1940

UWOMJ Volume 10, No 2, 1940

Western University

The University of Western Ontario
MEDICAL JOURNAL
VOLUME 10 NUMBER 2

Recent Advances in the Aetiology and Management of Early Essential Hypertension*

By GEORGE K. WHARTON, M.B., M.S., F.A.C.P.
London, Ontario

THE selection of hypertension for this discussion was made first to review with you newer concepts in ætiology and treatment, secondly to advise you to discard some unnecessary restrictions and, lastly, to present to you some observations which I made on a few cases of high blood pressure who were placed under thyroid medication as they showed other evidences suggesting low metabolism.

By hypertension we simply mean elevation of the blood pressure above normal. This elevation may be either in the systolic, diastolic or in both blood pressures. The systolic blood pressure readings may be very labile and the author has seen a drop of over 60 mm. Hg. within 15 minutes in a young man. The diastolic blood pressure reading should be taken to the fifth phase where it is less variable and more significant. This diastolic pressure represents the resistance against which the heart works. We must remind ourselves continually that elevation of blood pressure is a sign worthy of appraisal and not a disease in itself; it is the individual's attempt to compensate for circulatory changes. Treatment must be directed toward the fundamental circulatory changes rather than the lowering of the blood pressure itself.

The two chief factors controlling the blood pressure are peripheral resistance and cardiac output. Less important factors are elasticity of the larger arteries, the viscosity of the blood and the total blood volume. Blood pressure in the normal individual might be considered as the product of cardiac output and peripheral resistance. The cardiac output depends on the venous return as well as on the force and the rate of the heart. The peripheral resistance results almost entirely from the tonus as well as the contractility of the arterioles. In older arteriosclerotic patients there is a marked decrease in the elasticity of the vessel walls, therefore systolic blood volume cannot be accommodated by the expan-

*Read before Noon-day Study Club, London, Ont., Nov. 29, 1939.

sion of the vessels themselves, and the result is an increased systolic pressure.

Of all of these factors influencing blood pressure, it is well to concentrate our attention on the peripheral resistance which influences, or one might say, causes hypertension. Again let me stress that high blood pressure is the individual's symptom of peripheral pathology and not the pathology. Sodeman[1] considers three possible controls of arteriolar tone, *viz.*, nervous control through vasomotor nerves; or local change, or hormonal type. Prinzmetal and Wilson[2] also Pickering[3] have shown that increased peripheral resistance was due to a general vascular hypertonus which was independent of the vasomotor nerves, and that these vessels continued to be capable of dilatation and receptive to the influences of the vasomotor nerves. Vasaspasm is often seen in the eye-grounds of hypertensive patients, especially in the malignant type and in eclampsia, and no doubt plays a considerable rôle in persistent hypertension. Other factors will be considered later.

The study of these hypertensive patients should be directed toward the estimation of the amount of arteriolar as well as arterial changes. The prognosis for these patients, as well as their treatment, depends largely upon the extent of these changes as well as the ætiological factors producing the blood pressure. Study of the eye-grounds for spasm or arteriolar changes is extremely valuable for these changes parallel those in the kidney and brain. Repeated blood pressure readings must be taken, however, to obtain a true basal pressure. MacKenzie's[4] comments on temporary and slight elevations in blood pressure are worthy of note. He says to disregard these variations "as merely the result of emotion, nervousness or excitement at the time of examination is to overlook the true import of the findings. Any rise in systolic pressure (over 15 mm. above the average for the age) should be looked upon as indicating a potential or actual case of hypertension." Besides these examinations detailed studies of the heart, kidney and brain should be made for evidences of damage.

Hines and Brown[5] have devised the technique of the cold pressor test for measuring the blood pressure response to a standard cold stimulus. They consider it a satisfactory index of vasomotor reactivity. They found that 98 per cent of known hypertensives gave an abnormal or excessive blood pressure reaction to the cold stimulus. They believe that the response is based on generalized vascular constriction produced by a neurogenic reflex. Miller and Banger[6] did not find positive results in such a high percentage. They, however, found the response to be negative in the chronic nephritics, and suggest that the test may be used as a point in the differential diagnosis between chronic nephritis with hypertension, and essential hypertension with kidney damage.

Hypertension is a disease of the Occident and may be attributed to our civilization. Negroes in Africa, according to Dennison[7] and Chinese

according to Cadbury,[8] rarely show this condition. Moreover, foreigners who live in China have lower blood pressures than when living in other parts of the world (Tung[9]). Weiss and Prusmack[10] in their study found that in the American negro hypertension occurred a decade earlier and more often than in a corresponding white group. Schulze and Schwab[11] found the incidence of hypertension in the American negroes to be two and one-half times greater than in whites of the same economic group. Hines[12] has shown the influence of heredity by his cold pressor test which was positive five times as often in relatives of hypertensives than in other groups. All hyperreactors had one parent an hypertensive or an hyperreactor.

Other headings under which we will consider the ætiology of hypertension are neuropsychiatry, endocrine disorders and renal pathology. The neurogenic group may be further subdivided into neuropathology and psychogenic disturbances. Heymans[13] and Bouckaert and Heymans[14] and others have produced permanent hypertension in animals following bilateral denervation of the carotid sinus with also the section of the aortic nerves. Weiss and Baker[15] found an increased carotid sinus reflex in 70-78 per cent of cases of hypertension. According to Nowak[16] chronic cerebral anæmia may result in chronic hypertension. Hypertension also occurs with increased intracranial pressure which Cushing[17] considers to be due to cerebral anæmia. Raab[18] has shown that increased intracranial pressure acts by producing acidosis of the vasomotor centre, while on the other hand perfusion of this centre with alkalies lowers the blood pressure. Williams and Harrison[19] report cases of diphtheria, poliomyelitis, and encephalitis associated with brain stem pathology which showed hypertension occurring with the onset of these diseases. The exact mechanism of its production is uncertain. Alam and Smirk[20] found that exercising ischæmic skeletal muscles caused a well-marked increase in blood pressure which set in before the pain occurred and also with obstruction to the venous return. This effect is probably of reflex nature. In cases of cardiac infarction, a lowered blood pressure may occur which persists. Williams and Harrison[19] report a case where increased blood pressure occurred with the onset of angina pectoris and disappeared following coronary thrombosis. The blood pressure cuff, if pumped too tightly or kept on too long, may produce a reflex elevation of blood pressure.

Psychic factors play an important rôle in essential hypertension. The early symptoms of hypertension are often psychoneurotic in nature and emotional stress often precipitates hypertension or accentuates an existing high blood pressure. Moschowitz[21] described an hypertensive personality as one who is dynamic, excessively meticulous, loyal and sympathetic, hypersensitive, quick in temper and movement. Ayman[22] describes hypertensives as showing increased psychomotor activity.

They are forceful, hyperactive individuals with large, steady energy output and are sensitive and quick-tempered. Williams and Harrison[19] report a case with severe symptoms—(blood pressure 300/200, a cerebral crisis and vascular retinitis) associated with mental stress who later, with mental stress eliminated, became symptom-free and carried only a moderate hypertension. Dunbar[23] and Wolfe[24] call attention to increased nervous tension with spasm of both voluntary and smooth muscles, which disappear as unconscious conflicts are brought into consciousness. Here is an opportunity for the physician to render a real service to the patient. This tension is a part of the patient's defense mechanism. The gastro-intestinal, as well as in genito-urinary tract, may also show increased tonus in hypertension cases.

Under the endocrine disorders a review of the evidence for the influence of the pituitary, adrenal, ovarian and thyroid glands on the blood pressure will be discussed. Cushing's syndrome, which is associated with basophilic hyperplasia of the pituitary gland, has hypertension as a prominent symptom. Associated with this, there may be involuntary muscular contractions and even convulsions which may indicate increased muscular irritability. The urine shows an excess of prolan from these basophilic cells often with an absence of œstrogen. No conclusive evidence has been brought forward yet to show that there is a direct relationship between basophilic hypersecretion and the hypertension. The pituitary effect may act indirectly through the adrenal glands.

Oppenheimer and Fishberg[25] collected thirteen cases of suprarenal tumors with hypertension. Charles Mayo[26] was the first to remove an adrenal tumor with cure of a paroxysmal hypertension. Binger and Craig[27] more recently discovered an adrenal tumor while doing a sympathectomy for hypertension. Besides this evidence for the association of adrenal pathology with hypertension, injection of adrenalin gives a temporary elevation of the blood pressure due to peripheral constriction by the adrenalin acting on the myoneural junction. Acidosis and calcium ions increase this response. Overactivity of the adrenal medullary cells as seen in pheochromocytomata is usually periodic and gives the paroxysmal hypertension. The presence of the adrenals is essential in the hypertension associated with renal ischæmia of the Goldblatt's type.[28]

Many authors have remarked on the onset of essential hypertension with the menopause. Alvarez and Zimmermann[29] have reported on the association of "poor ovaries" and hypertension. Culbertson[30] has described vasomotor disturbances associated with the menopause mentioning fluctuations in arterial tone. The causation of this elevation in blood pressure with the menopause may be due to greater emotional instability, pituitary hyperfunctioning or ovarian dysfunctioning. Hypertension in patients with other menopausal symptoms is not

affected by œstrin therapy even though the other symptoms have cleared up (McDonald[31]).

Just how thyroid dysfunction affects the blood pressure was discussed by Goodall and Rogers.[32] The effect, according to these investigators, was a primary hypertension due to vasoconstriction produced by an increased adrenalin output. The second stage was prolonged hypotension, the result of vasodilatation from thyroid excess. In the late stage hypertension was seen due to cardiovascular changes and reduced thyroid activity. Alvarez and Zimmermann[29] report 18 cases with hypothyroidism associated with high blood pressure. Hadovsky and Goormaghtigh[33] report experimental arteriosclerosis with hypertension after thyroidectomy and feeding vitamin D. High systolic blood pressures are commonly seen in hyperthyroid patients as well.

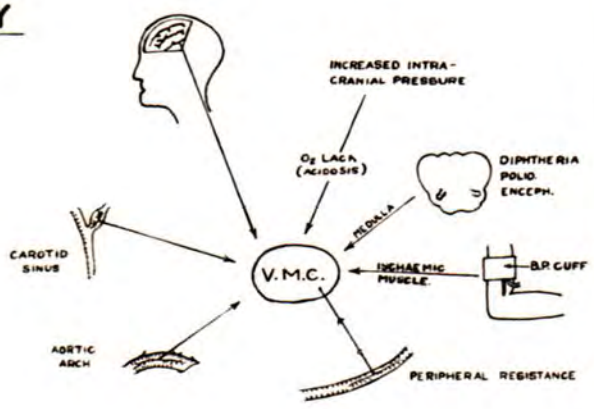
The kidney has long been accused of causing hypertension. Recently much light has been thrown on this relationship by Goldblatt and his co-workers,[34] who have shown that any pathological change which produces renal ischæmia increases the blood pressure. They have shown that an intact adrenal cortex is necessary for the maintenance of hypertension in these cases. Removal of the pituitary gland before the placing of Goldblatt's clamp prevents the development of the increased blood pressure. Katz *et al*[35] have shown that renal hypertension is produced whenever the ratio of ischæmic kidney substance to normally functioning kidney substance exceeds a certain value. Urinary obstruction, infection, circulatory disturbances such as renal arteriosclerosis or arteriolar sclerosis, or tumors, as well as chronic nephritis, may give rise to elevations in blood pressure. All except nephritis, and even this, may act by reducing circulation to the kidney. In the early stages arteriolar sclerosis is probably the result of hypertension, but in itself may further increase the blood pressure so that a vicious circle is set up. These types of renal pathology must be considered even if only to be ruled out in the diagnosis of essential hypertension.

