well as the other symptoms persisted, but the patient carried on until the fall of 1938.

About this time she started to bleed easily from the gums, and developed a swollen and painful left shoulder. On December 11th she had a marked attack of nausea and vomiting; the following day had fever and a severe headache. On December 13th she stayed in bed; next day attempted to work but was too weak to carry on and on December 15th she was admitted to the hospital.

On admission her temperature was 100°, pulse 80, respirations 20, blood pressure 118/88 mm.

On physical examination the patient was found to be well nourished and not acutely ill. The significant findings were:

(1) A highly nervous and easily excitable patient. Bleeding from gums, which were spongy in appearance; tongue coated. Tenderness over the left abdomen, extending from the costal margin to Poupart's ligament.

(2) Spleen enlarged about one finger below the costal margin.

(3) Swollen left shoulder which was painful on movement.

(4) R.B.C.—4,450,000. W.B.C.—6,400. H.B.—100%.

(5) Sedimentation rate—10 mm. in one hour.

(6) Urinalysis negative.

(7) Wasserman reaction negative.

This case report (with minor alterations) was read before the Staff Meeting of the St. Joseph's Hospital, London, Ontario on January 19, 1939.
In the differential diagnosis the following were considered:
1. Influential infection of the respiratory tract.
2. Tuberculosis.
3. Typhoid group fevers.
4. Undulant fever.
5. Rheumatic fever.

The patient was put to bed and kept under close observation. She was treated provisionally for upper respiratory infection. A consistent rise in temperature reaching 102° and 103° was observed every 6.00 a.m. It usually came down to about the normal level in the afternoon. The rise was associated with marked chills. There was also a corresponding rise in pulse rate from about 60 to 88.

Summarizing the findings: We had a young female suffering from (1) indigestion, (2) alternating constipation and diarrhoea, (3) bleeding from gums, which were spongy, (4) enlarged and painful spleen, (5) headache, (6) generalized aches and pains, (7) insomnia, (8) hysterical manifestations, (9) profuse perspiration, (10) swollen left shoulder, (11) coated tongue, (12) loss of appetite, and (13) fever, gradual in onset and of the undulatory type.

The relatively high temperature and the low pulse suggested the possibility of colon typhoid group, but for the undulatory type of fever. A provisional diagnosis of undulant fever was made and the patient was put on prontylin grs. X.T.I.D.

Two days later the report on agglutination test proved the presence of bacillus abortus in a dilution of $\frac{1}{220}$.

Patient was receiving 30 grs. of prontylin every day. On about the 10th day the temperature became normal and remained so. During the whole course of treatment the patient received a total of 435 grs. of prontylin.

During the course of the disease the blood count showed marked secondary anaemia. The R.B.C. was 3,700,000 and H.B. 76%. After the fever had subsided there was marked improvement in the patient's general condition as well as her blood picture, which on discharge approached her normal.

DISCUSSION

Undulant fever, also called Malta fever, Mediterranean fever, Bruce's Septicemia, etc., is characterized by febrile attacks which persist for weeks or months, with many remittances.

Undulant fever is an ancient disease. Hippocrates described a long-continued fever, which in all probability was undulant fever. In the 18th and 19th centuries Howard, Herinen and Davy gave descriptions of protracted and remittent fevers occurring in Malta; in all probability related to this disease. Much confusion was caused in Malta during the Crimean War by the presence of both Malta fever and typhoid. There, the disease was recognized as a specific entity. Bruce, in 1886, proved that Malta fever had a definite aetiology, when he dis-
covered the organism in the spleen. A year later he cultivated the organism on agar and was able to reproduce the disease in monkeys by inoculation. In 1904 a Commission was appointed by the British Government to investigate this disease. They showed that the organism leaves the body for the most part in the urine and that it is capable of existing for a long time outside the body. It was discovered also that the milk of many goats contained the organism, the Brucella melitensis. The organism is described as a coccus, some consider it a bacillus, others a coccobacillus. It is found in the spleen, liver, kidney and lymphatic and salivary glands. This disease, undulant fever, is not solely produced by Brucella melitensis. It is caused by Brucella abortus, of which there are two types: (a) bovine type, (b) porcine type. Any of these three major varieties can attack human beings. The resulting disease, in all, has a more or less similar or identical clinical course and pathology.

The organism is non-motile, possesses no capsule and produces no spores. Its growth is extremely slow, and with some strains cultivation is much more difficult than with others. Differentiation between different strains is very difficult, and they all seem to give positive agglutination reaction for Brucella abortus, there being no serological difference between the bovine and porcine varieties.

The Brucella melitensis and the Brucella abortus usually enter the system through the alimentary tract and produce septicemia. This, as some investigators believe, is of a transient character.

The organism may be found in the heart, blood and nearly all the internal organs. The marked enlargement of the spleen at times causes confusion with typhoid fever. Agglutinins are formed about the fifth day, and may be regarded as specific.

It is the general belief that one attack of Malta fever or undulant fever protects against a second attack. It is difficult, however, to be certain that the first attack is cured.

TREATMENT

Vaccine therapy has been employed for many years, but in man it has not demonstrated its usefulness, nor has it been carried out on a sufficiently large scale to permit the formulation of conclusions. Serum treatment in man has been attempted, but has never proven to be of any practical value in the treatment of undulant fever.

There is, as yet, no drug of relative safety that is specific against the causative organism of undulant fever. Quinine, salicylic acid and neo-salvarsan have been tried but without favourable results.

Mercurochrome has been used intravenously. The concentration of this drug which it is possible to obtain in the blood stream is not sufficient to destroy the causative organism. It is impossible to raise the concentration beyond this point as it has toxic effects on the body.

Acriflavine has been employed in a few cases, particularly in Italy;
the best effect was obtained if the drug was given in the maximum intravenous dose of 0.01 gm. per kilo of body weight. This dose may have to be repeated once or twice. The injection must be given slowly and care must be taken that the drug goes into the vein. Following this there occurs a decline, a rise and a final decline in the fever. The best results, according to Thurber, were obtained in patients treated during the early weeks of infection, especially before arthritic symptoms set in. On the other hand, several investigators, among them Simpson, reported that acriflavine has no appreciable effect on the course of the disease.

Methylene blue, Methyl violet and Thionin were used by several observers in the treatment of this disease. It seemed that methylene blue possessed little bacteriostatic power for Brucella abortus. Methyl violet and Thionin appeared most active against the strain of Brucella in the stool. It is usually administered in the form of pills coated with phenol salicylate from 25-200 mg., being given in the course of 24 hours. At the same time a retention enema of 300 cc. of from 1/25,000 - 1/100,000 dilution of the dye is given. This is continued for about a week. Lowell, Porton and Amoss believe that the administration of the dyes may assist in freeing the stools of the organism, thus they may be useful in chronic cases.

Stern and Blake have reported three cases treated with sulfanilamide. These patients exhibited rather typical symptoms of undulant fever, and in every case agglutination tests proved positive in high titres against the specific organism. Sulfanilamide was given orally in full doses, usually starting with 60 grains daily the first one or two days, raising the dose to 80 grains on the second or third day and lowering it to 40 grains on the fifth day and to 20 grains daily until the fever has been absent for six days. After this, a daily dose of 15 grains was continued for some time. Prompt clinical cure followed, the temperature reaching normal on the fourth day. Patients received about 550 grains of sulfanilamide in all.

