DR. ROBERT JAMES GRAVES (1796-1853)*
— A BIOGRAPHY

DAVID A. CLARK, B.Sc., Meds '50

Introduction:

It is written in the Holy Book that we should "praise famous men and our fathers that begat us". This evening seems a not inappropriate time for remembrance and reflection on a celebrated Irish clinician and physician, Dr. Robert James Graves, who can take his place rightly in the list of the fathers of Medicine (Sydenham, Fothergill, Haggart, Huxham, Cullen, Gregory, Frank) and who had the rare privilege of leading the advance of the modern school of practical medicine in Ireland.

For one brief period — hardly exceeding a third of a century — the medical schools of Western Europe and America looked to Dublin for a model. Padua, Montpellier, Leyden, Edinburgh, Paris — each in succession had been the Mecca of Medicine; for a short space of time Dublin, too, was to have her turn amongst holy places. That eminence was created by a few men, and knew no continuity; with their passing, her leadership passed to other centres unborn in the years of her flourishing.

His Life — Background & History:

The pedigree of the family of Graves in Ireland can be traced back to the period of subjugation of the county by Cromwell. His ancestor, Colonel Graves, an officer in the Protector's cavalry, at the time acquired large estates in the county of Limmerick. Graves was the youngest son of Richard Graves, D.D., Senior Fellow of Trinity College, Dean of Ardagh and Regius Professor of Divinity in the University of Dublin, and of Eliza, daughter of James Drought, D.D., also a Fellow of Trinity College whose family had long settled in the King's county. Robert James Graves was born in 1796. Little is known of his early childhood and youth. There were three sons, Richard, Hercules and Robert, who all passed through the University of Dublin with great distinction. The three brothers obtained, in three successive years, the gold medal in Science and Classics, then the highest distinction attainable by students.

In 1816, Graves, a tall dark-complexioned youth of ready wit and sarcastic tongue, graduated from the school of Physic in his 21st year, having taken every possible prize in his course on the way to his degree.

* Read at a meeting of the Osler Society, University of Western Ontario Medical School, London, Ontario, February 8, 1950.
of M.B. from the University of Dublin. Robert Graves was amply to repay Ireland for his ancestor's uninvited settlement. He had been a phenomenal student and the family means permitted a long tour of continental study—three years spent in visiting the best teaching centres of London, Edinburgh, Berlin, Gottingen, Vienna and Copenhagen, with vacation trips to France and Italy. Like other youths with well-lined pockets he had his adventures of which we may select three as exemplifying the character of the man who was to revolutionize medical teaching on two continents.

Story No. 1:

His faculty for language was such that in Austria he was taken for a German spy, and had to submit to ten days imprisonment before his correct identification procured his release.

Story No. 2:

Crossing the Alps en route to Italy, he shared a diligence with Turner, the painter. They travelled together for weeks sharing the same inns, eating, conversing and sketching together neither asking the other's name until it was time to part company. NOTE: Graves showed remarkable artistic powers and his sketches from nature were full of vigour and truth.

Story No. 3:

While sailing from Genoa to Sicily Graves' brig ran into foul weather. The sails were torn to ribbons and the crew was abandoning ship and passengers. Graves though abominably seasick, seized an axe and stove in the sides of the row boat and declared "It's a pity to part good company, so let's all drown together". He then took command of the ship, had the suckers of the pumps removed, and cut from his own boots the necessary leather valves. The crew returned to their duties, the leak was stopped and the vessel saved.

In this liberal education, which embraced the training of the school, the university, and the world, we can discover in part the foundation of his subsequent eminence. He had made himself intimate with the recent great discoveries and modes of thinking in every great school of medicine and had formed friendships with the leading physiologists and physicians of Europe, friendships which were continued throughout his life by means of correspondence.

Youth, vigour, determination; these are qualities to be found in many an Irishman. When to this is added "ce petit rien de superflu" which has allowed a first class education to be rounded off with several years of travel and experience, the whole fired by the daemon which, knowing that something ought to be done knows also what that something is, and is determined to get it done—the combination becomes irresistible.
Graves' Labours:

In 1821 Graves returned to Dublin and at once took a leading position; he was elected Physician to the Meath Hospital and became one of the founders of the Park Street School of Medicine. Graves' opening lecture to his students at the Meath Hospital in 1821 shook the complacency of the Dublin pundits. He boldly declared that many lives were lost each year owing to bad treatment by doctors whose teachers had never taught them to practise. He declared that students "walking the hospitals" in Dublin made their appearance there as critics rather than as learners, coming to hospital seeking entertainment rather than instruction and that many were annually dubbed doctors who had scarcely ever been called upon to write a prescription. Graves also avowed that the coarse, abusive language of Irish medical men must go, and that doctors, often accused of disrespect for the dead, were to show only humanity to the living.

Graves introduced into the Dublin School of Medicine the German method of clinical instruction. The hospital lectures given before his time both in Edinburgh and Dublin consisted of Olympian dissertations delivered in indifferent Latin by a lecturer to a class, who, notebooks in hands, took down and memorized every word. The aristocratic gulf between teacher and pupil was broken by Graves. The practice of medicine, he declared, could not be learned by hearsay; this was book-medicine or book-surgery at its very worst. Taking his class to the bedside he allotted to each student a patient, every detail of whose cure was to be studied and recorded from beginning to end of his stay in the hospital. Graves' student-practitioner was thus charged with the personal responsibility of investigating his cases for himself under the personal guidance of the teacher. This daily deliberation and anxious discussion concerning the nature and treatment of each case is peculiarly interesting and serves to accustom the beginner to habits of accurate examination whereby he is taught to interrogate nature for himself and learn the history and treatment of disease from direct observation. The student, obliged to give reasons for every plan of cure that he proposed, became accustomed to a rational and careful investigation of disease and enjoyed the most important of all advantages — the early correction of his errors. He thus commenced private practice with a sufficient degree of experience to render himself unlikely to commit any serious mistakes.

Graves the Teacher:

The style of his speaking was massive, nervous and forceful, unweakened by sentimentality and undisfigured by pathos. The teaching of Graves at the Meath gave great impetus to clinical study in Dublin. He was a great teacher and as such had command over the minds of men. He was thoroughly earnest, every word he uttered forced its way irresistibly. As a teacher he was an original investigator and hence commanded attention from his listeners.
Graves taught that while the successful cultivation of medicine required the most enlarged training of the mind, the study of disease could not be commenced too soon. After a certain period it was a grave error to divert the mind of the student from observation and study at the bedside.

Speaking on the sources of the medical art he philosophically stated that the possession and exercise of the healing art shed a kindly lustre over man's nature, and afforded him the means of practising the sweetest of all the offices of charity—curing his fellow-creatures; but if this be one of the goodliest fruits borne by the tree of knowledge, it cannot be attained, nor enjoyed by all; it can be reached only by him who, patiently labouring year after year, has perseverance enough to seek, by means of constant study and constant observation, this precious gift. His success as a teacher was justified by the success of his pupils and the growth of the School.

Having been elected a Fellow of the Irish College of Physicians he was subsequently appointed Professor of the Institutes of Medicine, from which chair he gave many lectures, chiefly on physiology. From 1828 to 1836 he wrote many philosophical essays in the "Dublin Journal of Medical Science" of which he was one of the founders and editors.