From the discussion so far, it has become evident that many factors must be considered in the management of early hypertension. Certain of these factors such as heredity and brain damage cannot be changed, while others in the environment and personality can be modified and improved. Also, it is apparent that the more arteriolar sclerotic changes that have taken place, the less help we can give.

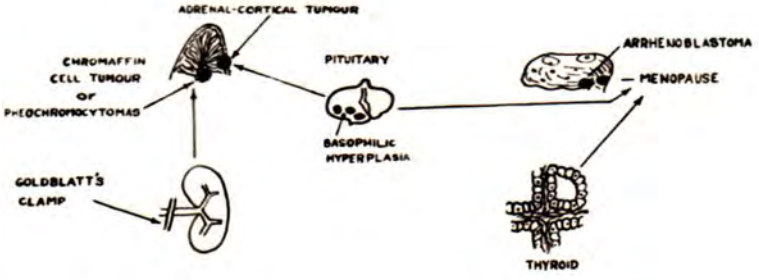
Patients are frequently worried about strokes, heart trouble, and kidney disease when they are told that they have high blood pressure. These patients are usually intelligent. We must consider our patients physically and psychologically and not be satisfied with a mere recording of the blood pressure. Our aim should be to reassure them about their general health and the blood pressure changes should not be discussed more than necessary and then always optimistically. A complete exami-

ETIOLOGY of HYPERTENSION

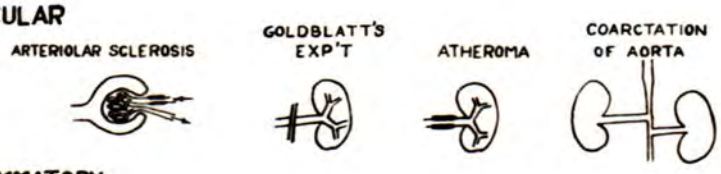
1. **HEREDITY**
2. **ENVIRONMENT**
3. **NEUROPSYCHIATRY**
   - a PSYCHOGENIC
   - b NEUROGENIC



4. **ENDOCRINE**



5. **RENAL**
   - a. VASCULAR



   - b. INFLAMMATORY
     - i.  PYELONEPHRITIS — $\bar{C}$ OR $\bar{S}$ STONES
     - ii. GLOMERULONEPHRITIS
     - iii. CHRONIC KIDNEY DAMAGE

nation reassures the patient that you know his condition and shows him that your opinion is not based on blood pressure readings alone.

An emotional state is often the precipitating cause of the patient's visit to the physician and the blood pressure readings consequently may be exaggerated. Negative replies to the common question, "Are you worried," mean little since the patient may not himself be conscious of a conflict and often projects his worries into hypochrondrical questions. To advise this patient not to worry is not only inadequate but futile. Let us first find out what is disturbing him, and help him to reorganize his life in a way that will give him hope. If we allow the patient to talk about himself as an individual rather than about his symptoms we will do much to find the solution of his problem. Ordering the patient to bed without the above preparation of confidence not only in you but also in his own future is dangerous. Otherwise we may only give him more time to think and magnify his problems. Bed does not necessarily mean rest and may even be detrimental. In your aim to bring about his relaxation, give him time to adjust his philosophy as well as his tempo of living. Rest periods at the same time each day and hobbies will do much to help even the severe hypertensive cases.

Weiss[36] ridicules some forms of treatment: "What," he says, "has been done in an effort to reduce the blood pressure? Because of an ill-founded idea that protein was responsible for hypertension and kidney disease, the patient was denied meat and eggs, and especially red meat, which for some reason was looked upon with particular dread. His diet was rendered even more unpalatable by the withdrawal of salt. Sympathy would doubtless have been extended to this half-starved fellow except that he probably was not able to eat anyway, his teeth having been extracted on the theory that focal infection had something to do with hypertension. Even before this he had sacrificed his tonsils and had had his sinuses punctured because of the same theory. In case some food had been consumed, the slight colonic residue was promptly washed out by numerous colonic irrigations, especially during the period when the theory of auto-intoxication was enjoying a wave of popularity. To add to his unhappiness, he was often told to stop work and exercise. Of course, he was denied alcohol and tobacco as well as coffee and tea, and as a climax to the difficulties of this unfortunate person, he may now fall into the clutches of the neurosurgeon, who is prepared to separate him from his sympathetic nervous system."

Barborka[37] in his recent book outlines three simple rules to follow in the diet: The patient should have adequate calories to maintain normal weight, adequate protein which is one gram per kilogram of body weight per day, and no excess of salt or any condiments. For severe forms of hypertension with renal or cardiac failure, more restrictions may be necessary.

No panacea for high blood pressure has been discovered. The treatment is largely symptomatic. Sedatives, especially the longer acting ones such as phenobarbital, are valuable. These sedatives should be spread out so that they will help the patient to relax, not given in massive doses at bedtime only. When these drugs are given frequently in small doses, the total amount per day will be less than required in massive doses.

Sodium or potassium thiocyanate has been used intermittently for many years. It produces toxic manifestations early in some cases and may even cause death. Griffith and Lindauer[38] report twenty-six cases of which only sixteen were properly handled and only ten showed good results. In these latter there was lowering of systolic and diastolic pressures as well as subjective improvement. Barker[39] found the optimal blood level of this thiocyanate was 6-12 mgm. per 100 cc. of blood; toxic symptoms began around 15 mgm. per 100 cc. of blood, and fatalities were known when the level rose to 40 mgm. per 100 cc. of blood. The general impression is that the use of this drug is dangerous unless followed with blood estimations of thiocyanate.

Evans and Loughnan[40] investigated thirty-three drugs which were on the market for lowering blood pressure. Of this group they found only six giving better results than a placebo. These drugs were as follows: bismuth subnitrate, iodine, iodide, sodium luminal, theominal, and potassium thiocyanate. Weiss[41] also questions the value of bismuth subnitrate.

Many surgical procedures have been suggested for hypertension. Three types of operation have been advocated: rhizotomy, adrenalectomy and sympathectomy. The mayo Clinic group[42, 43, 44] have done the first type with complete denervation of the splanchnic area believing that thereby they have dilated the splanchnic vessels, decreased the liberation of adrenalin and increased the renal blood supply. This procedure was done on a very select group of cases with enough favourable results to encourage them to carry along. Crile[45] has reported large series of cœliac ganglionectomies. He believes that the cœliac ganglion is enlarged in hypertensives and is the primary cause of high blood pressure. He says that 81 per cent of his series have returned to their former occupations with relief of cardiac pain and heart consciousness. Adrenalectomies have been done largely by the French surgeons without good results. Surgical removal of an unilateral diseased kidney often gives exceptional results. The real value of these surgical procedures cannot at the present be evaluated. Further work and longer periods of observation of these cases will alone answer the problem.

Diathermy and deep X-ray therapy over the carotid sinus have been tried on the continent with some good results (H. M. Thomas[46]).

Endocrine therapy has received very little attention in the medical literature. Albright[47] found no change in blood pressure levels when œstrin was given to hypertensive menopausal patients. In a previous paper the author has reported two cases of hypertension treated with thyroid therapy.[48] I wish to consider here five cases with their response to thyroid extract. The first case was diagnosed hypothyroidism without the typical myxœdematous changes. The blood pressure was within the normal range, being 118/68 mm. but with a relatively high diastolic pressure. After three weeks' treatment with thyroid extract, which gave relief of all of her symptoms, the blood pressure was 96/48 mm. Two other cases, one female age 42 and one male age 36, showed blood pressures of 152/116 and 154/104 mm., respectively. These readings were reduced with thyroid therapy to 142/86 and 142/84 mm. They discontinued the treatment and the blood pressures increased to their previous levels. In the former, the blood pressure again responded to thyroid medication; the latter was not treated further. Two other cases have been observed over much longer periods of time, two and one years, respectively, with pressures dropping from 160/114 and 186/120 to 124/72 and 136/84 mm., respectively, on thyroid therapy. Details of these cases are being held for a part of future publication elsewhere. All of these cases showed some evidence suggesting hypothyroidism, but their hypertension was a prominent finding. These results suggest a greater response of the diastolic pressure to this form of therapy than of the systolic pressure. No attempt to explain this response can be made at this time. This form of treatment has certainly a limited use. Probably with further study of a longer series of hypertensive patients, it will be possible to recognize an endocrine sub-group and remove it from the undifferentiated group of essential hypertension. However, this offers an interesting field for further clinical research.

SUMMARY

I have attempted to review the literature of the ætiology and treatment of hypertension. The results are not satisfying in that, even though many views are advanced, all are incomplete. Drastic restrictions in diet and activity are less valuable than we formerly thought. The patient's co-operative understanding of his own problem, with judicious use of sedatives, offers the best help we know. An attempt has been made to differentiate hypertensives on an ætiological basis. The term "essential" covers a cosmopolitan group which with increasing knowledge no doubt will be subdivided. The author suggests that one sub-group may be considered primarily an endocrine problem. Goldblatt has shown that another group is the result of renal ischæmia. Further observations are necessary before the use of endocrine products and surgical procedures may be generally applicable.

BIBLIOGRAPHY

[1]Sodeman, W. A.: Recent Concepts in the Pathogenesis of Diastolic Hypertension; Am. J. Med. Sc., 195:115; 1938.

[2]Printzmetal, M., and Wilson, C.: The Nature of Peripheral Resistance in Arterial Hypertension with Special Reference to the Vasomotor System; J. Clin. Invest., 15:63; 1936.

[3]Pickering, G. W.: The Peripheral Resistance in Persistent Hypertension; Clin. Sci., 209; 1935-36.

[4]Mackenzie, L. F., and Shepherd, P.: The Significance of Past Hypertension in Applicants Later Presenting Normal Average Blood Pressures; Assoc. of Life Ins. Directors of America, xxiv, 157; 1937.

[5]Hines, E. A., and Brown, G. E.: The Cold Pressor Test for Measuring the Reactibility of the Blood Pressure. Data concerning 571 normal and hypertensive subjects; Amer. Heart J., 11:1; 1936.

[6]Miller, J. H., and Banger, M.: The Cold Pressor Reaction in Normal Subjects and in Patients with Primary (Essential) and Secondary (Renal) Hypertension; Amer. Heart J., 18:329; 1939.

[7]Dennison, C. P.: Blood Pressure in Africa: Its Bearing Upon Ætiology of Hyperpiesis and Arteriosclerosis; Lancet, 216:6-7; 1929.

[8]Cadbury, W. W.: The Blood Pressure in Normal Cantonese Students; Arch. Int. Med. 30:362-377; 1922.

[9]Tung, quoted by Fishberg: Hypertension and Nephritis, 3rd Ed.; Lea Febiger, Philadelphia, 1934.

[10]Weiss, M. M., and Prusmack, J. J.: Essential Hypertension in the Negro; Amer. Jour. Med. Sc., Vol. 195:510-516; 1933.

[11]Schulze, V. E., and Schwab, E. H.: Arteriolar Hypertension in American Negro; Amer. Heart J., 11:66-77; 1936.

[12]Hines, E. A., Jr.: Hereditary Factor in Essential Hypertension; Ann. Int. Med., 11:593; 1937.

[13]Heymans, C.: Pressor Captive Mechanisms for Regulation of Heart Rate, Vasomotor Tone, Blood Pressure, and Blood Supply; New Eng. J. Med., 219-147; 1938.

[14]Bouckaert, J. J., and Heymans, C.: Carotid Sinus Reflexes: Influence of Central Blood Pressure and Blood Supply on Respiratory and Vasomotor Centres; J. Physiol., 79:49; 1933.

[15]Weiss, S., and Baker, J. P.: The Carotid Sinus Reflex in Health and Disease; Medicine, 12:297; 1938.

[16]Nowak, S. J. G., and Walker, I. J.: Experimental Studies Concerning the Nature of Hypertension; New Eng. J. Med., 220:269; 1939.