In the case referred to above sulfanilamide was given orally, starting with 10 grains on the first day, increasing the dose to 30 grains on the second day, and continuing it for 12 days—i.e., until the temperature was normal for three days. The next day it was reduced to 20 grains and then to 15 grains for three more days. In all, patient had received 435 grains of sulfanilamide. The administration of the drug in this case was not associated with any of the numerous toxic symptoms of overdosage, and the patient had no discomfort whatsoever.

Several clinics in the U. S. A. have employed artificial hyperpyrexia with success. Among them the Mayo Clinic has treated 9 cases. For this type of therapy the Kettering hypertherm was employed. This is an air-conditioned cabinet with controlled temperature and humidity. The process consisted of three sessions of fever at three-day intervals,
A CASE OF UNDULENT FEVER

maintaining at each session a sustained rectal temperature of between 105° and 106° F. for five hours.

The mechanism of the affect of this type of treatment is not clearly understood, and Thompson has shown conclusively that a sustained temperature of 107° F. for 24 hours does not kill the organism in vitro. The explanation must be in the activation or heightening of the body’s intricate protective mechanism. The average success is about 80% of the total cases treated. As a rule, fever therapy is not applied to patients over 50 years who have undulant fever, or to patients who have respiratory, metabolic or cardiorenal vascular disease.

SUMMARY

1. A case of undulant fever successfully treated by moderate dosage of sulfanilamide is reported.
2. A consideration of the history of undulant fever, including a discussion of the various therapeutic measures, is presented.

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Haemochromatosis

By S. Roy Korey, ’41

Haemochromatosis may be regarded at present as embracing a well-defined clinical syndrome whose aetiology is poorly understood. Sheldon establishes the following four signs as outstanding stigmata of haemochromatosis; the tetralogy is as follows: (a) enlargement of the liver, (b) severe diabetes, (c) bronzed pigmentation of the skin, (d) sexual hypoplasia.

The most constant of these signs are severe diabetes and enlargement of the liver. Cleveland reports 14 cases that came to autopsy in which there was no skin pigmentation as confirmed by biopsies but in whom there was generous infiltration of the viscera with pigment and almost invariably hepatic enlargement.

Before we discuss the aetiology of this disease, some description of the characteristic pigments concerned seems necessary. The two pigments responsible for the obvious discoloration of the skin and organs, both macro- and microscopically, are haemosiderin and haemofuscin.

Haemosiderin is an iron containing pigment. Reactions suggestive of iron in ferrous or ferric state have not been present and it is tentatively concluded that the 55 per cent iron content is in a colloidal combination with some organic substance. Its distribution in the organs is rather characteristic for there is manifested a tendency to affect the glands of internal and external secretions particularly. It is found plentifully in the liver, pancreas, parathyroid, thyroid, zona glomerulosa of the adrenal cortex, and the anterior pituitary. In the latter, the basophilic cells are most heavily impregnated and a possible reason for the sexual hypoplasia may be the destruction of these cells. This is somewhat supported by the obvious freedom of pigmentation in the germinal epithelium of the testis which appears in good condition. The pancreas which is seriously affected shows large amounts of haemosiderin, either as fine grains or amorphous masses present in the islet cells.

As we shall see later, it is significant that the tissues with higher activity and metabolic rates show more pigmentation than other tissues. The amount present in the musculature is concentrated more in the heart and striated muscles than in the smooth muscles. Of the striated muscles, the tongue, which is usually notoriously active, has more pigmentation than the quadriceps femoris. In addition, the widely scattered reticulo-endothelial system contains a great deal of pigment. The reticulo-endothelial cells about the vessels of the ducts of the testes are remarkably choked up with haemosiderin and perhaps act as a barrier for the testicular epithelium. The pigment is also found in the connective tissue of most organs. The relative immunity of the bone
HAEMOCROMATOSIS

marrow to pigmentation in this disease is an important point (vide infra). In the majority of locations the pigment is intracellular and gives the Prussian blue reaction with potassium ferrocyanide and hydrochloric acid.³

Haemofuscin is the other pigment concerned in haemochromatosis. It is dark, contains no iron but does contain 3.7% of sulfur, and is thought to be related to the melanin group. It may be the brown pigment of old age often seen deposited in senescent heart, for example. This pigment is found extracellularly and in the connective tissue and smooth muscle of the walls of the alimentary and genital tracts. It is present likewise in the blood vessels and heart walls.

AETIOLOGY

In a discussion of the aetiology, we involve ourselves in the deep waters of theory, but Sheldon has recently clarified the situation considerably and it is his view that is chiefly presented.

The general incidence of the disease is extremely low and is not yet adequately recorded. It is preponderantly present in the male, although not sex limited. There is some familial relationship and possibly a congenital factor is underlying. The age group most often affected is forty to forty-five years but there have been cases as young as 20 years. The age must be considered as that time when symptoms are first noticed. In the light of the theory that haemochromatosis is an inherent metabolic defect of the oxidative process (vide infra), we assume that the disease is one of slow growth and insidious onset of symptoms. Marble and Smith⁴ have shown that on a standard analyzed diet there was a positive retention of iron of 1.8 mg. daily if 16.9 mg. were given to persons with this disease in normal daily diet. In their series, the amount of iron retained and the amount excreted were the same for normal controls and diabetic controls as compared with individuals suffering from haemochromatosis. Other workers have agreed with the above results⁵,⁶ and the conclusion is that the iron present in haemochromatosis is not there because of abnormal retention of exogenous iron of diet. Because of the great iron increase and pigmentation which seem associated with the underlying pathological changes, we are forced into consideration of these as primary aetiological factors. Again, we must consider the pigments separately.

HAEMOSIDERIN. There are two possible sources of the haemosiderosis besides the abnormal retention of food iron which has been excluded: the excessive destruction of haemoglobin or the accumulation of intracellular iron. The former may offer six mg. of iron a day for storage in the form of haemosiderin. But we cannot find any abnormal destruction of blood or compensatory regeneration. There is no anaemia before the terminal debility. The location of the pigment is far from suggestive of this process for the bone marrow is relatively free, whereas
the pancreas and heart are both greatly affected. Compare this with the distribution seen in pernicious anaemia. There is no similarity. Then, too, experimental injection of great amounts of iron into a rabbit does not cause the disease or the hepatic cirrhosis and enlargement. Certainly liver cirrhosis itself is not a cause for there are many cases of cirrhosis without the semblance of haemochromatosis.

The accumulation of intracellular iron has much more in its favour and is at present the favoured theory.

We know that the iron in cytochrome is an integral part of cell oxidative processes. In this disease, the iron is supposed to assume an inert form and to cease taking an active part in oxidation. This would explain the cell death which though gradual is inevitable, for the iron collected in the immobile form crowds the cell until it bursts. As a result of parenchymatous death, the normal reparation by connective tissue replacement occurs and we now have accounted for the polyfibrosis seen in this disease. As mentioned before, the tissues with the highest metabolic rate are most deeply pigmented—another substantiation of the oxidation theory. Zondek and Karp have stated that an increase of intracellular iron is an indication of the cell's senescence. This is verified by the low amounts of iron pigment seen in new cells or its absence in cancer cells. To correlate this with the oxidative theory is not difficult if we realize that the iron in each cell is infinitesimal and its accumulation in an inert form requires a long time before it is pathological and responsible for much cell death. Therefore the older cells in this disease would be most deeply stained for they have been subjected to the defect the longest. They have found this so.