In 1843 his famous Clinical Lectures were published and he was elected president of the Irish College of Physicians. In 1848 he was elected Fellow of the Royal Society, the highest recognition of ability which British Science had to bestow. He was then in retirement and the distinction came as a fitting climax to a life consumed in the application of scientific method to clinical medicine. Four years later he died, too soon, of liver disease. He was only in his 56th year.

Graves' Contributions

Graves' permanent reputation chiefly rests upon his Clinical Lectures, 70 in number, which were published in 1848 and which shortly acquired a European reputation. They were deservedly popular and drew from Trousseau himself, the prince of French clinical lecturers, the warmest ecomiums; he called Graves "a perfect clinical teacher" and also advised his students to regard these clinical lectures as their breviary. He introduced many novelties such as "the pin-hole pupil", timing the pulse by the watch, and discarded the old antiphlogistic treatment of fevers. The lectures when read today are seen to have outstanding merit and reveal a very broad grasp of general topics. Graves had unusual powers of observation, he employed as aids a careful physical examination and a searching analysis. His diagnosis and treatment were based on an intimate knowledge of normal and pathological anatomy, physiology and chemistry.
Fever Contribution:
Fever had broken out in Ireland in successive epidemics in 1817, 1826, 1847. The treatment secundem artem consisted of repeated bleedings, purgings, sedation, and such a low course of diet as would cooperate with the other remedies. Graves was as revolutionary in his methods of treatment as in his teachings. Realizing that a starving man was in no shape to resist contagion he ordered his fever patients to be fed. The results were so soon apparent by the continued improvement of his fever patients in the convalescent wards that he suggested as his epitaph, "He fed fevers".

Tuberculosis Contribution:
Graves advocated an abundance of nourishing food and plenty of fresh air for tuberculosis patients. "Never abandon cases of consumption" was a note in prognosis.

Diarrhoea Contribution:
He used much common sense in the food he prescribed for children afflicted with diarrhoea.

Goitre Contribution:
The contribution for which he is best known is the one in which he described independently what is called today toxic or exophthalmic goitre—Graves' Disease. (This entity had been described 7 years previously by the old Bath physician Parry). The description of the three cases he had seen shows the pains-taking recording of minutiae based on his equally careful examinations. He described the thyroid enlargement, its elasticity and its variation in size; the persistent tachycardia with palpitation, the nervousness, emaciation, weakness, and the undue prominence of the eyes. "And yet there seems to be no certain grounds for concluding that organic disease of the heart exists."

Cholera Contribution:
In his papers on cholera, he gave a history of its progress and predicted correctly its arrival in Ireland. He urged the formation of a complete, world-wide network of medical observatories to record especially the rise, progress and character of diseases.

Opium Contribution:
He did immense good by teaching how opium should be used correctly and its special use in the treatment of peritonitis.

Graves according to Trousseau, was a perfect clinical teacher, an attentive observer, a profound philosopher, an ingenious artist, and an able therapist. Robert Graves commends to our admiration the art whose domain he enlarged, and the practice of which he rendered more useful and fertile.

As might have been anticipated, the efforts of Graves' mind were by no means confined to subjects purely medical. He showed a continued
sympathy for all the events of his time, and more especially for those which concerned the advance of civilization, discovery, and the struggles of a people for freedom in the military undertakings of his own country. His writings were characterized by careful preparation and singular knowledge of the history, topography, political condition, and material sources of various countries. Among the events of the time which most interested him may be mentioned the Hungarian Revolution and the War in Afghanistan. His history of the latter event is a good example of his powers of investigation and arrangement.

Conclusion:

This work would not be complete without mentioning the collaboration between Robert Graves and William Stokes at the Meath as staff men. The relationship between these men was admirable in its harmony. They entered the lists together, neither one jealous of the other’s distinction and each striving to strengthen their joint influence upon the pupils who year by year were drawn in increasing numbers to the clinics at the Meath. In their joint task Graves and Stokes changed completely the intellectual atmosphere of Dublin Medicine, stamping their personalities on the whole development of medical studies in the two schools. Sir William Osler, addressing the delegates to the Bicentenary of the School of Physiology at the Dublin Mansion House on July 5th, 1912, paid them tribute.

"I owe my start in the profession to James Bovell, kinsman and devoted pupil of Graves, while my teacher at McGill, Palmer Howard, lived, moved and had his being in his old masters Graves and Stokes."

Osler went on to say, "that the best life of a teacher is in supervising the personal daily contact of patient with student in the ward." Through Osler the leaven of the teaching of Graves and Stokes works still in Canadian, American and English centres of learning.

Hogan's bust, outside the Academy Library in Dublin, portrays the features and expressions of this daemoniac searcher after truth. There one can see force, intellect, and abundant energy. But there is another side which no marble can portray. It cannot reproduce for us the voice nor the warm-hearted sensitive nature of the man who, in an age of snobs, never forgot a kindness or a friend, however lowly.

After Graves' death the mantle of leadership which fell on Stokes was carried effectively for the next 25 years. He continued the work of Graves and gave to physical diagnosis its place in clinical medicine.

Yet, although its span of eminence was short, Irish Medicine had an influence that endures to the present day. Men die, but ideas live. Across a century of scientific progress, comes back the voice of Graves, speaking in his retirement:
"A short transitory existence has been allotted to our bodies: individuals die, generations pass away, but the common intellect of mankind fears not the same fate nor shares the same brief mortality."

**BIBLIOGRAPHY**


To each one of you the practice of medicine will be very much as you make it; to one a worry, a care, a perpetual annoyance; to another, a daily joy and a life of as much happiness and usefulness as can well fall to the lot of man. In the student spirit you can best fulfill the high mission of our noble calling—in his humility, conscious of weakness, while seeking strength; in his confidence, knowing the power, while regarding the limitations of his art; in his pride in the glorious heritage from which the greatest gifts to man have been derived; and in his sure and certain hope that the future holds for us still richer blessings than the past.

— OSLER, "AEQUANIMITAS."
THE PATHOLOGY AND PATHOGENESIS OF THE COLLAGEN DISEASES

JAMES MURRAY, MEDS. '50

The collagen diseases are a group of disease entities of unknown etiology characterized clinically by diffuse symptoms in all systems of the body and grouped together on the basis of their common pathological lesion. This group of diseases includes:

- Serum sickness
- Periarteritis nodosa
- Disseminated lupus erythematosus
- Scleroderma
- Rheumatic fever
- Rheumatoid arthritis

The pathological lesion common to all the above diseases is a fibrinoid degeneration of connective tissue. These lesions may occur in any organ of the body containing connective tissue, thus accounting for the diffuse nature of the symptoms. There are two phases of the lesion:

**Necrosis:**

In microscopic areas of the connective tissue the ground substance is first increased in quantity so that it becomes easily visible. The collagen fibres in the area, at the same time, become swollen and loosened in their structure. Their individual fibrils are separated by the increased ground substance, become granular in appearance, and may fragment. Fibroblasts and inflammatory cells in the area of necrosis are destroyed and merge with the necrotic debris, forming a smudgy patch. While undergoing degeneration the fibres and the ground substance become strongly eosinophilic, taking on the staining reactions of fibrin. This reaction gives the name "fibrinoid" to the necrosis although it is not known whether fibrin is actually present.

**Proliferation:**

In the tissue adjacent to the necrotic areas the fibroblasts proliferate and many new collagen fibres are laid down. This new fibrous connective tissue encroaches on, and gradually replaces, the necrotic area.

The actual lesion seen on pathological study is compounded of the above two processes. The proportion of each varies in the several diseases and gives rise to their clinical and pathological differentiation. The inflammatory response to the necrotic material is a further factor in the production of the lesion.