[17]Cushing, quoted by Nowak and Walker.

[18]Raab, W.: Central Vasomotor Irritability: Contribution to the Problems of Essential Hypertension; Arch. Int. Med., 47:727; 1931.

[19]Williams, J. R., and Harrison, T. R.: Clinical Pictures Associated with Increased Blood Pressure: A Study of 100 Patients; Ann. Int. Med., 13:650; 1939.

[20]Alam, M., and Smirk, F. H.: Observations in Man Upon Blood Pressure Raising Reflex Arising from Voluntary Muscles; J. Physiol., 89:372; 1937.

[21]Moschcowitz, E.: Cause of Hypertension of the Greater Circulation; J.A.M.A., 93:347; 1929.

[22]Ayman: The Early Diagnosis and Early Treatment of Arteriolar (Essential) Hypertension; New Eng. J. Med., 205:424; 1931.

[23]Dunbar, H. F.: Psychic Factors in Cardiovascular Disease; N.Y. State J. Med., 36:423; 1935.

[24]Wolfe, T. P.: Emotions and Organic Heart Disease; Am. J. Psych., 93:681; 1936.

[25]Oppenheimer, B. S., and Fishberg, A. M.: Association of Hypertension with Suprarenal Tumors; Arch. Int. Med., 34:623; 1924.

[26]Mayo, C. H.: Paroxysmal Hypertension with Tumors of Retroperitoneal Nerve: Report of a Case; J.A.M.A., 89:1047; 1927.

[27]Binger, M. W., and Craig, W. M.: A Typical Case of Hypertension with Tumor and Adrenal Gland; Proc. Staff Meet. Mayo Clinic, 13:17; 1938.

[28]Blalock, A., and Levy, S. E.: Studies on the Ætiology of Renal Hypertension; Ann. Surg., 105:826; 1937.

[29]Alvarez and Zimmerman: Blood Pressure in Women as Influenced by Their Sexual Organs; Arch. Int. Med., 37:597; 1926.

[30]Culbertson, C.: A Study of the Menopause with Special Reference to Its Vasomotor Disturbances; S.G.O., 23:667; 1916.

[31]McDonald: The Endocrine Aspects of Hypertension; Cleveland Clin. Quart., 6:63; 1939.
[32]Goodall, J. S., and Rogers, L.: Blood Pressure in Grave's Disease; Brit. Med. J., 2:588; 1920.
[33]Hadovsky and Goormaghtigh, quoted by Nowak and Walker.
[34]Goldblatt, H.: Studies on Experimental Hypertension: The Pathogenesis of Experimental Hypertension Due to Renal Ischæmia; Ann. Int. Med., 11:69; 1937.
[35]Katz, L. N.; Friedman, M.; Rodbard, S., and Weinstein, W.: Observations on the Genesis of Renal Hypertension; Amer. Heart J., 17:334; 1939.
[36]Weiss, E.: Recent Advances in the Pathogenesis and Treatment of Hypertension; Psychosomatic Med., 1:180; 1939.
[37]Barborka, C.: Treatment by Diet, 4th Edition, Lippincott; 1939.
[38]Griffith, J. Q. J. W., and Lindauer, R.: Theocyanate Therapy in Hypertension, Including a New Micromethod for Determining Blood Theocyanates; Amer. Heart J., 14:710; 1937.
[39]Barker, quoted by Griffith and Lindauer.
[40]Evans, W., and Loughnan, O.: The Drug Treatment of Hyperpiesia; Br. Heart J., 1:199; 1939.
[41]Weiss, S.: Recent Advances in Treatment of Arterial Hypertension; Med. Cl. North Amer., 1343; 1936.
[42]Adson, A. W.; Craig, Wm., and Brown, G. E.: Surgery in Its Relation to Hypertension; S.G.O., 62:314; 1936.
[43]Allen, E. V., and Adson, A. W.: Physiological Effects of Extensive Sympathectomy for Essential Hypertension; Amer. Heart J., 14:415; 1937.
[44]Craig, W. M.: Essential Hypertension: The Selection of Cases and Results Obtained by Subdraphragmatic Extensive Sympathectomy; Surgery, 4:502; 1938.
[45]Crile, G.: Two Years' Results of Treatment of Essential Hypertension by Celiac Ganglionectomy; Cleveland Clin. Quart., 6:49; 1939.
[46]Thomas, H. M.: Management of Early Essential Hypertension; Med. Cl. North America, 23:487; 1939.
[47]Albright, quoted by S. Weiss.
[48]Wharton, G. K.: Unrecognized Hypothyroidism; Can. Med. Ass. J., 40:371-376; 1939.

THE PSYCHOLOGICAL ASPECTS OF COD LIVER OIL ADMINISTRATION

Some authorities recommend that cod liver oil be given in the morning and at bedtime when the stomach is empty, while others prefer to give it after meals in order not to retard gastric secretion. If the mother will place the very young baby on her lap and hold the child's mouth open by gently pressing the cheeks together between her thumb and fingers while she administers the oil, all of it will be taken. The infant soon becomes accustomed to taking the oil without having its mouth held open. It is most important that the mother administer the oil in a matter-of-fact manner, without apology or expression of sympathy.

If given cold, cod liver oil has little taste, for the cold tends to paralyze momentarily the gustatory nerves. As any "taste" is largely a metallic one from the silver or silver-plated spoon (particularly if the plating is worn), a glass spoon has an advantage.

On account of its higher potency in Vitamins A and D, Mead's Cod Liver Oil Fortified with Percomorph Liver Oil may be given in one-third the ordinary cod liver oil dosage, and is particularly desirable in cases of fat intolerance.

Sciatica from Protruded Intervertebral Discs

By CHARLES A. CLINE, M.D.
London, Ontario

SCIATICA may be defined as a symptom, characterized by the complaint of pain in the posterior thigh and postero-lateral calf. It is presumably peripheral pain in the regions supplied by the sciatic nerve or of any of the roots of the lumbo-sacral plexus which form the nerve. The actual pathological change present in many, if not most, of the clinical cases of sciatica is unknown, and accordingly, as is seen in all conditions in which the ætiology and pathology are obscure, there is a multiplicity of curative methods. In a small group of cases, however, comprising perhaps 5 to 10 per cent or more of all the cases of sciatica, we have come to recognize a clear-cut syndrome in which the sciatic pain is due to the pressure of intervertebral disc tissue displaced posteriorly against one or more roots of the cauda equina.

ANATOMY

A normal intervertebral disc is composed of a semi-fluid gelatinous central nucleus pulposus which is encircled by a ring of dense coarse fibrous tissue, the annulus fibrosis. The annulus is intimately attached to the cartilaginous end-plates of the vertebrae immediately above and below each disc, and also blends with the strong anterior and posterior longitudinal vertebral ligaments. Each intervertebral disc has a certain internal pressure which prevents its collapse when the superincumbent weight is placed upon it. The total amount of spinal mobility is the summation of the mobility of each of the intervertebral discs. The function of the disc is to permit mobility of the spine, to cushion the central nervous system from trauma, and to transmit the body weight from one vertebra to another. Schmorl has made exhaustive studies of the pathological changes which occur in intervertebral discs. Extrusion of the nucleus pulposus may occur in any direction, following weakening of its surrounding tissues by developmental defect, disease or trauma. If the cartilaginous end-plate is weakened, protrusion may occur into the vertebral body, but these lesions rarely cause radiating pain. If the annulus fibrosis is weakened by disease or trauma, peripheral protrusion of intervertebral disc tissue may occur, sometimes slowly as a developing hernia, sometimes rapidly as a traumatic rupture. Schmorl found that small posterior protrusions into the spinal canal occurred in about 15 per cent of spines examined at necropsy, but felt that they were of no particular clinical significance. The earliest mention of extrusion of cartilage from an intervertebral disc was made by Virchow in 1857.

In 1911 Goldthwaite first directed attention to the possible importance of the condition in producing compression of the spinal nerve roots within the spinal canal. In the same year, Middleton and Teacher reported a case in which they attributed the patient's symptoms to protrusion of such an intervertebral disc. Adson in 1925, Stookey in 1928 and Dandy in 1929 all have reported cases in which they have removed intervertebral disc tissue which had been compressing the spinal cord. In 1936, Hampton and Robinson introduced the injection of lipiodol into the spinal canal in order to demonstrate roentgenographically intervertebral disc protrusions. This diagnostic procedure revolutionized the study of sciatica, and since that time many workers have reported hundreds of cases in which the diagnosis has been established and proved by subsequent operation. Love and Walsh state: "It may safely be said that, today, protrusion of intervertebral discs constitutes one of the major causes of sciatic pain. Indeed, it is quite as antiquated to make a diagnosis of 'sciatica' today as it is to make a diagnosis of 'headache'."

ÆTIOLOGY

It is the opinion of most authors that abnormal protrusion of an intervertebral disc into the spinal canal is in the majority of cases the result of trauma. It is probable that repeated trauma may be necessary in many cases to produce sufficient protrusion to cause the symptoms. In only about one-half of the cases, however, does the patient feel that the symptoms began immediately after the injury. About one-third of the cases give a history of injury within a few months of the onset of symptoms, while less than one-third recall no injury which may have produced the symptoms. The condition is three times more common in males, probably due to the increased liability to injury. It is interesting to observe that protrusions of intervertebral discs tend to group themselves in relation to the normal curves of the vertebral column in the region of the greatest convexity or concavity, particularly in the lower lumbar region, where about 90 per cent of protrusions occur. It is, of course, in this region that the greatest mechanical stress is placed on the vertebral column in heavy lifting or pushing. The condition occurs chiefly from 20 years to 60 years of age, most commonly in the fourth decade, with an average age of about 40 years.

SYMPTOMS AND SIGNS

The symptoms and signs of a ruptured lumbar intervertebral disc are so constant and characteristic that the presumptive diagnosis can often be made before radiographic and injection studies are carried out. As described by Barr: "The typical case is a vigorous man in his thirties who was perfectly well until, while lifting a heavy weight, he felt something snap in his lower back, and had immediate pain in his lumbosacral region. Some time thereafter he developed 'sciatica' in one leg,

which he describes as a deep-seated pain beginning in the buttock, radiating down the posterior thigh, the postero-lateral aspect of the calf, and occasionally going into the lateral border of the foot. Coughing and sneezing, bending forward to tie the shoes, and lying face down in bed cause marked increase in the radiating pain. There may have been two or three separate periods of disability, the first ones relieved by rest in bed; the last one, however, has yielded to no conservative measures, including back-strapping, heat, bed-rest, plaster casts and osteopathic manipulation. On examination the patient is found to stand with his trunk thrust forward and to one side, with most of his weight borne on the non-painful leg—'sciatic scoliosis.' The normal lumbar lordosis has been lost, and in its place is a fixed reversal of the lumbar curve, with prominence of the spinous processes of the third, fourth and fifth lumbar vertebrae. All motions of the lumbar spine are constantly restricted by fixed involuntary muscle spasm."

On further examination there is often some atrophy of the buttock, thigh and calf on the painful side, and extension of the lower leg with the thigh flexed on the abdomen shows pain and limitation of movement (Lasègue's sign). The ankle-jerk on the affected side is usually absent, while the other reflexes are normal. There may or may not be any sensory or motor change but, if present, it is usually most noticeable in the distribution of the common peroneal nerve. The intermittency of the symptoms of protruded intervertebral discs (86 per cent of cases of lumbar protrusion) suggests that the protruded material may return more or less completely to its normal position, either spontaneously or as the result of manipulation. This has actually been demonstrated by Schachtschneider and by Love and Walsh, and on kyphotic flexion the disc material is seen to draw in almost level with the posterior surface of the vertebral bodies. In these cases the possibility of transitory cure of symptoms by the manipulations of irregular practitioners undoubtedly explains some of the dramatic recoveries which have been reported.