HAEMOFUSCIN. This is reputedly a melanin. Melanin disturbance is seen in haemochromatosis where there is a melanosis of skin and a melanuria. There are other diseases in which melanin metabolism goes awry such as melanotic tumors, Addison's, and melanosis coli. Zondek related the accumulation of the haemofuscin to the premature senescence of cells, for he identifies the haemofuscin with brown atrophy pigment. We know that there are inherent melanotic metabolic errors and so it would not be overstretched our imagination to suppose that associated with the iron metabolic error there is a haemofuscin dysfunction. Boyd goes farther and says that haemofuscin is formed first and then converted into haemosiderin.

The present concept of the aetiology may be summed up as an error of metabolism in the intracellular oxidation, which may be inherited as a recessive characteristic but is not sex limited.

PATHOLOGICAL CHANGES

There are three major pathological changes, namely: (1) pigmentation of skin and viscera (vide supra), (2) degenerative changes in the organs affected, (3) polyfibrosis.
HAEMOCHROMATOSIS

Because of the accumulation of pigment, the parenchymatous cells involved die and are replaced by fibrous tissue. With the progressive loss of the islet cells of the pancreas there is a progressive diabetes which responds very irregularly to insulin therapy. The fibrosis of the liver increases its size and weight so that it becomes clinically palpable and may weigh up to 4,000 gms. There is universal lymph gland involvement and, later, splenomegaly may be demonstrated clinically.

PATHOLOGICAL PHYSIOLOGY

The normal iron content of the body is about five mg. In haemochromatosis, the liver alone may contain 20 gm. The entire body content ranges from 20-55 gm. This iron in the form of haemosiderin is located in all tissues except the blood, brain and colon. There is a general upset of the metabolism of metals as noted:

(a) Increase in calcium paralleling iron in the pancreas and liver. There is no rise in blood calcium but X-ray shows bony porosis and it is likely that the parathyroids are minimally affected.

(b) There exists an inverse ratio between potassium and calcium. In those tissues like lung, trachea, urinary bladder where calcium is depleted, the potassium concentration rises. Striated muscle, on the other hand, shows a decrease in potassium and a rise in sodium content.

(c) All tissues show an augmented copper content and this is harmonious with theory of interference in tissue oxidation for copper is intimately bound up with the role of cytochrome.

SYMPTOMATOLOGY

The onset of symptoms is gradual and the patient is most likely to complain of asthenia, general malaise, polydipsia and polyuria. These are referable to the diabetes. Neuritis, neuralgias, cataract, diabetic retinitis are also possible symptoms. As the disease progresses, the skin assumes a dark bronzed appearance with a slaty blue or metallic nuance. The pigmentation is not confined to the exposed parts nor is it present usually on the mucous membranes, both distinguishing features from Addison’s. If the diabetes remains untreated, the symptoms are those of severe diabetes. In addition, genital hypoplasia with impotence and a redistribution of public and axillary hair according to female lines occurs. There is a tendency to loss of sex identity. The symptoms increase in severity and the disease is usually fatal in about 18 months. However, there have been three confirmed cases which lived: 13, 9 and 8 years respectively. Satisfactory control of the concurrent diabetes will prolong life.

The outstanding physical sign is the enlarged palpable liver and later the splenomegaly.
DIAGNOSIS

The diagnosis is based upon the following data:

(a) General symptomatology of diabetes with Sheldon’s tetralogy present.

(b) Biopsy of the skin. In the deeper layers of the skin, when stained with Prussian blue, there may be seen brownish haemosiderin granules scattered throughout the section. Melanin and haemofuscin deposits may also be seen.

(c) Rous urinary test for haemosiderin-stained sediment.

The differential diagnosis between haemochromatosis and Addison’s disease is necessary. In the crises of the latter with dehydration, decreased blood volume, low sodium blood content, the diagnosis is easy. During the non-dramatic part of the course of Addison’s disease the lowering of the blood pressure, the morning nausea, the absence of an enlarged liver are the preferred differential signs. Skin biopsy with only melanin present is indicative of Addison’s disease, but must be weighed in the light of clinical findings.

TREATMENT

Treatment is purely palliative and control of the diabetes by insulin the best we have to offer. No form of iron deficient diet has appeared helpful in the past.

CASE REPORT

September, 1939.—The patient was a man 55 years of age. He had complained of general weakness and mental depression, the onset of which symptoms he had first noted in 1932. He was unable to work and complained of mental confusion and physical fatigue. Accompanying these symptoms were excessive thirst, polyuria with marked nocturia, insomnia and cold extremities. His weight had dropped in the period from 1929-32 from 220 pounds to 170 pounds. In 1935 he was treated for diabetes mellitus and his blood sugar was reduced from 400 to 222 mg. Early in 1938 the patient became conscious of increased weakness which prevented any but the slightest exertion.

At present his insulin dosage had been increased and he was treated with 20 units of protamine zinc insulin before breakfast and 5 units of standard insulin before breakfast and lunch. The blood sugar response was somewhat peculiar, for despite careful and repeated corrections of dosage on a standardized diet, the quality of insulin that may have been ineffectual one day would cause pre-shock conditions another day.

Physical Examination.—The most apparent finding on physical examination was a marked bronzing of the skin over the entire body but especially marked on face and hands. The color was dark brown with a bluish overtone. The lips were a dusky blue color. The mucous membrane of the hard palate showed a tan-brown splotch of pigmentation about 3 cm. in diameter.

The heart appeared essentially normal when the patient was first examined. The heart was examined daily and before discharge a systolic murmur was noticed. It was a soft blowing murmur, heard best in the mitral area with propagation to
HAEMOCHROMATOSIS

the left axilla. This suggested mitral insufficiency, and was in keeping with the increased general weakness with possible atonia of the heart.

The blood pressure on admission was 110/70. During the remainder of his stay in the hospital the pressure was maintained at 140/90. This was thought to be one of the main differential points in distinguishing the patient's condition from Addison's disease.

The liver was enlarged and quite palpable, extending two inches below the left costal margin. The spleen was also palpable and markedly enlarged.

Clinical Laboratory Findings.—There was at first a notable glycosuria which was eventually controlled. The examination of the blood was essentially normal.

To confirm diagnosis, a skin biopsy was done. The basal layer of the epidermis was loaded with melanin but on staining the section with Prussian blue no haemosiderin was found present.

Diagnosis.—The diagnosis of haemochromatosis was based on the existence of diabetes, pigmentation of the skin and enlargement of the liver. The negative skin biopsy, although disappointing, was somewhat less decisive in the light of Cleveland's work mentioned above. There was considered to be enough clinical evidence to establish a diagnosis of haemochromatosis.

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The Diagnosis of Organic Causes of Mental Disorder

By GEORGE EDGAR HOBBS, B.A., M.D.
Ontario Hospital, London

For the proper handling of any mentally ill person, whether it be in a mental hospital or under care in the community, the diagnosis is just as important as in the case of a physical illness. The first step in any diagnosis is to separate this group of patients where the mental symptoms are due to some organic pathology in the brain from the other large group where, to our present knowledge, no pathology exists and to whom we give the name psychogenic.

The diagnosis of the organic group has been made difficult by the fact that practically all text books attempt to subdivide these patients into groups dependent on their etiology; for example, delirium tremens due to chronic alcoholism, bromide intoxication, etc. The symptomatology of those patients has many factors in common no matter what the cause, and they fall quite readily into two large groups, both from the point of view of pathology and symptomatology. These groups are, namely, the acute or delirious group and the chronic degenerative group.