The pathology of the diseases mentioned above is as follows:

**Serum Sickness:**

Serum sickness is a reaction to injection of a foreign protein into a person previously sensitized and follows seven to fourteen days after the
injection. At the height of the reaction there is generalized lymphadenopathy, swollen joints and increased capillary permeability producing oedema, urticaria and albuminuria. Rich found necrosis, fibrinoid alteration and hyalinization of the media of the affected small arteries together with perivascular infiltration or infiltration of the entire wall with mononuclear and polymorphonuclear cells. These lesions of small arteries were found in kidney, bladder, skeletal muscle and lymph nodes.

**Periarteritis Nodosa:**

Periarteritis nodosa is believed to be a manifestation of hypersensitivity. In more than 25 percent of cases there is a history of a long standing allergy such as asthma, hay fever or hives. Clinically periarteritis nodosa is characterized by fever, sweating, tachycardia, malaise, fleeting oedema, progressive weakness, and diffuse joint, muscular or abdominal pain. The lesions occur in the walls of small and medium sized arteries and especially visceral arteries. The early lesions show a fibrinoid degeneration of the fibrous elements of the arterial wall and a proliferation of the lining endothelial cells. The later necrosis of the smooth muscle cells of the media is believed to be secondary to the fibrinoid degeneration of the ground substance and intercellular fibres of the connective tissue elements. In late stages of the lesion the tremendous proliferation of the fibroblasts and production of connective tissue encroaches on the lumen and raises the adventitia to form the characteristic nodule on the artery.

**Disseminated Lupus Erythematosus:**

Disseminated lupus erythematosus is a disease of unknown etiology occurring predominantly in young females. In many cases an erythematous rash appears on the face or other parts of the body at some stage in the disease. The skin rash, however, is but a superficial manifestation of a widespread disease of the body. The clinical manifestations are a prolonged irregular fever, recurrent involvement of synovial and serous membranes, depression of bone marrow function, and evidences of vascular alterations in the skin, kidneys and other viscera. In twenty autopsies Klemperer, Pollack and Baehr found lesions in all layers of the heart. In the pleura, peritoneum, spleen, kidneys and in the walls of blood vessels. In the heart, pericarditis occurred frequently. The characteristic changes were in the epicardium. Deeply eosinophilic substance appeared among the collagen fibres which was believed to be an alteration of the interfibrillary ground substance. The fibres lost their delicate wavy appearance, became straight and irregularly thickened. They were intensely eosinophilic and highly refractile. The usual sharp contrast between fibres and ground substance was obliterated. The ground substance appeared to have increased in bulk and to have become collagenized. There was a conspicuous proliferation of fibroblasts which were concentrated in the foci of altered collagen fibres.
Microscopic endocardial vegetations were found in 40 percent of cases and microscopic lesions in another 20 percent. In the early phase focal clumps of altered ground substance appeared in the superficial connective tissue layers of the valves just below the intact endothelium. These clumps appeared as homogeneous, deeply eosinophilic masses. With increase of the altered ground substance the protruding mass became grossly visible as a verruca.

Pleuritis was frequent. In most cases it was associated with pneumonia but occasionally it was seen with adherent pericarditis. In these cases the lesions in the pleura were identical with those found in the pericardium.

Perisplenitis and perihepatitis occurred repeatedly in the series. The capsular fibres and the newly deposited collagenous tissue exhibited fibrinoid degeneration as in the pericardium.

The characteristic lesion in the kidney was the alteration of the glomerular loops producing a "wire loop" appearance. The glomerular loops were irregularly thickened and deeply stained with eosin. In more advanced cases there was fragmentation of the loop and complete necrosis.

Lesions were found in the walls of blood vessels in every tissue in the body. Initially there was a deposit of homogeneous eosinophilic material within the intima, between the muscle fibres of the media, or within the adventitia, accompanied by fibroblastic proliferation which often narrowed the lumen. Further progression of this process led to the involvement of the entire vessel wall so that complete rings of fibrinoid masses were laid down lifting the endothelium from the media and choking the lumen.

**Diffuse Scleroderma:**

Diffuse scleroderma produces a diffuse fibrotic contraction and atrophy mainly of the skin but also of the pleura and pericardium. In this disease fibrinoid necrosis of the dermal connective tissue is very slight and scattered. The predominant change is a profuse proliferation of fibroblasts and collagenous fibres producing an induration or hardening of the skin. Contraction of this connective tissue results in atrophy and ulceration of the overlying skin. The proliferative phase of the fibrinoid degenerative process predominates almost to the exclusion of the necrotic process. There is little or no inflammatory reaction.

**Rheumatic Fever:**

Rheumatic fever is characterized pathologically by the Aschoff nodule. This develops in its typical form only in the myocardium, however similar lesions occur in the pericardium, endocardium, heart valves, subcutaneous nodules, pleura, periarticular tissues and synovial membranes. Fibrinoid degeneration of connective tissue elements occurs but is overshadowed by the proliferative and inflammatory responses.
The earliest evidence of injury is a fibrinoid swelling of the "ground substance" of the connective tissue of the heart. The staining reaction of the ground substance becomes intensely eosinophilic. Some few collagen fibrils may fragment but most of the fibres remain intact. Within two weeks the focal area of necrosis becomes surrounded with the typical Aschoff cells. Fibroblasts proliferate about the lesion and gradually replace it with scar tissue.

This same lesion occurs in the subcutaneous tissue. An excessive proliferation of fibroblasts and production of collagen fibres around the lesion results in the formation of the subcutaneous rheumatic nodule.

The presence of these lesions in the periarticular tissues results in the production of increased amounts of synovial fluid and gross oedema of the periarticular tissues resulting in the transient arthritis.

Rheumatoid Arthritis:

Rheumatoid arthritis is a diffuse disease of the body involving not only joints but skeletal muscles, heart and kidney.

In the joints the process is one of fibrinoid necrosis accompanied by inflammatory response and an intense proliferation of fibroblasts with production of collagen fibres.4 "The lining membrane of the joint is covered with a necrotic fibrinous layer which penetrates the adjacent connective tissue of the joint capsule. The connective tissue becomes edematous and a homogeneous substance forms in it which gives the staining reactions of fibrin. About this necrotic area the connective tissue cells swell and assume a morphology suggestive of giant cells. . . . After the disease has assumed a more chronic phase the superficial endothelial or flattened connective tissue cells undergo hyperplasia and form a thick pad on the surface of the synovial membrane. In the later stages the penetration of the synovial membrane by areas of fibrinoid degeneration may lead to necroses in this membrane and the formation of very cellular and vascular granulation tissue. . . . The capsular and periarticular connective tissue is diffusely swollen, and its fibres dissociated. Fibroblasts are abundant. . . . As the disease becomes chronic and tends to heal, restoration of the joint may take place without damage or, in the more severe types, bony or connective tissue ankylosis may remain, or the joint may be deformed without ankylosis. . . . The contracting synovial membranes and periarticular fibrous tissue render the joints stiff and may cause considerable deformity."

Aegerter and Long1 found pathological pictures of pure and classical fibrinoid degeneration in the subcutaneous nodules of rheumatoid arthritis. Baggenstoss and Rosenberg2 found myocardial lesions which they could not distinguish from those of rheumatic heart disease in sixteen out of thirty patients having rheumatoid arthritis. Only two of these patients gave a history suggestive of rheumatic fever. They also found glomerular endothelial proliferation in nineteen of the thirty cases necropsied.
The essential process in the pathology of all the above-mentioned collagen diseases is a fibrinoid degeneration of connective tissue. It is on this basis that they have been grouped. One other element common to the group has been proposed: a common pathogenesis due to response of connective tissue to anaphylactic hypersensitivity.