DIAGNOSIS

(1) *Examination of the Spinal Fluid.* A spinal puncture is performed at the lowest intervertebral space possible, and a sample of the fluid is tested for the total protein content. A value higher than 40 mg. per 100 cc. of spinal fluid strongly suggests the presence of a protruded disc, although a value lower than 40 mg. does not exclude the possibility of protruded disc. This increased protein is, of course, only found below the level of the lesion, and is the result of interference with the normal circulation of spinal fluid in this region. In the case of disc protrusion in the lowest part of the lumbar spine, it may be impossible to obtain spinal fluid below the lesion, and protein studies will therefore be useless. Manometric studies are usually attempted at the same time, and any evidence of dynamic block (lack of increase of spinal fluid pressure

on jugular compression) will be very suggestive of protruded intervertebral disc. The presence of increased protein content in the spinal fluid below the lesion, or any evidence of dynamic block warrants the use of lipiodol visualization to confirm the diagnosis.

(2) *Lipiodol Visualization.* The radiological examination after the injection of iodized oil is the most important step in the diagnosis. The lesion can be accurately localized and readily demonstrated on the radiograph. Barr reports that he has observed no permanent ill effects, in a series of over 150 cases, which could be attributed to the use of iodized oil in the spinal subarachnoid space. He specifies, however, that the oil should show no signs of deterioration and should be of a very light colour.

Technique: 5 cc. of iodized poppy-seed oil is injected into the lumbar subarachnoid space. After waiting for from two or three hours to a day or more, in order to allow the oil to fill the root sheaths, the radiological study is begun. Fluoroscopic visualization is performed on a tilt-table equipped with a Bucky diaphragm (in order to take detailed radiographs), which is manipulated to cause the oil to flow slowly up and down the anterior aspect of the subarachnoid space. The patient lies face down on the table and particular attention is directed towards maintaining the iodized oil in a single mass. If a filling defect is observed, repeated efforts are made to obliterate it, either by turning the patient from side to side, or by repeating the tilting process. A constant filling defect in any region is recorded by serial radiographs taken at various angles of rotation of the patient. Posterior protrusions usually produce a rounded filling defect one cm. or more in diameter, lying just lateral to the strong central portion of the posterior longitudinal ligament.

TREATMENT

After a thorough trial of conservative methods has failed, the logical treatment is laminectomy and removal of the protruding portion of the ruptured disc. This must be performed by a competent neurosurgeon, and the end-results are excellent. The pain is invariably relieved immediately and very few recurrences have been reported. The patients may be sent home within three weeks, under ordinary circumstances.

REPORT OF A CASE

D. C., a man, white, labourer, aged 57, was admitted to the Victoria Hospital, London, Ont., on March 30, 1939, with the following history: In September, 1937, while hauling tobacco leaves, he was seized with a sharp, stinging pain, localized to an area the size of a hand, in his right calf. This pain was very severe for a while, but after working the leg a bit he was able to finish his afternoon's work. There was no definite

relation of onset to injury. The next day the leg dragged to some extent, but the patient worked all day. Toward evening he was able to walk only with extreme difficulty. The next day he was unable to stand on the leg on account of severe pain. For the next six months he was treated by various doctors with no lasting relief; one year ago he attended the O. P. D. of Victoria Hospital and has since received regular physiotherapy, consisting of baking massage and electrical stimulation with some relief in pain and slight return of motor power.

Previous History: The patient had an attack of "sciatica" in his right leg 20 or 25 years previously which he attributed to a wetting; five years ago he had a similar attack. Both attacks cleared up in two or three weeks.

Examination: Reveals a marked atrophy of the muscles supplied by the right common peroneal nerve, with marked weakness of extension of foot and toes, of eversion and abduction of the foot, and some weakness of plantar flexion; the right ankle-jerk is absent; there is an area

Plate No. 1

of diminished sensation over the postero-lateral surface of the right lower leg and over the lateral part of the dorsum of the right foot. There is no tenderness over the sciatic nerve. There is a definite scoliosis of the spine with some leaning towards the good leg; there is no flattening of the lumbar curve, however, and little impairment of movement in this region. Radiographic examination showed a narrowing of the space between the fourth and fifth lumbar vertebrae on the right side, with tilting of the fourth lumbar vertebra.

On April 20, 1939, Dr. Norman Roome injected lipiodol into the lumbar subarachnoid space and radiographic examination revealed a persistent filling defect at the level of the intervertebral disc between the fourth and fifth lumbar vertebrae. A re-check several days later showed the same defect. (See Plates I and II.)

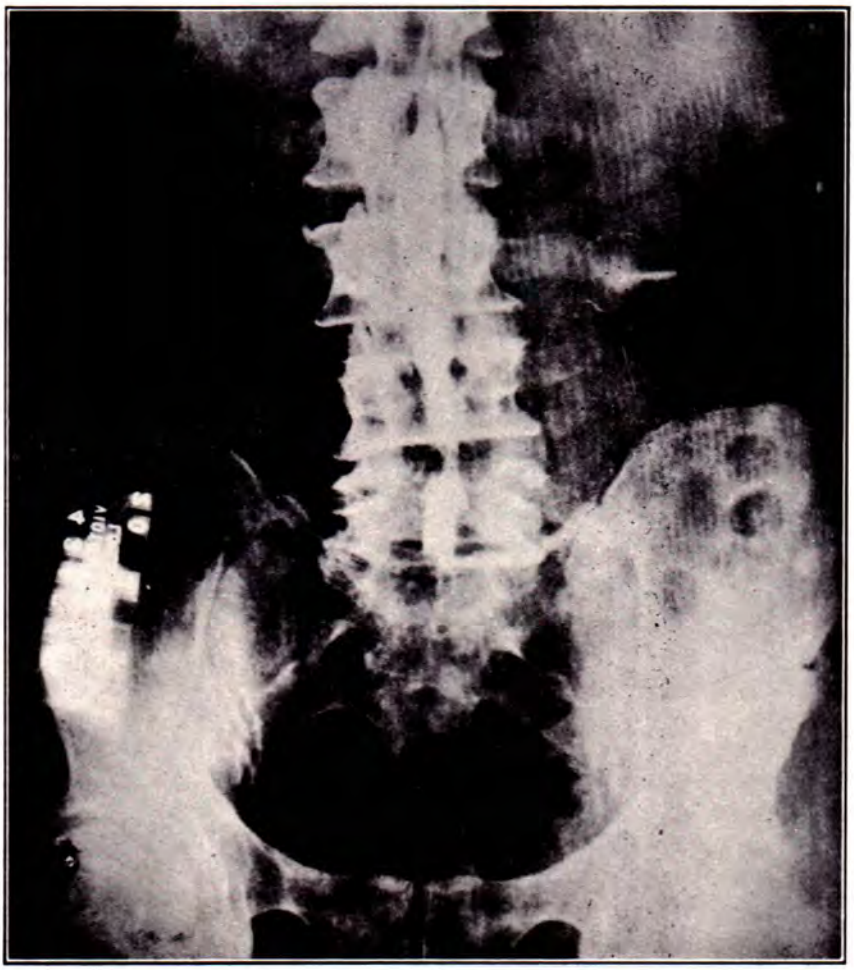


Plate No. 2

Subsequent Course: The patient refused operative interference because he had no particular desire to be able to work and the disability furnished a not too disagreeable handicap which enables him to continue on relief. He has received more or less constant physiotherapy with no change whatever in the physical findings, although he claims transitory improvement (increase in strength and sensation) occurs at times, to be followed by periods of relapse. Until the present time there have been no signs of untoward reaction from the lipiodol which presumably is still present in the subarachnoid space.

SUMMARY

A case is presented in which the symptoms and signs of "sciatica" are believed to be the result of protrusion of an intervertebral disc; unfortunately this diagnosis has not been corroborated by operation. Two other cases have occurred in this vicinity within the past few months, one of which was checked by operation. It is believed that this condition will be found to be a not uncommon cause for "sciatica" but, until further study sheds more light on the condition, a large group of cases remain which must, for a time, be placed in the "idiopathic" category.

Heparin—Its Applications*

By J. M. JANES

HISTORICAL: Attention was called first to heparin by Jay McLean in 1916, while working in Howell's laboratory. Howell prepared the substance from dog liver, found that it prevented coagulation and that it was probably a normal physiological substance. Charles and Scott, at the Connaught Laboratories, undertook extensive work on heparin and in 1933 they were able to secure it in a pure form on a commercial basis. In 1936, they isolated the active substance as a crystalline barium salt. D. W. G. Murray, through experiment plus clinical investigation and application, has made it a therapeutic agent of proven worth.

THEORETICAL: Howell and Holt stated that heparin could be designated as an antiprothrombin since they believed that it inhibited clotting by preventing the activation of prothrombin. It is now thought that there is a material in plasma and serum which by a reaction with heparin is converted or gives rise to antithrombin. This factor is non-dialyzable, destroyed by heating to 60° C. and found in the albumin fraction of the plasma. This is substantiated by Mellanby's work, which indicates that heparin does not prevent the conversion of prothrombin to thrombin but that it inactivates the latter after it has been formed. According to this worker, then, heparin is an antithrombin rather than an antiprothrombin.

The work of Murray, Jacques, Perrett and Best, and of Best, Cowan and MacLean has shown that heparin effects thrombus formation, lending support to one of Howell's beliefs that heparin increases the stability of the platelets in addition to its antiprothrombic function. The most recent research of Best and Solandt indicates that the effect of heparin on platelet agglutination lags behind the effect on blood clotting time.

NATURE: Heparin can be extracted from all the vascular tissues, although, for commercial purposes, it is at present being obtained from beef lung. It has been suggested that Ehrlich's mast cells are the site of its production. From a chemical point of view heparin is very similar in structure to chondroitin sulphuric acid. The empirical formula may be written $C_{25}H_{65}O_{50}N_2S_5$, in which the sulphur appears to be present in the form of SO_3H. Jorpes has pointed out that heparin is the strongest naturally occurring organic acid known, and as a result forms salts readily, *e.g.*, with the basic proteins such as the protamines. The latter will then precipitate heparin both *in vivo* and *in vitro*.

ACTION: The chief effect of the intravenous administration of heparin is to increase the clotting time. A definite concentration of

*Research Assistant in the Department of Medical Research, Banting Institute, University of Toronto.

heparin in the blood is necessary to increase the clotting time beyond 10 minutes; while an additional small increase in the concentration produces a tremendous further increase in the clotting time. The rapidity with which injected heparin is destroyed while circulating in the blood makes it necessary to administer it by means of a continuous intravenous drip (technique described below). It has been found that in patients whose clotting time has been raised to 20 minutes by the use of heparin the effect has completely disappeared in an hour following the cessation of the administration. At this time there are no demonstrable changes in the physical or chemical characteristics of the blood. Although heparin is effective in preventing the formation of clots, it has been shown fairly conclusively, both from clinical and experimental evidence, that it will not dissolve a clot already formed. Its value is in preventing further thrombus formation, at the same time allowing for organization of the thrombus and growth of new endothelium.

CLINICAL USES

Heparin finds one of its chief uses in the field of vascular surgery. Following embolectomy, D. W. G. Murray has used it to prevent further thrombus formation. In the repair of arterio-venous aneurysms and in the restoration of the continuity of blood-vessels following their accidental or intentional severance, its use has been attended with gratifying results. No elaborate technique, such as was advocated formerly, is necessary as long as 800 units of heparin are given intravenously before the blood stream is allowed to traverse the restored pathway, and that a continuous intravenous drip of heparin in normal saline or distilled water is begun as soon as possible following the operation. The administration of heparin is continued in this manner for from five to ten days. If hemostasis has been properly secured, there need be no fear of post-operative hæmatoma.