Acute or Delirious Group

In the acute or delirious group one is dealing with patients whose symptoms are due to an interference with function of the brain cells and in many cases the injury is transitory, leaving little subsequent damage. In this group the suddenness of onset and recovery is a characteristic feature. The symptomatology here is that of any delirium, namely, very vivid hallucinations involving any one of the senses, the visual and the auditory being the more common. A good example is the person who is suffering from pneumonia and may become delirious with hallucinations and clouding of his consciousness as a result of the toxin in the blood stream affecting the function of the brain cells.

The Chronic Degenerative Group

In this group the underlying pathology is the actual destruction of the brain cells, more particularly those of the frontal lobes. This destruction may be in the form of total damage to a wide-spread area, e.g., where a large area of the brain may disintegrate secondary to a thrombosis of the blood vessel to that area, or where there is diffuse microscopic degeneration of the brain cells, as found in general paresis. The symptomatology here falls into three general groups:

(a) Intellectual: There is a gradual deterioration of the patient’s mental ability. This is shown by defects of memory, errors of judgment, childish behaviour and a let-down in interest in personal tidiness and cleanliness.
(b) *Emotional:* There frequently is some decrease in the person's ability to control their emotions. This shows up by anger over the most trivial incidents, weeping without adequate cause, etc.

(c) In addition to the above two symptoms, one sees other symptoms which are probably more dependent on the personality make-up of the individual than on the actual pathological changes. The person with the gloomy outlook on life before his illness may become depressed, the happy, cheerful person euphoric, and the suspicious person shows paranoidal symptoms; for example, he may believe that someone has stolen his glasses when in reality he has forgotten their location.

Practically all cases of organic mental disorder have some combination of the two above-named groups of symptoms. They may appear alone or in company with each other. For example, delirium tremens gives a very typical example of the acute group; many cases of general paresis show symptoms characteristic of the second group; and Korsakoff's psychosis may be a combination of the two, the patient at times being quite delirious and confused and behind the whole is a picture of a gradual mental deterioration characteristic of the chronic organic group.

*Underlying Aetiology*

A number of conditions may be responsible for these mental changes. In the *acute group* the following are the more frequent underlying causes:

1. **Toxin**
   - (a) Endogenous, *e.g.*, uremia, eclampsia,
   - (b) exogenous, *e.g.*, alcohol (delirium tremens), lead, carbon monoxide, bromides, etc.

2. **Infections**—Almost any severe infection in any locality of the body may have as a counterpart mental symptoms due to the circulating toxin. The more common infections producing this, however, are pneumonia, influenza, puerperal infection and syphilis (the early meningovascular type).

3. **Trauma**—This may result in post-traumatic delirium.

In the *chronic degenerative group* the various factors most commonly producing actual destruction of the brain cells are the following: Syphilis (general paresis of the insane), senile and arteriosclerotic brain disorder, trauma, alcohol, and brain tumor.

It will be noted that several factors are listed in both groups; for example, syphilis may in its secondary stage produce a typical delirium and in its tertiary stage result in a definite infection of the brain tissue with deterioration of brain cells, producing general paresis.

When one has decided that a mental patient falls into one of the two groups mentioned above, then the next problem is to determine
which of the above factors are responsible for the mental symptoms. Some of these conditions have characteristics by which they can be identified and our diagnosis is made largely by a method of exclusion and adequate history. We will next consider in detail some of these conditions.

**Diagnosis of Causative Factors in Acute Group**

Further diagnosis in most cases depends on an adequate history of toxemia, e.g., alcohol, lead, carbon monoxide, etc. In the case of delirium tremens of alcohol it should be remembered that the mental symptoms appear only after consumption of large quantities of alcohol over a long period of time and are associated with an inadequate diet. The latter is particularly important as these symptoms are believed now to be due to a vitamin deficiency, particularly B_1_, rather than the specific toxin of alcohol. Care should be taken to exclude those patients where alcohol is a symptom of some other underlying disorder and not an ætiological factor; for example, a person who is depressed may take alcohol to excess in an attempt to lighten his mental symptoms.

In the case of bromide delirium the same holds true as in the case of delirium tremens. Bromide is chiefly taken for some nervous or mental upset and, even though a patient may take sufficient bromide to produce a delirium, this may simply act as a cloud over the other underlying condition. Mental symptoms from bromide usually follow the use of the drug in large doses over a long period of time. Certain people, such as those showing arteriosclerosis, are more susceptible to the effect of bromide than others. A blood bromide estimation is helpful in diagnosing this condition and should always be done in a delirium where one is unable to determine the true underlying cause. Mental symptoms may be expected when the blood bromide rises above 150 mg. per 100 cc. of blood.

In the case of mental symptoms due to infections the diagnosis is dependent largely on identification of the underlying infection elsewhere in the body, e.g., pneumonia, influenza, etc.

The diagnosis of meningovascular syphilis is not difficult. One frequently sees involvement of cranial nerves producing strabismus, ptosis, etc. Blood and spinal fluid Wassermann are usually both positive, and the cell count of the spinal fluid is increased in range from 100 to 500 cells per cubic millimeter. The colloidal gold curve is of the "luetie" type, the following being a fairly typical type of curve: 0123443210.

**Delirium following head injury** does occur but it is very rare to see a severe case of this type. It usually comes on as the patient emerges from unconsciousness. Care must be taken in diagnosis as minor blows on the head, quite insufficient to produce any actual structural change in the brain, may be a precipitating factor in one of the psychogenic group of mental disorders; for example, a developing schizophrenia may
break down completely after a very minor blow on the head. The depth and duration of unconsciousness are our best guides in the seriousness of damage to the underlying brain.

**Diagnosis of the Chronic Degenerative Group**

The diagnosis of *general paresis of the insane* is made by the typical physical signs which may be present, namely, loss of tone of the facial muscles, loss of expression, the pupils may be of unequal size, of irregular outline, and their reaction to light is often sluggish or lost, as may be the convergence reaction. There is a disturbance of speech which results in the patient’s slurring his words and finding considerable difficulty with such widely used test phrases as “British constitution” and “Methodist Episcopal.” The deep reflexes are usually disturbed and may be exaggerated. If spinal cord involvement accompanies the condition the patellar reflexes may be absent. A large portion of these patients suffer from convulsions during some stage in the disease and this may be the first symptom. In untreated cases the blood Wassermann is positive, the spinal fluid Wassermann positive, and the globulin of the spinal fluid is increased. The colloidal gold curve takes the typical paretic form, the following being a fairly typical type of curve:

5544321000.

In *senile brain disorder* one must make a diagnosis by exclusion of the other causes in this group, and by certain general characteristics of the condition. The onset tends to be gradual, extending over several years, and this condition rarely occurs before sixty years of age and in most cases after sixty-five or seventy. The occasional case may have short periods of acute confusion suggesting the acute organic group, but the majority follow a slow chronic course with symptoms of the chronic organic group.