Serum sickness, of course, is due to hypersensitive reaction to the injected serum. Periarteritis nodosa has been shown to develop following an allergic reaction to sulpha therapy. The elevation of the antibody titre to hemolytic streptococci in 90 percent of cases of rheumatic fever indicates a causal relationship between this infection and the disease process. A hypersensitive reaction has been suggested. Thus in several of the diseases there is evidence that anaphylactic hypersensitivity may play a role in pathogenesis.

It has been suggested that fibrinoid degeneration is a specific lesion of anaphylactic reaction. However, Klemperer pointed out that "although fibrinoid collagen alterations occur in allergy yet collagen alterations hardly distinguishable microscopically from those seen in allergy can be observed in situations which bear no relation to hypersensitivity—for example chemical or physical irritation such as squeezing the skin."

Concerning the pathogenesis of collagen diseases, Duff has concluded: "It seems reasonable to suppose that fibrinoid necrosis may be caused by the action of enzymes on the intercellular ground substance and fibres, but the release of the appropriate enzymes into the tissues may be determined in a variety of ways. The reactions occurring in hypersensitive tissues may be one of these ways but there are probably others as well. Accordingly, we can assume a similarity of pathogenesis among the various collagen diseases only in the last of the sequence of pathogenic events that occur within the tissues themselves. Morphological resemblances . . . cannot establish the theory of common pathogenesis. Further clinical and experimental investigation may be expected to establish some degree of similarity of pathogenesis, but in the present state of our knowledge and until further information has accumulated, the grouping together of the diffuse collagen diseases must be regarded as a purely morphological correlation."

BIBLIOGRAPHY

CORTISONE AND ACTH IN THE TREATMENT OF RHEUMATOID ARTHRITIS

DAVID B. MELTZER, MEDS. '50

This review is intended to cover the applications of cortisone (compound E) and ACTH to rheumatoid arthritis only. Those of us who were privileged to hear Dr. J. S. L. Browne in London recently will realize just how small a facet is the treatment of rheumatoid arthritis as compared with the broad implications of these two substances. The treatment of rheumatoid arthritis, however, is somewhat fundamental, since it first brought to focus the broader implications of these two substances in the field of the collagen diseases, and in disease in general.

Dr. Philip Hench of the Mayo Clinic brought public attention to the reversibility of rheumatoid arthritis in his Heberden Oration, given in Scotland on October 15th, 1948. He pointed out that the pathological anatomy is largely irreversible, but that the pathological physiology under certain circumstances is dramatically reversible, activated spontaneously, therapeutically, and accidentally.

Regarding spontaneous reversibility, it has long been noted that in the course of the disease, lengthy remissions occurred in a major percentage of cases—generally associated with an overall improvement in general health.

Regarding therapeutic reversibility, various agents—mostly non-specific—have shown some some effect on the course of the disease, particularly febrile reaction to foreign protein, starvation, or surgery of any kind. (Gold therapy is also effective but seems to be unrelated to Hench's present theories). From these effects there arose in Hench's mind the question as to what relationship such diverse reactions could have to one another, and to the disturbed physiology of rheumatoid arthritis. He concluded that they must, in some manner, motivate a biological reaction unrelated specifically to the particular manifestations of the disease.

Regarding accidental reversibility, it has long been observed that in the majority of cases pregnancy brings about a considerable degree of relief of symptoms and signs for the duration of the pregnancy. Similar observations have been made regarding hepatitis with jaundice. In this instance, irrespective of the concentration of bilirubin in the serum, relief, though only temporary, occurred in a large percentage of cases.

Hench concluded that anything concerning the etiology of rheumatoid arthritis must take into account the beneficial influence of pregnancy and jaundice, i.e. that the disease is a basic biochemical disturbance, accidentally corrected by some incidental biochemical change common to the above noted conditions and circumstances. From this basic theory
he became convinced that this disease, heretofore considered progressive and unremitting, should no longer be viewed with such pessimism, and indeed, that therapy could be effective.

The first attempts at therapeutic observation along these lines included the following:
1. Therapeutic pregnancy — this was effective in a large percentage of cases, but of course can hardly be used beyond the normal indications for childbirth.
2. Female hormones — a large variety of these were tried, but produced negative results.
3. Blood transfusions from pregnant females — here again few, if any, positive results were obtained.
4. Experimental jaundice — this produced a temporary relief in a majority of cases, but is, of course, too drastic as a general therapeutic measure.

From these attempts, attention was again focussed on the effect of jaundice and pregnancy. These two conditions, separately or together, produced amelioration of symptoms in a number of diseases, including rheumatoid arthritis, chronic arthritis with psoriasis, psoriatic arthritis, psoriasis with no arthritis, intermittent hydrops of the true and of the symptomatic type, rheumatic fever, primary fibrositis, migraine, hay fever, Addison’s disease, and even in some cases of myasthenia gravis.

Hench postulated the existence of an anti-rheumatic "substance X", unrelated to the sex hormones, and operating in a non-specific manner. This, then, was to be his guide in future investigations.

In January, 1941, Dr. Edward Kendall, another worker at the Mayo Foundation, investigating adrenocortical extracts, turned Hench's attention to the adrenal cortex as the possible source of his "substance X". Kendall had extracted a series of substances, with a view to treatment of Addison’s disease. These substances were named compounds A, B, C, etc. Some of Kendall’s earlier extracts of the adrenal cortex were used at that time, but compound E, or cortisone, which is 17-hydroxy-11-dehydro-corticosterone, was not available to Hench until September, 1948.

The first patient upon whom cortisone was used was a married female, 29 years of age, who had had rheumatoid arthritis for some 4½ years. There had been no satisfactory response to any of the multiplicity of treatments previously in vogue. Pre-treatment X-ray studies showed destructive changes in the right hip, with less extensive changes in other joints. Her sedimentation rate, by Westergren method, was as high as 108mm. in 1 hour. She was started on intramuscular injections of 100 mg. of cortisone daily, on September 21, 1948. On that day, walking was so painful for her that she was unable to leave her room. On September 23, she noted greatly decreased muscular soreness. On September 24, painful morning stiffness was entirely gone, and she was now walking
CORTISONE, ACTH IN TREATMENT OF RHEUMATOID ARTHRITIS

with only a slight limp. One week later, joint as well as muscular stiffness had virtually disappeared, and tenderness and even swellings were markedly lessened. The sedimentation rate was decreased to 86mm. in 1 hour. Lesser dosages of cortisone were administered, but these led to marked recurrence of symptoms.

Since that time, the treatment of 16 cases has been reported from the Mayo Clinic. The patients selected were all classified in the moderately severe or severe chronic polyarticular rheumatoid arthritic group, with disease of 4½ months to 5 years duration, not responsive to any previous therapy.

Special charts were kept before, during, and after administration of cortisone or ACTH, including a report on the examination of joints, and any biochemical tests. Moving pictures were taken, as well. For control, the therapeutic substances were replaced by a fine aqueous suspension of cholesterol, identical in appearance with the therapeutic agents. The time of interchange was unknown to the patients, and to the three clinical observers evaluating the results. Upon checking the time of administration of the control and of compound E, it was observed that no clinical change occurred subjectively or objectively when the control substance was given, and conversely when the control substance replaced compound E, the articular and muscular symptoms recurred in a few days, and the sedimentation rates rose. The substance used during the latter parts of the experiment was compound E acetate, prepared by the chemists of Merck and Co. in cooperation with Kendall and his associates at Mayo's. This substance, by the way, is still very expensive, and very limited in supply.