Heparin has a very important use in cases of pulmonary embolism. In the experience of D. W. G. Murray, no recurrences have occurred in cases which have been treated following the initial embolus or emboli. Heparin can be used also in a prophylactic way in cases which, statistically, show a high incidence of embolism, *e.g.*, following nephrectomy for a hydronephrotic kidney with a dilated renal vein. It is well to remember that factors, other than blood-clotting, must be taken into consideration in cases of thrombosis and embolism, *i.e.*, trauma, venous stasis and dehydration. Measures which will counteract these are indicated. A low protein diet is also of value.

Some of the best results from the use of heparin are seen in patients suffering from thrombophlebitis. The more acute the condition, the more dramatic is the usual outcome. The sequence of events is as follows: disappearance of pain often in the first twenty-four hours, disappearance of redness, gradual reduction of the swelling and gradual

disappearance of tenderness on palpatation over the vein involved. Ten days' treatment is usually advocated, although in recent cases five days have been found to be sufficient. Movement of the extremity is encouraged toward the end of the course.

Heparin may be used in blood transfusion. It may be used *in vitro* or the donor may be heparinized and the transfusion done directly. In the clinical laboratory, too, it has many uses. It has none of the disadvantages of oxalate and citrate. It can be recommended for use in the determination of plasma lipids, phospholipids, cholesterol and blood calcium. It is of value in diluting fluids for cell counts (especially for platelet counts).

Possible Clinical Uses: Since the destructive bone lesions in osteomyelitis are thought to have an infective thrombotic basis, the use of heparin, together with a chemotherapeutic agent, in this disease has been suggested. At the present time, this combination is being used in the treatment of cases of subacute bacterial endocarditis. To prevent clotting in this disease is to prevent the formation of a nidus for the organisms and thus render them susceptible to attack by such drugs as sulphapyridine and sulphanilamide. The use of heparin has been suggested in coronary thrombosis, cerebrovascular thrombosis and lateral and cavernous sinus thrombosis. We are at the present time treating successfully a case of thrombosis of the central vein of the retina.

EXPERIMENTAL USES

Heparin has uses in the experimental laboratory, especially in cross-circulation work. Jacques has recommended 35 units /kg./ hr. with an initial injection of 35 units /kg. as a satisfactory method for heparinizing a dog. (Howell's original unit was the amount of heparin which would keep 1 cc. of cat blood fluid in the cold for 24 hours.) Widström has used heparin to prevent the formation of adhesions in experimental pleurisy.

TECHNIQUE OF ADMINISTRATION

The technique of administering heparin* to a human case is briefly as follows: An intravenous injection of normal saline (or distilled water) is started and allowed to run long enough to note whether or not there is any reaction. Heparin is then added to the intravenous flask in quantities sufficient to make a concentration of 15 units per cc. of the vehicle. By means of G clamps the dropper is regulated to 24 drops per minute. If it is imperative to obtain a response immediately 200 units of heparin in 5 cc. of saline (or distilled water) are injected into the intravenous tubing near the needle. An endeavour is made to keep the clotting time somewhere between 15 and 30 minutes. To do

*The heparin used is from the Connaught Laboratories and is put up in 10 cc. vials containing 1,000 units per cc.

this it may be necessary to alter the original rate to 16-20 or even 28 drops per minute, so that the desired clotting time may be maintained for the particular case. At present, an investigation is being carried out to determine if age, weight or fever have any influence on the dosage required. The level of the clotting time being the chief concern, the concentration and the rate are adjusted to attain the desired result *(e.g.*, in cardiac cases a higher concentration and slower rate are used). There is no hard and fast rule as yet regarding the dosage. It is advisable to determine the clotting time at least twice daily and to be sure that the rate of administration is as constant as possible.

The possibility of reactions from the preparation as it is being made now is most remote. Its chief disadvantage is its cost, which amounts to about $5.00 per day. The next step in progress in this work will be the synthetic preparation of heparin with a marked reduction in its cost.

SUMMARY

A brief résumé of the history of heparin, its nature and method of action has been presented. The uses and possible uses of heparin have been discussed. A technique for its administration to human beings has been outlined.

* * *

The author, who is indebted to Dr. D. W. G. Murray for much of this material, wishes to thank him for the opportunity of assisting in this work.

The work, both clinical and experimental, which is being done with heparin is being aided by a grant from the Banting Research Foundation.

REFERENCES

Best, C. H., and Solandt, D. Y.: The Time Relations of Heparin Action on Blood Clotting and Platelet Agglutination; Proc. Can. Physiol. Soc., page 1; Nov. 1939.

Charles, A. F., and Scott, D. A.: Studies on Heparin: Observations on the Chemistry of Heparin; Biochem. J. 30, 1927, 1936.

Howell, W. H., and Holt, E.: Two New Factors in Blood Coagulation; Am. J. Physiol., 47, 328, 1918.

Jacques, L. B.: Heparin; The University of Toronto Medical Journal, 16, 185, 1939.

Jorpes, E.: Heparin and Its Clinical Use As a Substitute for Oxalates and Citrates With Special Reference to Blood Transfusion; Acta Med. Scandinav. Supp., 89, 139, 1938.

Mellanby, J.: Heparin and Blood Coagulation; Proc. Roy. Soc., B-116, 1, 1934.

Murray, D. W. G., and Best, C. H.: Use of Heparin in Thrombosis; Annals of Surgery, 108, 163, 1938.

Murray, D. W. G.; Jacques, L. B.; Perrett, T. S., and Best, C. H.: Heparin and Thrombosis of Veins Following Injury; Surgery 2, 163, 1937.

Lumbar Anaesthesia in Obstetrics

By R. J. FRASER, M.D.

Hamilton, Ontario

LUMBAR anæsthesia was used for the first time in obstetrics by Corning of New York, in 1885. Four years later it was used on the European continent, for the same purpose. With the discovery of Novocain by Einhorn in 1904, much was added to the safety of the procedure. But it still remained in obscurity, until about twelve years ago, when the method was revived by Pitkin and others. A wave of undue enthusiasm and indiscriminate use resulted for a time, until the present recognized indications and limitations were established. To Pitkin, Labat, Babcock, Koster, Sise, and many others must be given the credit for establishing lumbar anæsthesia in its present position. In this country the names of Parry and Wilinsky should not be omitted. Pitkin is largely responsible for popularizing it on this continent, while Maxon has clarified the details of technique. With special reference to obstetrics, the names of Pitkin, Cosgrove, Hall, Gleason, Pithon, Cheval, Delmas, Dujol, and others should be mentioned. If such men as these have found the method desirable in obstetrics, we may be safe in assuming that it should have a definite place in this special field.

With high lumbar anæsthesia as used in upper abdominal surgery, there are certain possible dangers which are not encountered in the low anæsthesia necessary in obstetrics. With higher blocks there is the possibility of vasomotor collapse or interference with either the cardiac or respiratory mechanisms. These three eventualities are discussed below.

The Vasomotor System. From the vasomotor centre in the floor of the fourth ventricle a constant stream of vasoconstrictor impulses pass down the spinal cord and out through the white rami communicantes. The white rami emerge from the anterior or motor roots of the spinal nerves, from the level of the first or second thoracic to the second or third lumbar, and run to (or through) the corresponding ganglia of the sympathetic chain. The impulses pass over postganglionic fibres to the blood vessels of the two great body cavities, or back through the white rami to the spinal nerves, in which they travel to the blood vessels of the rest of the body. Lumbar anæsthesia acts upon this system from below upwards. Below the third lumbar nerves, there can be no effect upon the blood pressure. There is no fall, therefore, in sacral anæsthesia. As motor block advances to higher levels, more and more of the white rami are blocked, until at the first thoracic segment all have been paralyzed and every blood vessel in the body has lost its tone. A fall in blood pressure, roughly proportional, to the number of white rami

affected is inevitable. Interference with the cardiac and the respiratory functions also plays a part in the fall of the blood pressure.

The Cardiac System. Under normal conditions the rate and force of the heart beats are regulated by two opposing nerve influences, one depressing, the other accelerating cardiac activity. The first of these is represented by the vagi nerves which arise in the midbrain and are distributed to the heart. Their function is to slow the beat and lessen its amplitude. The vagi are never blocked by lumbar anæsthesia. The second influence is represented by three or more cardiac accelerator or augmentor nerves. Unlike the vagi, these are frequently affected by high lumbar anæsthesia. Although these nerves arise from the three cervical sympathetic ganglia, the impulses which they carry proceed from the cardiac centre in the medulla, downward through the cord, to the first four or five thoracic segments. They emerge from the cord with the anterior roots of these segments, passing to the corresponding thoracic ganglia of the sympathetic chain, and thence upward, to the cervical ganglia. Motor block to the fifth thoracic nerves cuts off many of these impulses, and all are cut off when the first thoracic is reached. The resulting interference with cardiac efficiency results in a further fall in blood pressure.

The Respiratory System. From a bilateral centre in the floor of the fourth ventricle intermittent impulses initiate respiration. They flow down the cord, to emerge at two levels, thoracic and cervical. The intercostal nerves represent the thoracic outflow and form part of the anterior roots of the twelve thoracic nerves; they supply the respiratory muscles of the thorax. The phrenic nerves, which innervate the diaphragm, arise in the neck, deriving their fibres from the third, fourth and fifth cervical nerves. The respiratory mechanism when involved by spinal anæsthesia is paralyzed from below upwards. There is no respiratory impairment until the anæsthetic blocks the lowest thoracic nerves. From this point cephalward there is progressive difficulty produced until at the first thoracic level the entire chest wall is blocked, and respiration is carried on by the diaphragm alone. The patient is dyspneic, but still has sufficient respiratory exchange to maintain life. Should the anæsthetic advance, until it blocks the roots of the phrenics, respiration ceases, and life can be sustained only by efficient two-way artificial respiration, which must be continued until the block wears off.

Summation of these three dangers is shown in Fig. 1, which makes evident the safety of low lumbar anæsthesia as practiced in obstetrics and illustrates the dangers of high anæsthesia. In summary it can be said that with spinal anæsthesia limited to the third lumbar segment there is no possibility of any of these dangers occurring. Anæsthesia limited to the tenth thoracic segment has little danger but above this the danger rapidly increases, and only patients with good cardiac re-

serve should be subjected to high lumbar blocks for upper abdominal surgery.