Separation of cases of *cerebral arteriosclerosis* from the senile group is not always possible and the end result of the two conditions may be very similar. The onset in the arteriosclerotic type is usually from fifty to sixty-five years of age. It may be more rapid and is frequently characterized by considerable fluctuation in the mental symptoms in contrast to the slowly progressing change of senile dementia. Periods of confusion during which the patient shows symptoms of the acute organic group may appear at intervals but behind this is the slow change of the chronic organic type of symptomatology. Cerebral vascular accidents are common, but are not absolutely necessary for diagnosis. The blood pressure is elevated in about half the cases and retinal arteriosclerosis can usually be demonstrated.

*Trauma* is a rare cause of mental deterioration of the chronic organic type. The author has seen only one unquestionable case in about two thousand psychiatric cases. Again, one must keep in mind the possibility of a minor head injury occurring in patients who already have cerebral arteriosclerosis or a syphilitic brain infection. The symp-
toms produced may be the result of these conditions rather than the actual head injury.

Brain tumor is again a relatively rare cause of mental symptoms of the chronic organic group. The frontal lobe tumor is the one that gives the greatest difficulty in diagnosis, as mental symptoms may be the only change that the patient shows for a considerable period of time. These should be kept in mind if all other causes of gradual mental deterioration have been excluded.

The diagnosis of chronic mental deterioration due to alcohol (Korsakoff's psychosis) can usually be made largely from the history and the exclusion of other conditions listed above.

In this paper we have attempted to give the main points in the diagnosis of the organic causes of mental disorders and have made no attempt to go into any of the conditions in detail. The following case histories are quite typical.

CASE REPORTS

CASE I., S.B.—MAN AGED 39 YEARS

This is a patient whose early history is essentially negative and who appears to be definitely above average in intelligence, completing High School at an early age, followed by University. The history of his present illness dates back about two years and the onset was very gradual. It was noted that he repeated conversations which he had mentioned. He had been a very excellent bridge player and he now began to forget what was trump. He began to tell the same story over and over again. He had been an excellent bookkeeper but he now began to get the figures completely jumbled. There was a definite deterioration in his personality and he was found occasionally picking cigarette butts up out of the gutter, and spent a great deal of his time borrowing tobacco from his friends and if refused would become exceedingly angry and threatening.

This is a picture of gradual mental deterioration with a loss of control over his emotions. The mental test carried out at the time of examination showed him to have a mental age of 11 years and 3 months, and an intelligence quotient of 70. Thus it would appear that there has been a marked dropping in his mental ability. This case would seem to fall quite definitely into the second group and, therefore, to find the underlying cause, one must consider the various factors present. The man is too young for the arteriosclerotic and senile group. There is no history of trauma. He does not use alcohol and there is nothing to suggest brain tumor. This leaves only syphilitic brain infection, which diagnosis was made entirely on the history and irregular pupils, with loss of reaction to light. The diagnosis was confirmed by blood and cerebral spinal fluid test.

CASE II., H.R.—MAN AGED 45 YEARS

His developmental history was essentially negative. He has always been a stable type of individual and a good, steady worker. Two weeks ago he went downtown and did not return, and was away for three days, arriving home in the early hours of the morning. On his arrival he appeared to be confused, could not give an adequate story of his whereabouts, and appeared rather dirty and untidy. Because of the disappearance, he was interviewed by the police and suddenly became excited, thinking that he heard them running about outside the house, firing rifles at him, threatening to kill him, mutilate him, etc. This period of excitement lasted two days and cleared up as rapidly as it came on.

At the time of examination he was quite clear mentally and one could not demonstrate any definite evidence of mental disorder. This case is fairly typical of the acute or delirious group with auditory hallucinations of a terrifying nature being the most outstanding symptom. Careful check-over excluded practically all the causes mentioned above. There was no evidence of any toxemia, the man was not an alcoholic, and there was no suggestion of any infection that might be a factor. Syphilis was also ruled out by a blood Wassermann test. Thus from
symptomatology and further investigation it would appear that the only condition remaining was that of head trauma. X-ray examination of the skull showed three linear fractures. It was subsequently established that the man had been hit over the head when an effort was made to hold him up and thus his symptoms were in the nature of a post-traumatic delirium.

CASE III. E.M.—FEMALE AGED 56 YEARS

This patient’s history was essentially negative up until two years ago. At that time it was noted that her memory was gradually failing. She was having periods when she was slightly confused, she lost interest in her family and home, became very childish in her actions and was quite content to sit in one chair day in and day out. Mental examination at the time showed her to be quite disoriented, not knowing where she was, had no idea of the day, year or month. Physical examination showed the reflexes to be slightly increased on the right side, and the blood pressure to be 140/102. Ophthalmoscopic examination showed the arteries to be small and tortuous and the veins show arterial nicking.

From the history this woman’s symptoms are fairly typical of the chronic organic group, and by further investigation it is quite obvious that this is due to arteriosclerosis associated with hypertension.

CASE IV. A.B.—MALE AGED 21 YEARS

Early history was essentially negative. He progressed normally at school and obtained his Entrance at fourteen years. Two years ago he was in a serious automobile accident, when he was thrown out of a rumble seat. There was very little superficial evidence of damage and no skull fracture, but the patient was unconscious for eleven days and very drowsy for a month. During this time he had several periods of acute excitement when he was quite confused and probably hallucinated. Following this accident he had to learn to speak again and had difficulty in using his right arm and right leg. In addition, it was noted that he was very childish in his behaviour. It was quite certain before his accident he was normal.

At the present time examination shows diminished sensation of the right arm and leg, speech indistinct, and reflexes on the right side slightly increased. Mental examination shows him to have a mental age of 10 years and 10 months, and an intelligence quotient of 69. This case presents no difficulty in diagnosis but is included to show the type of symptomatology and finding that one may run into following a severe brain damage.

REFERENCES


Abstracts

OESTROGENIC HORMONE THERAPY
By T. N. A. Jeffcoate
B.M.J.; September 30, 1939

The author discusses the various signs and symptoms of oestrogenic hormone deficiency, and the technique and dosage of various oestrogens in such varied conditions as menopause and climacteric, senile vulvitis and vaginitis, genital hypoplasia, amenorrhoea, uterine inertia, breast conditions and other rarer evidences of oestrogenic deficiency. It is pointed out that hormone therapy, though still in a crude state, has already passed beyond the stage of "gland extracts," and that success depends on careful selection of cases and the observance of physiological principles. Stilboestrol, a new synthetic oestrogen, is an adequate substitute for the natural oestrogen, and possesses advantages in that it is cheaper and equally active when given orally.

—W. A. Hargan, '41.

THE RESPONSIBILITY OF THE MEDICAL PROFESSION IN THE MOVEMENT FOR BIRTH CONTROL
By G. W. Kosmak
J.A.M.A., 113:1553, 1939

The profession has grossly neglected this subject, and the time has come to intervene and guide hysterical birth control movements into the proper channels. The problem is not new. It dates back many centuries, but has changed from a personal matter to a social and economic one. It has provided a fertile field for commercial exploitation and quackery.

A committee on contraception was appointed by the A.M.A. No direct legislation followed, but it signified at least a step in the right direction. The committee reported that although many means of contraception are available none is 100% reliable, nor should be represented as such. Some of the methods in common use are: use of the co-called "safe periods," medicated douches, jellies, suppositories, continence, coitus interruptus, foam powders and condoms. The latter are regarded as the most effective.

It is essential that the physician be familiar with the necessary procedures, whether he limits his participation to the strictly medical indications for contraception, or whether he is ready to acknowledge the desirability of spacing children or limiting their number. Education of the profession in this matter should begin with the medical student.

—L. C. Bartlett, '41.