An initial dose of 300 mg. of the acetate was given, followed by a daily dosage of 100 mg., which is the equivalent of 89 mg. of cortisone. This dosage is still regarded as tentative. A maintenance dosage is used after the initial optimum improvement. This varies from 75 mg. down to 24 mg. To date, however, in severe cases, flareups have been noted with an increased sedimentation rate when the maintenance dose is less than 75 mg. Additional measures, such as analgesics, physiotherapy, and the like, were used as required, but in all cases there was no necessity for such measures within several days to three weeks. The patients were encouraged to become ambulatory as soon as possible, and to carry on a normal routine of living. One particular case, that of a Rochester physician, was treated on an outpatient basis; he returned to his practice, and came in daily for injections.

Effects of Administration of Cortisone

1. Initial effects on muscles, and joints. In each case there was a marked reduction of stiffness in muscles and joints, decreased joint aching or tenderness on motion, and significant improvement of function. The pattern of improvement showed at first a decrease in muscular and artic-
cular stiffness, often within 48 hours, then a decrease in pain and tenderness, and in most cases this was followed by a complete or almost complete disappearance of swelling. Where flexion deformities were present to a mild degree only, there was a disappearance of these within 10 days.

2. General effects. These included an increase in appetite, often a gain of weight, and most patients showed improved strength and a marked sense of well being. One case went on to a degree of euphoria of psychotic proportions. This euphoria has been considered as being more than just due to the loss of pain, and as being positive, including an increased mental capacity and mental activity. This effect has since been observed by psychiatrists in treating some mental diseases with cortisone.

3. Withdrawal Symptoms

In 9 cases, where the control substance was substituted, 8 showed a prompt increase in sedimentation rate and a return of symptoms within one or two days. The 9th showed an increased sedimentation rate, but the symptoms did not return. Those cases in relapse had a prompt return of improvement when cortisone was again administered.

4. Laboratory observations.

(a) Sedimentation rate—there was a decrease in all cases, averaging 2-3 mm. per day. There was a decrease to normal levels in most cases within 10 to 35 days.

(b) Serum proteins—in those cases where there was a decrease in globulin and a reversal of A/G ratio, the trend was towards normal.

(c) 17-keto steroid excretion—in all cases this was reduced to low or even subnormal levels.

(d) Corticosteroid excretion—this was increased in each case.

(e) Hemoglobin—values rose significantly in those patients who were anaemic.

(f) Erythrocyte count—this increased 1/2 to 1 million within a few weeks.

(g) Articular biopsy—this was done in one case, and after 43 days of administration of compound E, there was definite evidence of healing and much less evidence of inflammation than in the pre-treatment specimen.

5. Effects of repeated or prolonged administration. A special observation was made in the case of the physician. A residuum described as "arthritis in miniature" occurred occasionally for a few days at a time. In the original case there were minor articular flareups.

When larger dosages were used, sudden gains of weight occurred, which were lost just as suddenly by a spontaneous diuresis. Other cases showed acne, mild hirsutism, with rounding of facial contours. In one female patient there was a cessation of menses. The newspapers mention psychoses, diabetes, and so forth, from cortisone administration. However, I have been unable to find any record of such cases in the literature.
The original case also complained of a transient epigastric pain. This was easily controlled. There has also been noted a transient oedema, particularly pretibial, disappearing either spontaneously, by change of dose, or by oral potassium nitrate. There is no report as yet from the Mayo Clinic on the effect of cortisone therapy on electrolyte and water balance. One case showed a rise in blood pressure, which may perhaps be related to an increased blood volume.

There is a further report on treatment of rheumatoid arthritis with ACTH, of 8 cases, by Regan, Grokoest, and Boots, from the Edward Daniels Faulkner Clinic of the Presbyterian Hospital, New York City. Here, divided dosages were used, administered every 6 hours, with a view particularly to finding a minimum dose to prevent relapse.

One case, an elderly female, was given 25 mg. daily in two doses, and this was sufficient to prevent remission, up to the time of publication. In another case, that of a male, aged 39, there was a remission from an initial dosage of 60 mg. daily for 6 days. He was then given 15 mg. daily as a maintenance dose, and mild symptoms recurred. The other 6 patients were given an initial dose of 100 mg., then 40 mg. daily for 6 to 10 days. The subjective response in each case confirmed the results obtained by Hench, and similar relapses occurred upon removal of ACTH, with one interesting exception, that of a female who developed euphoria to the extent of mania, for which electric convolution therapy was required. Her relapse did not occur until 25 days later.

Two patients of this group manifested subcutaneous rheumatoid nodules. A pre-treatment biopsy was taken from one of these nodules, and a nodule of equal size left on the other arm. In two weeks this nodule had fragmented into smaller nodules. Thirty-five days after the start of ACTH treatment, part of one of these nodules was removed. It showed large central areas of fibrinoid necrosis, and there was much less lymphocytic infiltration than in the previously biopsied nodule. In both patients the nodules decreased in size.

In those cases of the group showing flexion contractures of recent origin, there was a prompt return of full extension, and in those of more than 5 years duration, there was considerable improvement. It was noted also that flexion contractures did not recur so rapidly on removal of ACTH as did other symptoms.

Two of the patients showed an increase in heart size, apparently not associated with sodium retention. In the 6 other patients, no sodium restriction was employed, and there was no increase of heart size, although there was a slight haemodilution.

The New York group made some observations on chemical changes. They found that on 60 mg. ACTH daily there was marked sodium retention, with a small increase of potassium excretion, and little change in serum sodium and potassium. These changes were associated with weight
gains; when the dosage was lowered, a sodium diuresis occurred, and the weight gain progressed more slowly, and ceased with a dosage of 15 mg. daily, at which level remission of symptoms was less complete. An increase of uric acid excretion has been noted, apparently not accompanied by any significant increase of urinary nitrogen excretion. Changes in serum protein were similar to those observed by the Mayo group, as were the changes in sedimentation rate.

Some other interesting observations were made. In 3 patients, following treatment for 10 to 20 days, there was a fall in total serum globulin and euglobulin, and one patient had a positive cephalin flocculation test before treatment, which became negative after treatment. Observations were made on immunological changes also. It is known that 50% of rheumatoid arthritic patients show a positive agglutination test for alpha hemolytic streptococci, and 60% to 70% for sensitized sheep cells. Little change was observed in any of these patients in these respects during the period of treatment, which was 10 weeks at the most.

An elevation of fasting blood sugar level occurred in two patients, the rise being from 85 to 120 mg. %, on a dosage of 60 mg. ACTH daily. When the dose was reduced to 40 mg. daily, a return to pre-treatment levels occurred with symptoms still in remission.

Mental changes and evidences of hyperadrenalinism were seen to be similar to those reported by Hench. One patient, who was being treated in New York for disseminated lupus erythematosus, died from a pulmonary infarct, and at autopsy the adrenals were seen to be three times the normal size. In those patients with ulcers on the skin, there was a decreased ability to form granulation tissue. This is seen in hyperadrenalinism also. Ragan and Meyer have postulated that rheumatoid arthritis is a disease of mesenchymal tissues, which are overactive, and that specific steroids depress the activity of mesenchymal tissues, so depressing the host response which causes occurrence of the disease.