Summation of Danger Factors in Lumbar Anæsthesia

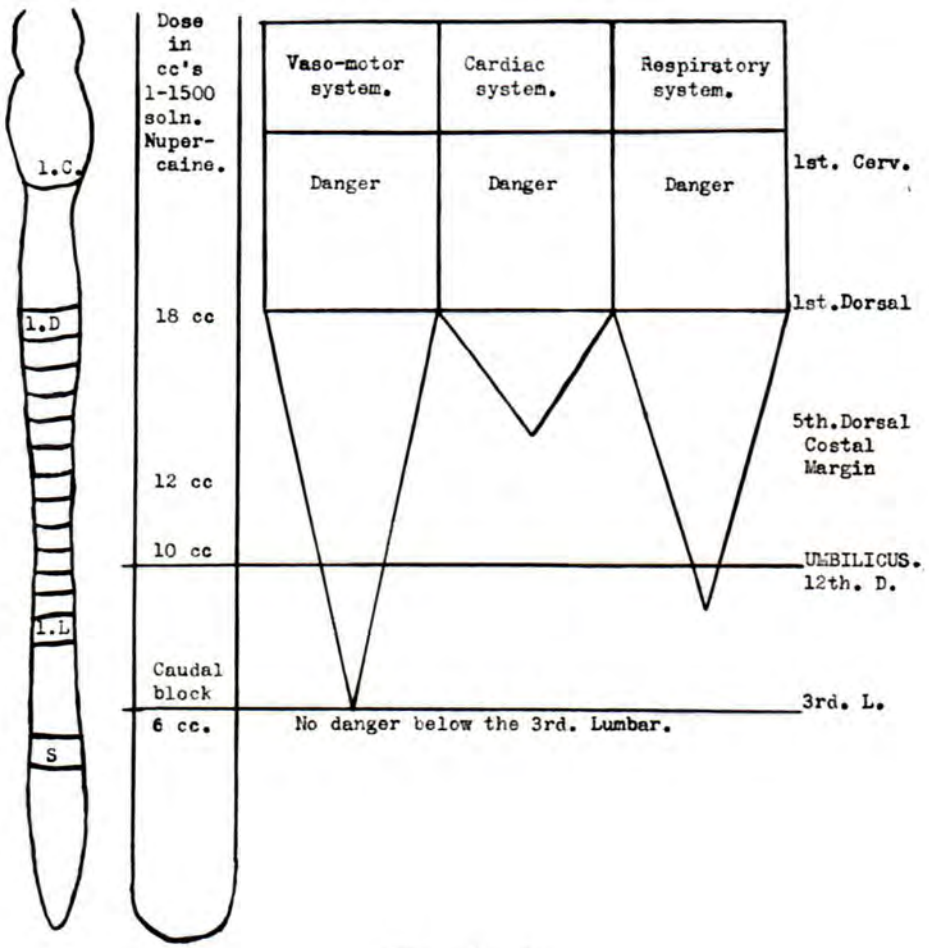


Figure No. 1

Now that the danger factors have been stressed, let us consider methods of avoiding them. Of first importance would be the selection of patients. Only those with good cardiac reserve should be considered for mid or upper abdominal work, but myocardial damage is no greater to the low lumbar anæsthesia, necessary on vaginal delivery. On such patients it probably has less danger than any other form of anæsthesia, providing a hyperbaric, or isobaric solution is used, with its proper technique. Of second importance would be the selection of the dosage of the drug to be employed; and the rule here is minimum dosage always. The next important consideration would be the control of the level of the drug in the cerebrospinal fluid by any recognized method; of these,

three will be briefly outlined. They are, first, the site of puncture or optimum interspace injection; the second, volume control including barbotage, and the third, very important, is gravity control.

All solutions used for lumbar anæsthesia may be divided into three classes; these are HYPERBARIC, or solutions with a specific gravity greater than that of spinal fluid; these have the tendency to sink in the spinal fluid. The second are ISOBARIC solutions which have the same specific gravity as spinal fluid, and are not influenced to any extent by gravitation. The third are HYPOBARIC solutions, with a specific gravity, less than that of the spinal fluid, and these have a tendency to rise. All technique is based upon the above three facts. It is therefore necessary to know the baricity of the drug in solution to be able to attain and maintain the desired level of anæsthesia. If this can be done, the result will be a safe lumbar anæsthetic, devoid of danger to the mother or the child.

The methods of using and controlling hyperbaric, isobaric and hypobaric solutions in obstetrical lumbar anæsthesia will be outlined, together with the volume control.

The use of a hyperbaric solution is as follows: the injection may be made either in the sitting or the lateral decubitus position; the position after the injection with minimum dosage may be horizontal. When larger doses are used, as in abdominal section, the Fowler position should be employed. An example of this type of solution is novocain crystals dissolved in spinal fluid and reinjected into the subarachnoid space. The dosage in vaginal delivery is 50 to 100 mg. and for abdominal delivery 100 to 150 mg. With this type of solution the level of anæsthesia can be controlled by interspace injection, barbotage or gravity control, or a combination of these. The 50 mg. dose is dissolved in two cc. of spinal fluid, while the 100 mg. dose is dissolved in three cc. of spinal fluid, and the 150 mg. dose is dissolved in four cc. of spinal fluid. With the larger dosage the head and shoulders should be elevated on a pillow. The Trendelenburg position is used only to attain the proper level of anæsthesia, then the table should be leveled off or Fowler's position used, depending upon the dosage of the anæsthetic drug and the level of the anæsthesia that is desired.

The use of an isobaric solution is as follows: the injection may be made either in the sitting or lateral decubitus position; the position after the injection is immaterial, since an isobaric solution is not influenced by gravity, and the height of anæsthesia cannot be changed by posture and the desired level is obtained by interspace selected, dose used and the volume of solution injected, or by barbotage. An example of this type of solution is Pontocain, which mixed with an equal volume of spinal fluid is considered to be isobaric. The dosage for vaginal delivery is 8 to 12 mg. or one cc. diluted with an equal volume of spinal fluid.

The use of a hypobaric solution is as follows: the injection must

be made in the lateral decubitus position only. It has been our practice to keep the head slightly lower than the hips when the injection is being done. After the injection the patient is then placed on her back, and after the desired level of anæsthesia is obtained the use of the Trendelenburg position is employed. An example of this type of solution is Spinocaine, the dose for vaginal delivery being one cc. mixed with one cc. of spinal fluid. For abdominal delivery the dosage is increased and mixed with larger quantities of spinal fluid. For lower abdominal work 1.5 cc. spinocaine mixed with 1.5 or 2 cc. spinal fluid will usually be found sufficient.

With volume control another hypobaric solution is used; it is Nupercaine, 1:1500 solution, and must be injected with the patient in the lateral decubitus and slight Trendelenburg position. The injection is usually made between the fourth and fifth lumbar vertebrae, without withdrawal of any spinal fluid, and when completed the patient's position must not be changed for five minutes; then she should be placed in the opposite lateral decubitus position before being placed on her back, and finally put in the Trendelenburg position. The dose for vaginal delivery is six to eight cc. Higher dosage will have to be used for abdominal work. The dosage of this drug will be found in Fig. 1. Lately I have been using this solution, and after the injection the patient is placed immediately in the dorsal decubitus position, with Trendelenburg. So far no untoward results have been encountered and the duration of anæsthesia has been less and probably not so intense as with other solutions.

All injections for vaginal delivery will be found satisfactory between the fourth and fifth lumbar interspace. The injection to be made when the cervix is three-fourths to fully dilated.

There will result complete anæsthesia of the cervix, vagina, vulva, perineum, and anal region, together with good relaxation of these parts. Thorough examination of the patient becomes possible and the application of forceps when necessary can be more accurately done. We believe that extraction is accomplished with less shock than with any other type of anæsthesia. Uterine contractions are lessened to some extent, but these can safely be controlled by the administration of pituitrin. After delivery the patient is transported back to her room in a position depending upon the baricity of the drug used. Fluids may be taken during and after delivery, and meals may be given normally, unless there is sufficient reason for withholding them.

Maxson has pointed out the safety of small doses and has this to say: "The results of 50 to 75 mg. dose of novocaine, the action of which is limited carefully to the sacral nerve roots, has been so satisfactory, and the procedure is so entirely free from any morbidity, that it can without hesitation be advised."

In a personal communication, R. W. Johnstone made the following

remarks: "I think that in general the objection to spinal anæsthesia in obstetrics is not so much concerned with ordinary vaginal delivery as with Cæsarian section."

After carefully weighing the text of the two above statements, it would seem that low dosage properly controlled is absolutely free from danger and experience of twelve years' usage in the field of obstetrics by the author has born out this fact.

With the use of this type of anæsthesia in obstetrics I have had no difficulties and no anxieties; in fact, the way has been made easier both for the patient, the accoucheur and myself. I do not consider it necessary to take the blood pressure in normal or forceps delivery. If, however, this type of anæsthesia is used in Cæsarian section it is well to carefully supervise the patient; the blood pressure should be recorded during the operation and, if necessary, suitable measures taken to maintain its level. For this purpose Ephedrine ½ gr. and Pitressin ½ cc. may be given before the operation is commenced and again about 15 to 20 minutes later, the same dosage of both is repeated, or earlier if the blood pressure begins to fall.

The author is of the firm opinion that best results will be attained in obstetrics if this type of anæsthesia is employed in certain cases, namely, those with respiratory infections both acute and chronic or those with toxemia or myocardial damage or diabetes. He uses it almost routinely with primipara in normal unassisted or forceps deliveries and does not hesitate in giving a second lumbar injection if he considers it necessary.

SUMMARY

1. Since lumbar anæsthesia has been developed to a point of safety and its technique is based upon anatomical and physiological principles, there appears to be no logical reason for withholding its use in obstetrics.

2. With low lumbar anæsthesia, as practiced in vaginal delivery, there is little if any encroachment upon the vasomotor, cardiac or the respiratory systems; hence its safety.

3. This type of anæsthesia should not be used as a routine procedure, but should be used where it will be particularly useful, as in primiparae, or in certain pathological conditions as respiratory infections, both acute and chronic, the toxemias of pregnancy, myocardial disease, and diabetes.

4. There is no tendency to increased hæmorrhage, and the babies are not affected by its use. There is less asphyxiation with lumbar anæsthesia than with any other type.

5. The dose of the drug should be minimum, the injection made low, sitting or lying, with hyperbaric and isobaric solutions; the lateral decubitus position for injection of a hypobaric solution.

6. After twelve years' usage of this type of anæsthesia with no

complication or fatalities, I think it is one of the safest types of anæsthesia to be employed in vaginal deliveries which terminate spontaneously or are assisted by forceps.

* * * *

I wish to thank Dr. Parry for his teaching and encouragement, and Drs. Woodhall, Playfair and Nash for their pleasant professional association. I would also like to thank Dr. Nash for his valuable assistance in producing the medical motion picture, "Lumbar Anæsthesia in Obstetrics," that we had the pleasure of making together. Finally, I would like to thank Dr. Crane for his valuable assistance, both past and present.

REFERENCES

1. Maxson, L. H.: Spinal Anæsthesia; J. B. Lippincott Co., 1938.
2. Pitkin: Personal communication.
3. Johnstone: Personal communication.
4. Thomson, Torrance: Spinal Anæsthesia; Trans. Med.-Chir. Soc. of Edin., 110: 49, 1939.

A NEW AND FORWARD STEP IN THE TREATMENT OF SYPHILIS

The December 16th issue of the Journal of the American Medical Association contains two articles, an editorial and a report of the acceptance of Sobisminol, a new bismuth product for the treatment of syphilis.

Sobisminol was developed by Hanzlik *et al* and is marketed under license from Stanford University. It is available for both oral and hypodermic administration.

Given orally, Sobisminol Mass appears to have an anti-syphilitic effect comparable to that produced by Sobisminol Solution and other soluble compounds of bismuth administered parenterally.

It is well absorbed; usually well tolerated; produces few undesirable side actions and tends to eliminate some disadvantages attendant upon hypodermic administration.

Sobisminol Mass and Sobisminol Solution have been subjected to extensive pharmacologic and clinical study. The investigations indicate that these products have a wide margin of safety whether given orally or intra-muscularly; that they are promptly absorbed with considerable uniformity; that bismuth is excreted at such rates and in such quantities as to indicate that, while there is little accumulation of bismuth, the quantities retained are adequate for the systemic action of bismuth, including a sustained anti-syphilitic effect while the product is being administered.

Clinically, according to published reports, administration of Sobisminol Mass and Sobisminol Solution in recommended dosage is followed by a rapid (aver. 4-5 days) disappearance of Treponema Pallidum from surface lesions and rapid (aver. 10-12 days) involution of the lesions of early and benign late syphilis.

Sobisminol Mass has been administered orally daily for periods of many months without producing cumulative toxic effects. It can be used wherever bismuth therapy is indicated in the treatment of syphilis, including its use with one of the arsenicals or in alternate courses with arsenicals, according to the preference of the clinician.

Sobisminol, under the Cutter and Lilly labels, will be available in certain sections of the Dominion of Canada and under the Squibb label throughout. Squibb also has available a test kit which provides materials for checking urinary bismuth excretion.