A NEW METHOD OF TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS
Preliminary Report
By S. R. Kelson and P. D. White
J.A.M.A., 113:19, 1939

The authors have treated six patients with subacute bacterial endocarditis and one patient with acute bacterial endocarditis, all of whom had four or more positive blood cultures for streptococcus viridans. Heparin and sulfapyridine were used in combination, following a technique described whereby 10,000 units of heparin are administered in 500 cc. saline by uninterrupted intravenous drip day and night for fourteen days, and four to six grams of sulfapyridine is given daily by mouth before and during the use of heparin and for one week afterward. Blood transfusions are given if there is anemia. Only three patients were able to take the heparin for more than a week, and these showed a striking improvement and have since been free of any evidences of disease (19 weeks). Of 246 control cases none remained free of signs and symptoms for that length of time, and afebrile periods were rare for as long as five weeks once fever had set in. The treatment is in the experimental stage and can do harm, but the possible benefits may well outweigh the risks in this almost universally fatal disease.

—J. A. Chikovsky, '41.
SULPHUR THERAPY IN ARTHRITIS

By BERNARD I. COMROE

Medicine, 18:2, 1939

After a most comprehensive summary of the literature dealing with sulphur therapy in arthritis, and a discussion of its pharmacological action, the author presents the results of a three-year period of treatment of 30 cases of osteoarthitis and 30 of rheumatoid arthritis. The results indicate that the treatment is no better than physiotherapy, removal of focal infection, vaccine, etc., but that if no improvement is obtained with these conservative methods a cautious administration of sulphur may be considered.

The intravenous, intramuscular or combined routes of injection were employed with no noticeable variation of results. Intravenous injections should be made very slowly. Vigorous massage should follow intramuscular injections. The presence of indole in the urine of arthritic patients would seem to indicate the oral administration of sulphur, due to its major role in the detoxication of this highly toxic substance. Contrary to many reports, it was found that cystine determination of the nails was of no assistance in judging which patients would benefit by sulphur therapy.

The occurrence of two cases of acute coronary occlusion during the course of therapy indicates the great danger of its use in patients with cardiac disease.

—JOHN LINDSAY, '43.

THE EFFECT OF LIPIODOL IN THE SUBARACHNOID SPACE

By HOWARD A. BROWN AND JESSE L. CARR


This article is a review of the experimental and clinical literature on this subject, as well as a report of the authors' findings in the spinal cord of a patient who had had lipiodol injected six months previously.

Although there is much disagreement in the literature, the bulk of the evidence supports their own findings, that both gross and microscopic pathological changes may occur in the nervous system following the injection of lipiodol into the subarachnoid space. No persistent subjective complaint or objective neurological finding has been demonstrated, although the oil is known to remain in the spinal canal for periods as long as 10 years. Nevertheless the authors feel that any substance producing such changes in the nervous system cannot be regarded as harmless, and that the indiscriminate use of lipiodol in the spinal canal should not be encouraged.

—D. KEELEY, '41.

EXTRAPLEURAL PNEUMOTHORAX

By HORACE BINNEY


In this article the authors discuss the frequency with which anemia accompanies pregnancy, and point out the close relationship of maternal and fetal erythropoiesis. They review 525 non-selected cases of pregnancy, of which 275 received no therapy and 250 were treated with iron preparations. Also included in the study were 100 infants, only 50 of whose mothers received therapy. One of the chief problems was to find an iron preparation which would not upset the already unstable gastro-intestinal tracts of the pregnant women. Many iron preparations were found to be effective. They recommend ferrous sulphate in combination with vitamin B complex, since it does not upset the gastro-intestinal tract. They conclude that the
Anemias of both mothers and infants can easily be prevented by prophylactic iron therapy, thereby reducing maternal complications and infant mortality.

—D. Keeley, '41.

SELECTIVE ACTION OF URINE AND SERUM FROM PATIENTS WITH MALIGNANT TUMOURS ON EMBRYONAL AND NEWLY GROWING TISSUES

By T. H. Elsasen and G. B. Wallace

Science, 250, 1939

When the urine of a man with testicular tumour was injected intravenously into pregnant rabbits abortion occurred about the fifth day. Similar results were obtained from injections of either urine or serum from patients with other embryonal tumours. These results led to a test of the effects of urine and serum from patients with various types of malignancy. A suitable series of controls, including patients with non-neoplastic conditions and pregnant women, gave uniformly negative results, while in all known cases of neoplasia the test was positive. Massive doses of antuitrin S and oestrin failed to produce the same effects.

Confirmation of this work would make available a simple test for malignancy, providing it is positive in the early stages of the neoplastic process.

—Myra Mackenzie, '40.

ELECTROSURGICAL OBLITERATION OF THE GALL-BLADDER WITHOUT DRAINAGE (THOREK'S OPERATION)

By Hamilton Bailey and R. J. McNeill Love

B.M.J., September 30, 1939

These two eminent surgeons state that they are compelled to admit that in changing their technique for treatment of gall-bladders they have made a change for the better. The essential difference in the Thorek operation is that the portion of the gall-bladder attached to the liver is left so attached, and its mucosa destroyed by electro-coagulation. Since the integrity of the liver as an encapsulated organ is not interfered with, drainage of the peritoneal cavity is not necessary. This results in an operation carrying a much smaller mortality, less post-operative pain, and a shortened convalescence.

In Thorek's series of 376 unselected cases the mortality was 0.5%. The average mortality of the standard operation in skilled hands is 2%. The authors cite a series of 129 unselected cases of their own, with no mortality, and an average hospital stay of 20 days. They state that it is exceptional for the wound to heal by other than first intention.

—J. G. Stapleton, '41.

LYMPHOSARCOMA OF JEJUNUM

Brief Case Report

Lymphosarcoma is an uncommon form of malignancy, usually arising in lymph glands, and, clinically, is almost identical with Hodgkin's disease. The following case, which was autopsied at Hamilton General Hospital in July, 1939, deserves a few comments, not only on account of the rarity of the condition, but also on account of the rarity of its location.

The patient was an Italian male, 67 years of age, who died after a month's illness, and was diagnosed as bilateral cerebral hemmorrhage with myocardial degeneration. He had suffered from bilateral facial paralysis and symptoms of coronary thrombosis. The night before he died he had a sudden severe pain in his lower abdomen, which suggested a perforation. In the absence of rigidity, the pain was considered referred.

At autopsy, a tumour mass of the jejunum was found, about a foot from the end of the duodenum. This mass was firm, white and irregular, and measured 6 cms. long by 12 cms. in diameter. The lumen of the intestine was patent, and at one point there was a perforation about 3 mms. in diameter. Microscopically, the tumour was a typical lymphosarcoma, made up almost entirely of lymphocytes. One wonders how such a tumour could start at a point where the lymphoid tissue is comparatively scarce. Metastases were found in the myocardium, stomach, adrenal, kidney and pancreas. Although no pathology could be found in the brain, the patient's cerebral symptoms were probably caused by emboli of tumour cells. The cause of death was apparently a generalized peritonitis, due to perforation of a lymphosarcoma of the jejunum.

—J. W. Babb, '41.
Editorial

On September 3, 1939, Great Britain issued a declaration of war and slowly a startled world realized once again that man's inhumanity to man was still in existence. We, who have chosen the cause of Medicine, may find it difficult to rationalize a state of war, with the ideals of life which we wish to retain. On careful examination of this situation, we can plainly see that if we wish to maintain our ideals we must fight for them.