The metabolic effects and mode of action of cortisone and ACTH are undergoing exhaustive investigation. To date, little has been published. Dr. Hans Selye has shown in his experiments on the anaphylacticoid reaction to eggwhite in rats that cortisone and ACTH effectively inhibit the reaction. He has also pointed out that a similar inhibitory effect can be noted with the use of the antihistaminic drugs. In his work he has found that D.C.A. and compound E acted antagonistically, and he suggests that D.C.A. produces a partial hypocorticoadrenalism by a blocking action on the target organs to the action of cortisone. Similar effects are seen with L.A.P. (an impure anterior pituitary extract) to those of D.C.A., although an enlargement of the adrenal cortex is brought about by it, just as by ACTH. Selye therefore postulates an anterior pituitary principle antagonizing the ACTH effect, and producing a D.C.A.-like effect, and he relates this to a group of diseases which he has called the diseases of adaptation. In this group he includes nephrosclerosis, myo-
carditis, hypertension, and rheumatic changes, all of which conditions can be simulated by the administration of D.C.A. and L.A.P. to experimental animals. As early as 1944, Selye pointed out that a pathogenetic relationship existed between the adrenal cortex and the allergic, rheumatoid, and other collagen diseases. In the light of the action of cortisone and ACTH, it appears very probable that adrenal-cortical and pituitary derangements are involved in the pathogenesis of this group of diseases. In this regard, some patients who have been treated with ACTH and cortisone for rheumatoid arthritis, who also had hay fever or asthma, were greatly relieved of symptoms of the latter.

Godlowsky has recently published a very interesting theory regarding the action of ACTH. Numerous observers have noted an eosinopenia following administration of cortisone and ACTH. Godlowsky has suggested that the eosinophils may possess the transportation ability of the specific antigen. Since ACTH and compound E produce definite improvement in allergic conditions, the idea is put forth then that the eosinopenia temporarily eliminates the antigen from the antigen-antibody reaction. He suggests that an answer may be sought in the electrolyte regulation—that inflammatory reactions commonly are seen to show quantitative alterations in potassium and sodium equilibrium, and this, he suggests, may occur in the eosinophils to such an extent that their surface tension is altered, causing them to marginate in the capillaries, and so to be temporarily eliminated from the circulation.

To summarize, a review of the treatment of rheumatoid arthritis with cortisone and ACTH, and a summary of some of their clinical and laboratory effects has been presented. It must be emphasized that in a severe case, at any rate, relapse occurs on discontinuation of treatment, and that prolonged administration has its complications. Hench has likened this to the treatment of diabetes with insulin. He has not claimed a cure for rheumatoid arthritis, but rather has shown an approach to its treatment, and to its pathogenesis. Certainly it must be conceded that large inroads are being made into the understanding of the collagen disease group, and that an entirely new field of investigation and therapeutics has been opened.

BIBLIOGRAPHY

Physiology of the Nervous System

J. F. Fulton
Oxford University Press, New York, 1949, 667 pp., Illus. 140

This is an extremely well-written book. In this third edition the author has taken great pains to organize the material on this important subject. Each chapter is divided into the following sections:

1. Brief historical data.
2. Anatomical considerations linking the physiology with the neuroanatomy of the topic.
3. Overall physiological considerations.
4. Details of the general considerations.
5. Clinical applications.

The book as a whole is too extensive for students taking general physiology. However, the summaries of each chapter are extremely useful in obtaining a general picture of the neurophysiology section of the course.

—R. Lyons, '52

Communicable Disease Control

G. W. Anderson and M. G. Arnstein

Since the 1941 edition of this book researchers have met the threat of disease, and war facilitated scientific developments. The highly qualified authors will satisfy the student as well as Health Officers and Public Health Nurses.

The epidemiology and control of the major diseases are arranged under headings and subheadings in an orderly pattern. For each disease an excellent summary is made and supplemental reading is listed. A few well-chosen and comprehensive graphs are included.

This organized, down-to-earth book should become the handbook of every medical student and physician for the study and control of disease.

—W. Beattie, '52

Histology

A. W. Ham
J. P. Lippincott Company, Philadelphia, 1950, 756 pp., Illus. 445

Here is a book designed not only to teach but to facilitate the reader's understanding. It deals therefore, to some extent, with the problems of learning histology, as well as the subject-matter of histology itself.

The student studying histology for the first time has a limited knowledge of gross anatomy, physiology and pathology, hence much explanatory material concerning such subjects has been included to integrate the student's work. The book is especially suitable as a guide in the laboratory because common artefacts, staining techniques and other difficulties are ironed out at the beginning.

—J. Beger, '53
THE TEMPORAL BONE AND THE EAR
T. H. BAST AND B. J. ANSON
Charles C. Thomas, Publisher, Springfield, 1949, 447 pp., Illust. 165

In their studies of the anatomy of the adult ear and temporal bone in man, the authors found it increasingly evident that no matter what course the investigation took, either new morphological features were established or features were found to have been erroneously presented in the past.

This volume is organized on a developmental basis and it is very comprehensive. It can be considered as the latest word in a field that is still controversial. Each point made is supported by a photo-micrograph or illustration. If the structure of the ear is your particular interest, this book warrants your close attention.

—J. WALKER, '53

CLINICAL ENDOCRINOLOGY
(for Practitioners and Students)
LAURENCE MORTIN AND MARTIN HYNES.
Cambridge

This is a simple, practical and authoritative book on a subject which both student and practitioner find difficult. It is easily read and contains no specifications, only facts with stated physiological or pathological bases. All the foregoing reasons and particularly the last, combine to make this book the type of text valuable to the student. Although concise, it is also complete.

From the practitioner's point of view in particular the limits of hormone therapy are emphasized. A list of British and American proprietary hormone products is also given.

Each subject is dealt with under the routine headings of Anatomy; Physiology; Pathology — (a) tumour, (b) hypersecretion; Definition; Etiology; Clinical Features (including illustrative pictures); Differential Diagnosis; Complications; Treatment and Prognosis.

Due to the inter-relation of the different hormones the book has been written and arranged to facilitate cross reference, including an exhaustive index. Since Diabetes would have doubled this conveniently sized book, the subject has been omitted.

Certainly, this is a book that will facilitate the study of a difficult subject.

—J. G. FRID, '50

PHYSIOLOGY OF HEAT REGULATION
EDITED BY L. H. NEWBURGH

Few students or practitioners will wish to read every word of this book. However, all who have wondered how the Eskimo keep warm or how the Japanese survive in their hot, wet climate, will find many pages of interesting and informative reading.

Compiled from information obtained during wartime research, the book is divided into two parts. The first tells of the human response to climatic environment; the second, how and why clothing acts as a thermal barrier. For those interested in special sections, detailed references are provided in this very excellent book.

—J. STEPHENSON, '52

THE PERSONALITY OF WILLIAM HARVEY
G. KEYNES

One receives a brief but interesting glimpse of the life of this great man as gleaned from the writings of his contemporaries. In addition, reproductions of several portraits of Doctor Harvey are compared and interpreted.

This booklet is the text of the Linacre Lecture (Cambridge, 1949) and should interest any student of medical history.

—K. BANDEEN, '51
DIFFICULTIES IN DIAGNOSIS OF MALNUTRITION
S. O. Waife
Am. Pract. 1: 225-227, March 1950

The first step towards a proper diagnosis of the varied conditions included in the term "malnutrition" is a description of the clinical condition in terms of what nutrients are present in inadequate amounts, the degree of the deficiency, and the time during which the state has existed.