Cancer of the Breast: Its Aetiology, Prognosis and Treatment

By J. LEVINE, '40

ÆTIOLOGY

THE cause of cancer of the breast, like that of all cancer, is as yet unknown. Considerable speculation as well as a good deal of experimental work have been devoted to this problem with the result that some of the old ideas on the subject have been pretty well exploded while some new theories have appeared that seem to be worth considering.

The question of the rôle of *chronic cystic mastitis* in the ætiology of cancer of the breast is one which has long puzzled medical men. As Trout[13] points out, we are not even agreed as to what chronic cystic mastitis is. Some pathologists see it in almost every post mortem examination, while others find it in comparatively few cases. A discussion of its relationship to cancer of the breast would therefore require first a more exact definition of the condition. Trout divides it into two types which unfortunately cannot be distinguished clinically. One is "mazoplasia," a term denoting a physiological aberration of the breast which usually occurs normally at or about the menopause. The other is "mastopathy," which is a precancerous, desquamative, epithelial hyperplasia.

Patey,[7] in his admirable survey of chronic cystic mastitis, shows that historically we have passed through three stages in regard to its carcinogenesis: (1) In the middle of the nineteenth century it was considered benign by such men as Paget, Gross and Valpeau. (2) In the period of Reclus and Schimmelbusch at the turn of the century it was considered a dangerous form of epithelial hyperplasia for which the breast was amputated prophylactically. (3) The modern period in which opinion is fairly evenly divided.

The evidence which accounts for *our* present uncertainty may be considered under three headings: (1) experimental, (2) histological, and (3) clinical.

Animal experimentation seems to prove the importance of chronic cystic mastitis in the development of cancer of the breast. It has been demonstrated and confirmed that continuous, large doses of estrin in mice and rats causes proliferation of duct systems, dilatation with secretion, cyst formation and epithelial proliferation, all of which are characteristic of chronic cystic mastitis. Lacassagne has shown that these hormones might go further and even cause cancer, the ease of its development depending on the hereditary susceptibility of the strains of mice used in the experiments. But opposed to this is the fact that in the human there is no history of uterine disturbance which one might

expect with an excess of estrin and there is no rise in the estrin level in the blood or urine. Thus, we have no proof of the over-secretion of estrogens in patients with cancer of the breast.

The *histological* evidence is of two types: (1) Evidence of the changes of chronic cystic mastitis in breasts removed for cancer, and (2) Unsuspected cancer in breasts removed for cystic disease.

The incidence of chronic cystic mastitis in the general population as reported varies all the way from 15 per cent (McFarland) to 93 per cent (Borchardt and Jaffe). This wide variation is probably due to the fact that consideration is not always taken of variations in the breast in individuals at different ages and in different phases of sexual life or of the menstrual cycle. This makes interpretation of figures difficult because the authors do not give their criteria for the diagnosis of chronic cystic mastitis.

Cheattle states that 20 per cent of all cancer of the breast arises from chronic cystic mastitis. He claims that the whole sequence from desquamative epithelial hyperplasia, to cyst formation, to benign neoplasia, and finally to cancer may be traced histologically. Bloodgood, however, has removed 222 breasts for chronic cystic mastitis and has not found cancer in any of them. Fraser, on the other hand, found chronic cystic disease in about 20 per cent of his cases of breast cancer. In his cases the chronic cystic mastitis seemed to be arranged concentrically about the carcinoma and therefore was probably secondary to it.

While experimentally and histologically chronic cystic mastitis seems to be linked with cancer of the breast, when we turn to the *clinical* evidence we find that grave doubts are raised. Clinically, chronic cystic mastitis is hard to diagnose and the nodularity which is thought to be so very characteristic may be due to many other factors such as atrophy, changes in the consistency of the fat or of the supporting connective tissue, vascular changes in the menstrual periods, etc.; while the pain which is also considered to be typical may frequently be functional. At the same time a breast may actually have the proliferative changes of chronic cystic mastitis without any of the clinical findings. Because of this the only cases to follow for acceptable clinical evidence are those with demonstrable cysts or biopsy to confirm the diagnosis. Using this as a criteria, Bloodgood and others found only two per cent of cases of cancer of the breast arose in breasts with chronic cystic disease.

To sum up, while animal experimentation and histological studies tend to prove that there may be some relationship, the risk of cancer in clinically recognized chronic cystic mastitis is slight.

The question of the influence of *estrogens* on cancer of the breast has long been disputed. Although we know that they cause cancer in

mice of the proper hereditary strains, we do not understand the mechanism. In view of our ignorance of the fundamental biological activity of the estrogens with respect to the onset of cancer, and since there is no definite proof of their effect on human breasts, it seems premature to draw conclusions on this point. Cramer, however, warns that "estrogen therapy extending over several years does involve a risk of cancer, especially in susceptible individuals; that is to say, in women with a family history of mammary cancer." This should be borne in mind in using estrogens therapeutically.

Seeking a *specific carcinogenic compound* which might be the cause of cancer of the breast, Twort[14] found oleic acid to be the most effective stimulant, causing sebaceous cell hyperplasia and hyperplasia of the surface and follicular epithelium in the skin of the mouse. These results are suggestive because sebaceous cells and breast cells are both modified epidermal cells. Biologically, breast cells are nothing more than sebaceous cells which have differentiated to perform a special function. Twort did not attempt to induce cancer of the breast because he was unable to simulate natural conditions, but his findings may explain why non-lactating or under-lactating breasts may predispose to cancer. In the event of insufficient or non-lactation there is decomposition of the excretory products and consequently liberation of oleic acid and other fatty acids. The products of decomposition are unable to find their way to the surface and lie "in situ" in the gland acini and ducts until removed by body fluids and wandering cells. If oleic acid and its related fatty acids act carcinogenically on the secreting cells of the breast (whereas they only caused hyperplasia of the sebaceous cells of the skin) it may be because they are acting in particularly favourable surroundings. Milk is well known as a carrier of growth stimulants and is not deficient in vitamins so that it may favour the exertion of malignant influence by the fatty acids.

Kennaway and Sampson, investigating the same problem, have shown that a reduced derivative of cholesterol is capable of producing cancer just as effectively as some of the coal tar and other phenanthrene compounds. Cholesterol is present in the ducts of the non-lactating breasts of the virgin as well as in the secretion of the lactating breast and in the absence of the normal drainage that comes with lactation it may undergo the reductions that would lead to the development of carcinogenic properties. Childbirth and lactation would constitute accordingly a natural protection against this endogenous carcinogenic agent.

Further experimentation along the same line was conducted by Bogen.[2] He also felt that there was some relationship between retained mammary secretions and cancer of the breast. To prove this, he took a group of mice which had just borne litters and separated half of them

from their young before they had suckled. None of the group which was suckled by their young developed cancer, whereas the group which was separated from their litters developed cancer of the breast in 55 per cent of the cases. Another group of mice had the nipples on the left side ligated; 33 per cent of these developed cancer on that side but the control group developed no malignancy. Bogen does not mention the hereditary strains of the mice used in his experiments but it seems likely that they were of a cancer susceptible strain.

A thorough survey of the *vital statistics* relative to cancer of the breast was also made by Bogen and his findings tend to confirm his experimental work. He points out that many errors may be made in interpreting figures by failure to properly account for regional variations in cancer incidence which must be corrected in terms of the percentage of females in the population of the territory, the percentage of women in the cancer age, etc. Adequate differences in the incidence of cancer of the breast have been found between many countries and also the various states of the United States, even after these corrections have been made. In every case it has been found that the incidence of breast cancer is in almost perfect inverse ratio to the birth rate.

It has been repeatedly noted in recent years that cancer of the breast is relatively much more frequent in single than in married females (Stevenson). It appears also to be true that among married women cancer of the breast is more often encountered among nullipara than among multipara and there are indications that it is even less frequent among those who have had a large number of children. If childbearing and lactation tend to prevent cancer of the breast it may be readily expected that the incidence of cancer of the breast in recent years would rise in most places with a falling birth rate and that countries with a higher birth rate, such as Japan or Mexico, would still have a low incidence of cancer of the breast. This trend is proven statistically.

Superficial enquiry also emphasizes the fact that breast cancer is more prevalent in countries where early weaning of the infant is the rule and less often met with where breast feeding is more prolonged.

Not only is breast cancer found with disproportionate frequency in single women but it is also more prevalent among women who have had miscarriages, stillbirths, or for some reason, although pregnant, have failed to nurse the young. There have also been suggestive reports of cancer in the unused breast and not in the contralateral lactating breast.

In view of these findings, we may conclude that the retention of milk and other secretions in the breast may be a factor in the ætiology of many if not all cases of cancer of the breast.

PROGNOSIS

The prognosis in cancer of the breast, as Boyd[3] points out, cannot be guided by the microscopic appearance of the tumor but depends mainly on the clinical features of the case.

However, for a proper interpretation of these clinical aspects a good clinical classification of the disease is required. Several attempts have been made to produce such a classification. Possibly one of the best of the recent attempts to classify the stages of this disease is that of Schenck,[11] which is reproduced below in abbreviated form:

STAGE I: Freely movable tumor less than three cm. in diameter, definitely localized, skin uninvolved, axilla clear, no other metastases.

STAGE II: Freely movable tumor between three and six cm. in diameter, skin uninvolved, one to three small nodes in axilla, no other metastases.

STAGE III: Tumor is six cm. or more in diameter, the skin is involved, there are more than three nodes in the axilla or one adherent or ulcerated node in the axilla, and there are metastases in other tissues, particularly ribs, the pleura, the mediastinum, the lungs and the spine.

STAGE IV: (The stage of recurrence following treatment)

1. Local Recurrences: skin, scar, stitch hole, subcutaneous tissue, residual breast (incomplete operation).
2. Regional Recurrence: axilla, supraclavicular fossa.
3. Opposite Breast and Regional Nodes: mammary gland, skin, axilla, supraclavicular fossa.
4. Distant Metastases: to chest, bone, etc.

If a case presents characteristics of more than one stage it is always considered to belong in the more advanced stage. Thus, a tumor which is five cm. in diameter (Stage II) but is fixed to the skin (Stage III) is considered to be in Stage III.

With a classification such as this it is possible to compare various methods of treatment. Up until now results in one clinic have varied from those in another because of different criteria of operability. But with a clinical classification it will be possible to compare various methods of treatment as applied to cases in the same stage of the disease and to forecast the outcome of our cases with more accuracy than at present.

Scarff and Handley[10] examined the results in 172 cases of radical mastectomy followed for 10 years in an attempt to arrive at a scientific basis for determining the prognosis in cancer of the breast. While they found the histological grading of the tumor to be of some value, the

most important factor in determining the prognosis in their series of cases was the presence or absence of axillary metastases. When the axilla was not involved they had 72 per cent five year and 45 per cent ten year cures. When the axillary glands were involved they had only 18 per cent five year and 9 per cent ten year cures. There were almost three times as many cases in the latter group as in the former. These investigators also observed, contrary to the generally accepted idea, that age does not influence prognosis. Their cases in the younger age groups fared equally as well as the older age groups.

TREATMENT

Halsted, in his classical report in 1897, concluded that no woman up to that time had been cured of cancer of the breast. At that time he also described his radical operation in which breast, fascia, muscles, and axillary contents were removed. Many modifications of his procedure have appeared but in essence the operation is unchanged.

The treatment of breast cancer may be considered to consist essentially of: (1) prevention if possible, (2) removal of the malignant growth from the chest wall in such a manner that local recurrences are decreased or eliminated, (3) proper handling of cancer that has extended beyond the chest wall. The latter two may be grouped as the active treatment.

Prophylaxis: Until the cause of cancer is discovered we can never hope to prevent it. However, we can try to care for some conditions which we know may become malignant. If a duct papilloma is discovered it is generally accepted that local amputation of the breast followed by a course of radiation therapy is advisable. Where the patient is found to have chronic cystic mastitis we find ourselves on less firm ground. All cases should be kept under observation, particularly if the breast is painful, if the disease is localized in the upper and outer quadrant, or if the masses are growing. If there is no improvement with estrogenic therapy and proper support, amputation with biopsy should be considered. Results of the biopsy determine whether a radical or more conservative type of amputation be employed.