As students, our position at present may not be in the fighting line; we have a duty to perform first. Our duty now is to make the most of our daily opportunities and so prepare ourselves for a service of greater importance than any we, at present, could give. Carlyle made the statement, "Our main business is not to see what lies dimly at a distance but to do what lies clearly at hand." If we keep this thought before us, we will prepare ourselves to render aid in a far superior manner in a situation where our aid will definitely be demanded.

On Christmas, 1916, Sir Wm. Osler wrote the following article, published in Lloyd's Weekly, entitled "The Silent Unit":

"There was a famous paradox in antiquity . . . a grain of wheat falls noiselessly to the ground, the same thing happens with the second, the third, the fourth and so on for the thousands of grains that make up the bushel. But collect the grains again and drop the whole bushel, and behold! a great noise. It seems difficult to explain how the sum of many thousands of silences could result in one great sound. The Silent Unit, the single grain, will win the war. In the world's crisis it is the spirit of the individual worker, in trench or camp, in factory or school, that keeps the mouth shut, the heart fixed, the hand steady. . . . Let this message be heard above the din of battle and the clash of machinery. The Silent Unit will win . . . in quietness and confidence will be your strength."

Let us take heed of these words of Osler. At present we are the Silent Unit. Let us be content to prepare ourselves for the activities that may lie ahead.
In Memoriam

JOHN ALEXANDER MACGREGOR, M.D.
F.A.C.P., F.R.C.P. (C), LL.D.
1872 - 1939

IN 1883 Western graduated its first medical class, consisting of one, lone member. Nine years later, in the class of '92, there was graduated a young lad of 19, John Macgregor. This youthful physician was fired with a noble enthusiasm for the profession, in the long pursuit of which he was to keep the ideals of the Hippocratic Oath as a constant guide. His life was to bring him tragedy and love, the opportunity of unselfish service and the cruel blessing, appreciated and desired by so many great men, of going down in the mighty surge of life instead of struggling to a pitiable end in the shallows of helplessness and decay.

On graduation Dr. Macgregor was too young to try his Medical Council exams and begin practising. He therefore obtained an appointment as demonstrator in Anatomy at the Medical School, for one year.
OBITUARY — DR. J. A. MACGREGOR

He then moved to Kent Bridge, where he married and succeeded in building up a creditable country practice, so fruitful to a young man who believed the purpose of a doctor was primarily to doctor. Still in search of practical experience and possibly adventure, he went to Minden, Nebraska, at that time scarcely more than a rough pioneer town. In a few years he returned to Canada and began practice in Dutton, where he remained until 1905. His sincerity and undoubted ability again earned for him the respect and confidence of his neighbors. His great scientific curiosity and feeling of almost sacred obligation to his patients prompted him to set out on his country calls supplied with a microscope, a small centrifuge and any other instruments which he thought might prove of assistance in diagnosis or treatment. He proceeded to set up his laboratory in the patient’s home, to the impressed amazement of the onlooker, in the utmost innocence, entirely free of imposture or deceit, which he so strenuously abhorred.

In 1905, when he began lecturing at the Medical School, he found a deplorable lack of equipment and material with which to work. This condition he promptly endeavored to improve by buying a microtome and microscopes for use in the school. His special, or unspecialized work as we would consider today, was in pathology, physiology, bacteriology. Pathology and physiology remained the basic subjects of all his future teaching, to which pair he was continually referring his students as the essentials of a complete and proper understanding of many medical problems.

He entered the department of Medicine in 1912, and became professor in 1920. Internal medicine, which became of especial interest, supplied the subject for the majority of the papers which were to gain for him such a wide and notable reputation.

Dr. Macgregor was an ideal teacher. He admitted no half-way points, but presented decidedly and finally his own opinions on any subject which arose. Although authoritative, his manner had nothing about it of the belligerent dogmatist; he was in possession of an extensive array of facts which he expected the students to accept until their own efforts had yielded better ones. He had learned that work and observation, plus more work and more observation, operating from a solid foundation of facts were the only tools that could be safely used in building an habitable edifice for the physician’s sound judgment and expert treatment. He considered it the students’ responsibility to employ their own workmen on the raw material which he so freely supplied.

In 1925 Dr. Macgregor was made Professor Emeritus and in 1931 received an LL.D. from Western. Of his other degrees and honors, may be mentioned: F.A.C.P. (1919); F.R.C.P. (C) (1931); president of the O.M.A. (1925-6); honorary member of the Harvey Club of London and the A.K.K. fraternity.

The loss which the Medical School has suffered in the death of
Dr. Macgregor will be fully appreciated only as time passes and his true beneficence is realized in retrospect. He was the trusted counsellor to many young doctors, giving generously of his sound professional judgment, encouraging and stimulating. His knowledge of modern medical books seemed to be unlimited and the opinion which he passed on them was always reliable and accurate. At least one new book was carefully read every week and the essence of it retained, to be available on a moment’s notice to librarian or student. The Medical School library has indeed suffered a severe blow from the loss of Dr. Macgregor’s expert guidance and personal interest in its affairs. The private medical library which he had built up is probably one of the finest of its kind ever formed. Many societies and clubs around the school have for years been relieved of embarrassing deficits and enabled to accomplish receding objectives through the gratuitous aid of Dr. Macgregor. Avoiding publicity, as an imposition and a well of fraudulent gush, he gave quietly wherever he saw a need.

To countless families and generations of families, his memory as a personal friend, adviser and doctor will remain alive for many years. The number of demands made on his time and his generous response speak eloquently of the esteem in which he was held and the lofty character of one who followed the highest code of professional ethics possible. Conservative, a lover of fine music and quiet family life, enthusiastically fond of hockey and boating, he still subordinated all of these pleasures to his sense of duty and integrity of mind. Expressive of his sincere opinions, in a manner not to be misunderstood, and acting warmly on personal impressions, he made many close friends and impressed his personality indelibly on everyone he met.

—JOHN LINDSAY.
Books in Review

PRINCIPLES OF HÆMATOLOGY

By Russell L. Haden, M.A., M.D.

Chief of the Medical Division of the Cleveland Clinic, Cleveland, Ohio;
Formerly Professor of Experimental Medicine in the University
of Kansas School of Medicine, Kansas City, Kansas.

(348 pp., illustrated with 155 engravings and a coloured plate, $4.50.
Lea & Febiger, Philadelphia, 1939.)

As stated in the preface, this book has been written with the idea
of helping to simplify the study of the disorders of the blood for the
student and physician. It is based upon the premise that clinical
hematology is simple if the fundamental principles on which the vari­
atations of the blood depend are thoroughly understood. In promoting
an understanding of such principles, the author has succeeded admir­
ably. The first part of the book deals with blood formation, the struc­
tures and properties of the various blood cells and the technique of blood
examinations. This is followed by a chapter on the mechanism of
anæmia and polycythæmia which is particularly instructive. The
abnormalities affecting the leuкоocytes are clearly described. Finally,
100 case records illustrating the clinical manifestations, differential
diagnosis and treatment of the blood dyscrasias are presented.

The lack of coloured plates is more than compensated by the distinct
photomicrographs and the many original charts and drawings which
are a feature of the book and which provide graphic conceptions of the
relationships within the hematopoietic system.

This work is a valuable addition to the literature on hæmatology.

—E. M. Watson.