There are four stages of malnutrition:
(1) Inadequate supply to meet the demand due to inadequate food consumption; malabsorption; impaired utilization or storage; excessive loss and increased requirements. These in turn may result from anorexia, diarrhoea, cirrhosis, glycosuria, hyperthyroidism or fever.
(2) Decreased bodily reserves.
(3) Impaired function.
(4) Development of anatomical lesions.

Clinical methods for determining these states are varied and in some degree nonspecific.

The author submits the following outline for clinical and laboratory examination:
(1) Medical history and physical examination. (Bodily thinness is the most important factor here.)
(2) Dietary history (including tables and analysis).
(3) Chemical tests, both simple and somewhat complex, of blood and urine.
(4) Functional tests (dark adaptation visual-acuity, ergometry, electrocardiogram).
(5) Others: thickness of skin, X-ray of a child's wrist and capillary fragility.

The author hopes that these thoughts will stimulate further interest in a complex and neglected aspect of medicine.
—Elizabeth O. Harrison, B.A., '52

WEIL'S DISEASE
Sidney Leibowitz et al

Histories of five cases of Weil's disease (Leptospira icterohemorrhagica infection in man) are presented with autopsy findings in fatal cases.

Diagnosis was made on basis of serum agglutination tests in four of five cases and by microscopic examination of lung scrapings in post mortem examination in fifth.

Certain unusual clinical features were noted in one or more patients. These include maculo-papular skin eruptions, pyelonephritis, persistent impairment of urinary concentrating ability and severe alopecia.

In two cases occupational contact with rats was clearly shown; in the other three no proof of rat contact was obtained.

Penicillin treatment was employed with one patient, but it is impossible to assess the value of therapy in this case.
—Gus Buck, '52
ABSTRACTS

STUDIES ON HEADACHE
M. MARCUSS E N AND H. G. WOLFF
Arch. Neurol. & Psychiat., 63: 42-51, Jan. '50

An attack of migraine comprises two physiological phases. The first or pre-headache phenomenon is accompanied by cranial vasooconstriction. It is manifested by visual disturbances, paresthesias, and dysarthria.

A lowering of the pain threshold of the pain-sensitive arteries is responsible for the headache which occurs during the second phase, at which time there is vascular dilatation.

Carbon dioxide, a powerful intracranial vasodilator, has been found effective in decreasing or abolishing the vasoconstrictor phenomena of the migraine attack.

A carbon dioxide and oxygen mixture makes these effects more pronounced and may prevent progression to the headache stage. It is believed the increased blood flow, saturated with oxygen, corrects an oxygen deficiency in an area where the neuronal impulses originate which set up the compensatory vasodilatation. The gas mixture must be inhaled before the pain threshold falls in order to derive the desired effect.

—A. L. ROBERTSON, B.A., MEDS '52

ETIOLOGICAL SIGNIFICANCE OF PULMONARY CALCIFICATION AT UNIVERSITY OF TORONTO
T. G. HEATON
C. M. A. J., 62: 252-4, March '50

In the past five years it has been increasingly realized that conditions other than tuberculosis can cause pulmonary calcifications, and in particular that calcifications can be caused by fungus infections of lung, such as coccidiomycosis, aspergillosis, and histoplasmosis.

A total of 122 cases, showing pulmonary calcifications radiologically, was found by an X-ray survey in which 8,144 chest films were taken of students, male and female, at the University of Toronto in the fall of 1948. This is a much lower incidence of calcification than is found in most parts of the United States.

Sixty-three unselected individuals showing pulmonary calcification were skin tested: 36 of these reacted to histoplasmin; 33 reacted to tuberculin. This together with a growing weight of evidence in the literature, suggests that pulmonary calcification is often due to Histoplasma capsulatum rather than to M. tuberculosis. Certain other fungi are also thought to cause pulmonary calcification.

Because histoplasmosis is a disease closely resembling tuberculosis, treatment and control measures will be very similar in the two diseases. For practical purposes there is nothing to be gained by attempting to differentiate between the two diseases in the stage of calcification. But histoplasmosis should be kept in mind in the differential diagnosis of persistent pulmonary infiltrates in Canada as in the United States.

—HOWARD FRIESEN, B.A.
Meds '52

SURGICAL TREATMENT OF FOCAL EPILEPSY


Focal Epilepsy is the result of the presence of an epileptogenic focus in the periphery of the brain. Penfield believes that this focus is situated in an area of ganglion cells whose circulation is interfered with so that the life of the cells is threatened, the partial anoxia causing increased spontaneous neuronal activity. Such foci are associated with meningoencephal scars, local cortical atrophy, local microgyria or expanding lesions such as brain tumors, cerebral abscesses and cysts, as the result of head injuries, birth injuries or local infection.

To aid the surgeon in diagnosis he has at his disposal:
1. Roentgenography which reveals asymmetry of the skull or cranial hemiatrophy suggesting birth injury.

2. Pneumoencephalography revealing local cerebral atrophy.

3. Electroencephalography which will indicate the location of the epileptogenic focus in a large number of cases.

One of the best guides to localization of the focus is the seizure pattern and electrographic study by a specialist.

Penfield stresses that for surgical therapy to be effective it is not only necessary to cut adhesions or remove a tumor or a cyst but also to remove the epileptogenic focus in the adjacent partly-involved tissue.

In a series of 76 cases operated on between 1939 and 1944 Penfield and Steelman reported one fatality due to infection and of the remaining 75 cases followed up, 59 had cortical excision and 16 had craniotomy alone. Of the former group only 11 felt no benefit at all; 15 being completely free of seizures; 18 almost free; 8 were 50% improved, and 7 only slightly improved. Of the latter group there was not a single successful case.

Penfield emphasizes that a focus causing occasional seizures may also adversely affect the brain development and function. This can be ameliorated by removal of the focus.

Radical excision offers hope for cases of focal epilepsy which are not controlled by medication.

—John Nixon, '50

SEX-HORMONE RELATIONSHIPS IN SCHIZOPHRENIC MEN
R. G. Hoskins and G. Pincus


It has been known for some time that schizophrenic psychosis is marked by abnormality in the psychosexual field. Commonly, libidinal evolution halts at the homosexual level or, if this period has been surpassed in the pre-psychotic period, the regression that marks the onset of the psychosis reverts the patient to this homosexual or lower stage.

It has been suggested that the deficiency of adult masculinity in schizophrenic men could be due in some measure at least to abnormality in sex-hormone relationship of a chronic form. The authors themselves believe this hypothesis is not completely true but rather caused by an abnormal ratio between androgens and oestrogens, i.e., too much oestrogen or too little androgen, or both. This imbalance is also found in non-schizophrenic males who have homosexual activity.

Both women and men secrete oestrogens and androgens in the urine. On the test group of 29 schizophrenic men, 23 normal men and 11 normal women, tests for androgens, oestrogens and 17 ketosteroids were done biochemically.

Results:
Normal Androgen: Oestrogen ratio in males is 4.1:1; females is 1:1.

Hebephrenic Schizophrenic: Close to normal male.

Simple and Paranoid Schizophrenic: Between male and female.

Other types of Schizophrenics: Close to female.

A further study on the five schizophrenics with the lowest androgen: oestrogen ratios showed this group to be less aggressive than normal. The four with the highest androgen-oestrogen ratio were quite aggressive, with homosexual tendencies.

The schizophrenic males showed a lower oestrogen output than women but significantly higher than the normal male. The androgen output in this group was lower than normal male but significantly higher than the female, i.e., a schizophrenic shows a trend to femininity but is more masculine than a normal female.

—Keith Phillips, '50
MELANCHOLIA

T. T. STONE AND B. C. BURRIS
J.A.M.A., 142:165-168, 1950

When seen and treated early, melancholia offers an excellent prognosis. Fifty cases of melancholia are reported: 38 melancholia (involutional), 10 mental depression (manic-depressive), and 2 psychoneurotic depression. Each of these had been diagnosed and treated erroneously for an organic disease. Time lapses from the original diagnosis until a correct one was made varied from 3 months to 3 years.

The early signs of melancholia in these cases were "(1) psychomotor retardation; (2) no clouding of consciousness, and (3) staring expression with glassy eye appearance and masked facies. The symptoms were (1) anorexia, (2) loss of weight, (3) insomnia, (4) nervousness, (5) ideas of self-depreciation and self-accusation and (6) last but not least, the patient's feeling better in the late afternoon and evening." These signs and symptoms appear in no other disease except melancholia.

Eighteen patients received, besides other therapies, a complete course of E.C.T. Forty-eight of the fifty patients recovered fully from melancholia.

ELGIN ROBERTS, '50

---

So long as the body is affected through the mind, no audacious device, even of the most manifestly dishonest character, can fail of producing occasional good to those who yield it an implicit or even a partial faith. — OLIVER WENDELL HOLMES.

(From a criticism of homeopathy and quackery)

---

In these days when science is clearly in the saddle and when the knowledge of disease is consequently advancing at a breathless pace, we are apt to forget that not all can ride, and he also serves who waits and who applies what the horseman discovers.

— HARVEY CUSHING
A VOLUNTARY AGENCY AND CANCER

By JONATHAN C. MEAKINS, C.B.E., M.D., F.R.C.P.

President, Canadian Cancer Society

The encouragement of an intelligent interest in any aspect of health or disease is justifiable if one has reason to believe that as a result of interest and knowledge there will accrue to our people better health and greater freedom from disease. The acceptance by our people of the importance of certain health matters has, over the past 25 years, contributed increasingly to such benefits.

Vaccination against smallpox and inoculations for communicable diseases such as diphtheria have eradicated the first of these and brought the second under satisfactory control. The pasteurization of milk and tuberculin testing of cattle have given our children a freedom from the threat of milk-borne tuberculosis that we ourselves did not enjoy a quarter of a century ago. These are only a few of the steps in medical progress which we have taken in our own lifetime. Without public health education such progress could not be made.

Where, however, do we stand in the matter of public education as related to cancer? If we create an intelligent interest in cancer at least two benefits to our people may be expected. First the efficacy of our present treatment methods might be enhanced, which is to say that a greater number of people might be cured of cancer if they were to receive treatment in the earliest stages of the disease rather than when it had extended beyond hope of cure. And second, by giving moral and financial support to those who have dedicated their lives to cancer research, we might see ourselves approaching more rapidly that day when the cause of the disease is understood and when curative treatment for all cases of cancer is at hand.

To these ends the Canadian Cancer Society as a voluntary organization is dedicating its efforts. A sincere attempt is being made to acquaint our people with the importance of early diagnosis and stress is being laid upon four symptoms which, if noticed by any one of us, should mean a visit to our doctor for his opinion:

1. A lump in the breast.
2. Unnatural bleeding from any body opening.
3. Any sore of the skin or mouth which will not heal.
4. A persistent change in bowel habit such as diarrhea or constipation.
Any of these symptoms can be indicative of one of the common forms of cancer which can be effectively treated. Cancer of the breast, the uterus, the skin and mouth and of the bowel represent a challenge in early diagnosis. With adequate treatment in the early stages of these forms of the disease we know that there is a much greater hope for cure.

Any other facts which the lay public may learn in one way or another about cancer are of no measurable value to the nation’s health. If, however, the individual through his own interest, wishes to delve more deeply into the subject of cancer as a disease and the problems associated with finding the cause and the cure, there is nothing on earth to prevent his so doing. It is not the function of the Canadian Cancer Society, however, to educate our people in the many complexities associated with diagnosis, treatment and research. Such matters lie in the realm of professional, not lay education.

Each of us watches with interest the progress of research into the cause of and toward a "cure" for cancer. Such progress is not to be measured in terms of what is accomplished from week to week, but in terms of what is accomplished over 10 and 20-year periods. The story of research and the untiring efforts of our scientists are told in a very fair and enlightening manner in the new documentary film, Challenge: Science Against Cancer. The federal government has done a valuable public service in having this film produced. The fact that it was made in Canada not only for our own government but also for that of the United States emphasizes that Canadian research workers are taking an important part in the international efforts to control one of the most baffling diseases which besets mankind.

The Canadian Cancer Society is giving its full support to this research by contributing $200,000 to the work of the National Cancer Institute each year. The remainder of the funds raised by the Society are spent on education and on welfare services to needy cancer patients. As a voluntary health agency the Canadian Cancer Society will continue to do its full share in the promotion of the health of our Canadian citizens.


---

*Health is that state of mind in which the body is not consciously present to us; the state in which work is easy and duty not too great a trial; the state in which it is a joy to see, to think, to feel, to be.*

**Andrew Clark**
MODERATION ON VACATION

This is the time of year when vacation folders, road maps, classified advertisements for cottages and cabins, suntan lotions, insect repellents and dark glasses come into prominence. Summer holiday thoughts are in the minds of all—the office worker, the laborer, the housewife, the children, the butcher, the baker and the candlestick maker. Some are already at the lake or in the hills, some are looking forward to a week or two away from it all during July and August, others prefer the cooler days of September. But nearly everyone is at least thinking about it.

No one wants to be a spoilsport and burden holidayers with a list of "don'ts". After all, it's probably healthier to suffer a dose of sunburn in a care-free manner than to remain physically well and worry away the time. But we are spoilsport enough to utter a word of caution: take it easy. Too many return from their holidays in need of rest instead of full of vim. The man or woman who sits behind a desk or a typewriter fifty weeks of the year can't expect to spend a high-speed vacation engaging in vigorous sports to which he or she is unaccustomed and emerge refreshed. It just isn't natural. If you're going to change your usual mode of living during those one, two or three weeks, go at it gradually.


A HALF CENTURY OF HEALTH PROGRESS

In looking back over the period 1900-1949 it must strike all of us that far too many of the newsworthy events of that unsettled era were scarcely indicative of progress. Some spheres of human activity, however, offer in retrospect a happy contrast to the general picture. One of the most notable of these spheres is that of health where advances have been plucked even from war and pestilence.

The past half century has seen incredible advances in medical science and in its application, in public health and in the acceptance and appreciation of public health measures, in health education and in the awareness on the part of each of us that health is a precious possession which, like democracy, is worth fighting for.

Recently Metropolitan Life's Dr. Louis I. Dublin stated that "the fine Canadian health record for 1949 is the fruit of many substantial advances in the fields of medicine, particularly developments in chemotherapy, in surgery and the effects of public health teaching. There is a substantial basis for optimism with regard to health conditions for 1950 and after."

Half a century of health progress has shown us that health is not merely the absence of disease or infirmity but a state of complete physical, mental and social well-being. It is up to all of us during the second half of the century to work toward the full realization of that ideal.