ESSENTIALS OF PATHOLOGY

By Lawrence W. Smith, M.D., and Edwin S. Gault, M.D.

(With a foreword by James Ewing; 886 pp., illustrated, coloured
plates, $9.00. 1938: Appleton-Century.)

The Masters of Pathology have been and still are prone to relegate
their subject to the realm of a purely independent and abstract science.
Satisfied with their philosophical-pathological musings, they have been content to leave the important problem of close clinical application to be solved by a more recent school of teachers.

The urge of these scientists to aid in the accurate diagnosis, prognosis and logical treatment of disease has superseded their innate love for abstract rationalization. The authors of “Essentials of Pathology” are indeed deserving of a position of prominence and respect in this more modern group of morbid anatomists.

The fundamental factors relevant to the common disease entities and capable of helpful practical application are clearly and concisely set forth. Theorization is confined to those more plausible hypotheses, which to date have received the approval of the largest number of workers. These intrinsically abstract dissertations are vitalized and brought into the sphere of the clinician by the presentation of appropriate and clearly illustrative case histories. The process of visualization is materially aided by an unusual number of accurately prepared illustrations of gross and microscopic material drawn from the clinical problems quoted. Replicas of radiographic films and pictures of processes in the living patient are included at most suitable places and derived from these same sources.

Such a work will materially aid the busy clinician, who desires to refresh his memory upon certain pathological facts that may have been thrust into the limbo of the subconscious by the pressure of purely clinical interests. The parallels between the cases cited in this book and those in his own practice will enable him to envisage a firm pathological foundation upon which the clinical superstructure can be accurately and helpfully erected.

For the undergraduate, this book will facilitate the bridging of the seemingly infinite gap between the purely pre-clinical science of pathology and the realm of his early clinical experiences.

In conclusion, it may be truthfully stated that Dr. Smith and Dr. Gault have taken a definite and further step forward to an improved understanding and better co-operation between pathologist and clinician, between teacher and student.

—J. B. McKay.

A TEXT BOOK OF HISTOLOGY
By E. V. Cowdry
(Second Edition, thoroughly revised.)
(Lea & Febiger, Philadelphia; 600 pp., illustrated, coloured plates, $7.00. 1938.)

This book provides an excellent approach to the physiological, pathological and clinical subjects of the medical curriculum. The author, a distinguished Canadian, who has devoted his life to his science, has broken away from the old-fashioned, strictly morphological way of
presenting histology to medical students, and has replaced it with a
dynamic, unified course, leading directly to an understanding of the
living human body. The cells are shown as vital units whose activities
are correlated by the great integrating systems, such as the bloodstream,
with its various nutrient, energizing, protective and hormonic elements,
and the nerves. Everywhere the functional significance of cells and
intercellular substances is stressed. The book abounds in practical illus­
trations, charts and tables, and there is a good bibliography to aid the
student in selecting modern scientific papers. The summaries at the
end of each chapter are much appreciated. The student is led to think
for himself, to ask questions of Nature and to seek answers thereto by
the use of modern technics.

Professor Cowdry's educational foundation was laid at the Univer­
sities of Toronto, Chicago, and Johns Hopkins. As Professor of Anatomy
at the Rockefeller Medical College at Peking, China, he played an impor­
tant part in establishing modern medical science in the Orient. He has
carried on exhaustive histopathological researches not only at the Rocke­
feller Institute in New York, and a number of American Universities,
but also in Asia, North, East and South Africa, the West Indies and
other parts of the world. He has written many papers on histological
and other subjects, and has edited a number of large and important
volumes, including General Cytology, Special Cytology, Arteriosclerosis,
Human Biology and Racial Welfare, and Problems of Aging. He has
held many important posts, including that of Chairman of the Medical
Section of the National Research Council. He is now Professor of
Cytology in the School of Medicine of Washington University, St. Louis,
where, with an abundant time schedule, ample staff, and splendid
facilities of all kinds, he is taking brilliant advantage of his opportuni­
ties to develop his teaching and research interests.

—C. C. Macklin.
To Study the Phenomena of Disease without Books
is to Sail an Uncharted Sea.
—Osler.

RECENT ACCESSIONS TO THE MEDICAL SCHOOL LIBRARY

November 28, 1939

Abbott—Classified and annotated bibliography of Sir William Osler's publications. 2nd ed. 1939.
Allen—Sex and Internal Secretions. 2nd ed. 1939.
American Medical Association—The Vitamins. 1939.
Bacon—Anus, Rectum, Sigmoid Colon; Diagnosis and Treatment. 1938.
Beck—Introduction to the Rorschach Method. 1937.
Bensley & Bensley—Handbook of Histological and Cytological Technique. 1938.
Best & Taylor—The Physiological Basis of Medical Practice. 2nd ed. 1939.
Bivin—Pseudocyesis. 1937.
Callander—Surgical Anatomy. 2nd ed. 1939.
Couch—Surgery of the Hand. 1939.
Cowdry—The Problems of Ageing; Biological and Medical Aspects.
Cushing—Meningiomas. 1938.
Fishberg—Hypertension and Nephritis. 4th ed. 1939.
Flack—Surgeons All, by Harvey Graham (pseud.). 1939.
Fluhmann—Menstrual Disorders. 1939.
Franklin—A Monograph on Veins. 1937.
Fulton—Physiology of the Nervous System. 1938.
Guthrie—The Psychology of Human Conflict. 1938.
Haden—Principles of Hematology. 1939.
Heffron—Pneumonia. 1939.
Herelle—Bacteriophage and Its Clinical Applications. 1930.
Herelle—Le phénomène de la guérison dans les maladies infectieuses. 1938.
Horrall—Bile; Its Toxicity and Relation to Disease. 1938.
Just—The Biology of the Cell Surface. 1939.
Kopetzky—Surgery of the Ear. 1938. (Loose-leaf.)
Kydd—Bibliography of Rural Medicine. 1938.
Lewis—Research in Medicine.
Long & Bliss—The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds. 1939.
McClendon—Iodine and the Incidence of Goitre. 1939.
McLester—Nutrition and Diet in Health and Disease. 3rd ed. 1939.
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McNally—Toxicology. 1937.
McPheeters—Injection Treatment of Varicose Veins and Hemorrhoids. 1938.
Mansfield—Materia Medica, Toxicology and Pharmacognosy. 1937.
Munro—Cranio-Cerebral Injuries. 1938.
Murray—Bones. 1936.
Northrop—Crystalline Enzymes. 1939.
Noyes—Modern Clinical Psychiatry. 2nd ed. 1939.
Park & Williams—Pathogenic Micro-Organisms. 11th ed. 1939.
Ranson—The Anatomy of the Nervous System. 6th ed. 1939.
Reynolds—Physiology of the Uterus. 1939.
Rosett—The Mechanism of Thought, Imagery, and Hallucination. 1939.
Salle—Fundamental Principles of Bacteriology. 1939.
Schilder—Psychotherapy. 1938.
Strecker—Alcohol; One Man’s Meat. 1938.
Terry—Fever and Psychoses. 1939.
Walker—The Primate Thalamus. 1938.
Winternitz—The Biology of Arteriosclerosis. 1938.
Witherspoon—Clinical Pathological Gynecology. 1939.
Zinsser—Immunity. 5th ed. 1939.
Zinsser & Bayne-Jones—A Textbook of Bacteriology. 8th ed. 1939.
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