Education of the public to the importance of early investigation of lumps in the breast is also an important measure in the prevention of cancer of the breast. However, care should be taken not to produce a cancerophobia.

Active Treatment: Too much controversy is carried on concerning the relative value of surgery and radiation in the treatment of breast cancer. They are not rivals. We should properly regard them as two highly valuable agents to be combined in proper proportions in any given case.

Allen[1] points out one way of determining whether to emphasize radiology or surgery in a particular case. He claims that prompt regression of tumor size by small total roentgen dosage before the appearance of a radioepidermatitis defines the tumor as radiosensitive. This is found in about 15 per cent of cases and suggests an anaplastic lesion which early invades the lymphatics and indicates the continuation of radiation as the primary method of treatment. In 20 per cent of cases the tumor is radio-resistant as shown by lack of response to a dose of 3500 r given in ten days. These require operation as the primary method of treatment. Sixty per cent fall somewhere in between and should be irradiated as far as possible and then operated upon.

Whether or not radiation should be used preoperatively is a moot point. In favor of it, the arguments are presented that it makes operable many cases of questionable operability, that it acts directly on the cancer cell, making the young, active cell dormant and less likely to be transplanted by undue manipulation, and finally that it confines the activity of the malignant condition by developing fibrous connective tissue around the cancer cells, diminishing their nutrition and causing the death of some of them. Opponents of it claim that preoperative radiation takes too long to give and the cancer has time to spread, that it weakens the resolve of patients to submit to operation when they find the mass melting down under the X-ray machine, and that if it is not given expertly the skin may be burned, causing postponement of the operation.

There does not seem to be much question that radiation should be given postoperatively, although 25 per cent of a representative group of 72 British surgeons use no radiation at all (Gordon-Taylor). Its value is conclusively proven by Portmann,[8] who analyzed the results in a series of 405 cases of radical mastectomy performed by Dr. George Crile. Thirty per cent of these fell into Stage I, according to our clinical classification, 25 per cent into Stage II and 45 per cent into Stage III. 170 cases were treated by operation only and of these five year cures occurred in 100 per cent of Stage I, 50 per cent of Stage II, and none of Stage III. In all, 30 per cent of these cases lived five years or more. 235 cases had postoperative radiation, 25 per cent falling into Stage I, 31 per cent into Stage II, and 44 per cent into Stage III. In Stage I 100 per cent again lived five years so that irradiation was of no benefit here, but 70 per cent of Stage II and 10 per cent of Stage III had five year cures so that we have ample evidence that postoperative irradiation is of value in prolonging the lives of those patients in whom the disease has spread beyond the breast itself.

In addition to its life-saving properties, radiation is of incalculable value in making more comfortable the patient who is pain-wracked with bony or other metastases or who has a foul, sloughing ulcer which heals rapidly under X-ray treatment.

Numerous modifications have been proposed since Halsted originally introduced his radical operation in 1897, but none of these vary much from the original in essentials. We will not go into any detail concerning the surgical procedures but it may not be amiss to discuss briefly some of the principles which govern them.

The object of the operation is to remove the malignant growth and as much as possible of the adjacent muscular, fascial and lymphatic tissue in such a fashion as to eliminate or reduce the possibility of local recurrence or extension of the cancer beyond the chest wall.

The incision used should satisfy the following requirements: (1) It should give free and wide access to the axilla, (2) it should permit wide skin and fascial removal, and (3) it should give access to the epigastric triangle. An incision which satisfies these is one extending from the humeral groove to the centre of the epigastric triangle, crossing the costo-sternal articulation at the level of the ninth rib.

In performing the operation an attempt is made to do as much of the dissecting as possible without touching the breast or malignant growth itself until the last possible moment. The reason for this is to avoid contact implantation by hands or instruments. Chase[4] has found cancer cells on the scalpel, gloves, sponges, and even in the saline solutions used in these operations. He is of the opinion that a large portion of the failures in cases treated surgically result from too much handling of the growth. He feels that there would be more successes if more care was taken to leave the breast itself alone until the last possible moment and if all instruments, gloves, etc., used on the malignant tissue were discarded after use so as not to contaminate the rest of the field.

Closing the wound after such an extensive operation is a rather difficult procedure technically and frequently skin grafts are required. An interesting variant on the usual methods is that of Trout.[13] He ties radium into the axilla, screening it from the blood vessels by means of a drain and leaves it there for 24 hours. He also advocates tying radium into the area supplied by the internal mammary artery because dissection cannot usually be performed thoroughly in this area. In this way he hopes to destroy those malignant cells which may have been left behind

CONCLUSIONS

Experimentally and histologically, chronic cystic mastitis seems to bear some relationship to the cause of cancer of the breast but this is not borne out by clinical evidence.

Vital statistics, experimental work and clinical evidence point to a definite relationship between retention of mammary secretion and cancer of the breast in women who are hereditarily predisposed. The

fatty acids and the reduced derivatives of cholesterol have been suggested as the specific ætiological agents in cancer of the breast.

The need for a generally accepted clinical classification of cancer of the breast has been discussed and one is suggested as having considerable value.

The presence or absence of axillary metastases has been found to be the most important single factor in the prognosis of breast cancer. Histological grading and the age of the patient are also of some value.

Proper treatment of known precancerous lesions and education of the public are important prophylactic measures in control of cancer of the breast.

Evidence for and against preoperative irradiation is presented and it is concluded that it is of value in selected cases.

The need for postoperative irradiation is stressed in those cases in which the disease has spread beyond the chest wall.

Some of the principles of surgical treatment are discussed and the importance of avoiding contact implantation is emphasized.

BIBLIOGRAPHY

[1]Allen, L. G.: Radiology, 32:63, 1939
[2]Bogen, E.: Am. J. Pub. Health, 25:243, 1935.
[3]Boyd, W.: Text. of Pathology, 2nd Ed., Lea & Febiger, Philadelphia, 1936.
[4]Chase, H. C.: S. G. & O., 67:97, 1938.
[5]Gardner, W. U.: Arch. of Path., 27:138, 1939.
[6]Gordon-Taylor, G.: Practitioner, 1939.
[7]Patey, D.: S. G. & O., 68:575, 1939.
[8]Portmann, U. V.: Cleve. Clin. Quart., 6:116, 1939.
[9]Raven, C. J.: Brit. M. J., 1:611, 1939.
[10]Scarff and Handley: Lancet, 2:582, 1938.
[11]Schenck, G.: Surgery, 5:567, 1939.
[12]Taylor: S. G. & O., 1939.
[13]Trout, H. H.: J.A.M.A., 111:2189, 1938.
[14]Twort, C. C., and Bottomley, A. C.: Lancet, 2:776, 1932.

Abstracts

MANAGEMENT OF ACUTE BOWEL OBSTRUCTION

By OWEN H. WANGENSTEEN

Ann. Int. Med., 13: 6, 1939

It is becoming generally recognized that the mechanical effects of distension upon the bowel wall, the loss of fluid and electrolyte by vomiting, and the loss of blood in strangulating obstruction are the agencies causing damage. Management must aim to obviate these effects. The old axiom that the high obstructions are the most serious should be altered. Low obstructions hold greater risk to life since sustained intraluminal pressure threatens viability of the bowel wall. Vomiting nullifies this in high obstruction. All low obstructions need early decompression of the bowel to maintain a normal blood flow. Blood loss is a factor to be considered in all strangulating obstructions.

Saline solution, transfusion of blood, and oxygen are adjunct methods of treatment, all of which have their indications. Operation is still the most dependable agent in the relief of mechanical obstruction, but suction applied to an indwelling duodenal tube renders operation unnecessary in certain types of cases.

—A. M. JOHNSON, '40.

TREATMENT OF PNEUMOCOCCIC PNEUMONIA

By LEON SCHWARTZ, H. F. FLIPPIN AND W. G. TURNBULL

Ann. Int. Med., 13: 6, 1939

This is a comparative study of the efficacy of various forms of treatment of 351 adult pneumococcic pneumonia patients treated at the Philadelphia General Hospital between August 15, 1938, and May 16, 1939. In all patients included in this report a typed pneumococcus was recovered from the sputum or blood stream.

Mortality rates of 31.5 per cent, 10 per cent, and 9 per cent were obtained with non-specific, serum, and sulfapyridine treatment, respectively.

The total mortality rate of the series, 12.5 per cent, is compared to that of approximately 35 per cent for the past few years. It may be that some reduction in virulence of pneumonia has occurred, although this could scarcely be marked enough to account for these results.

—R. H. CRAM, '41.

INFARCTION OF THE LUNG

By THOMAS H. BELT

Brit. Heart Jour., 1: 4, 1939

This report is concerned with a series of 1,990 consecutive necropsies in which special attention has been paid to the dissection of the pulmonary arteries. These cases may be regarded as fairly representative of hospital cases. There were 155 cases of hemorrhagic infarction of the lung. Pulmonary embolism was regarded as the immediate cause of 136 of these infarcts.

In 22 (14 per cent) a massive pulmonary embolus was the main diagnosis, and most of these were after operations or fractures. In 74 (47 per cent) heart disease appeared to be a predisposing factor.

A potential source of emboli was demonstrated in 116 (75 per cent) of the infarct cases. Means of identifying emboli at autopsy are discussed, and evidence adduced to show that embolism of the pulmonary arteries is of very common occurrence, while primary pulmonary thrombosis is relatively rare.

—J. W. BABB, '41.

TOTAL, DIFFERENTIAL, AND ABSOLUTE LEUCOCYTE COUNTS AND SEDIMENTATION RATES

By OSGOOD *et al.*

Arch. Int. Med., 64: 1, 1939

This paper supplies some accurate data to replace the old figures which have been copied from text-book to text-book. The paper is one of a series on hæmatologic standards from birth through adult life. The subjects were a carefully selected, normal, native group, mainly between 19 and 30 years of age.

The results are tabulated in detail and statistical and smoothed means and ranges have been worked out. The results show that there is no significant difference with age or sex in this group. For clinical purposes it is considered that the 95 per cent ranges of values are the most useful and these are given. The leucocyte count given is 4,000 to 11,000 (95 per cent range). The proportion of lymphocytes is higher and of neutrophiles lower than in the text-book figures. The sedimentation rates form a skew curve, with the greatest number of determinations falling in the lower ranges. Probably the rate of 15 mm. in 45 minutes represents the strict upper limit of normal values.

—J. G. STAPLETON, '41.

GONORRHŒA, VALUE OF SULPHANILAMIDE SERIOUSLY QUESTIONED

By P. S. PELOUZE

Am. J. Syph., Gonor. and Ven. Dis., 23: 48, 1939

The author deprecates an attitude toward new remedies for gonorrhœa which he has been able to observe for a number of years—an attitude which welcomes each new remedy with enthusiasm, forgetting the nature of the disease itself, which is such that no panacea can ever cure all its manifestations. He believes that far too many of the "studies" of the action of sulphanilamide in gonorrhœa have been superficial and poorly controlled, and is not inclined to think that the new drug gives any better end-results than former methods. One thing new which he views with alarm is the rapidity with which discharge and other open symptoms of the disease may be controlled. This, he states, is lulling many physicians and patients alike into a false belief of cure, when the patients are really asymptomatic carriers. The old criteria for identifying gonococci in smears no longer hold when sulphanilamide is used, he believes, and cultural methods (relatively inaccurate) must be used instead.

USE OF VITAMIN C IN TREATMENT OF LEAD POISONING

By H. N. HOLMES, E. J. AMBERG AND K. CAMPBELL

Science, 89: 322, 1939

This preliminary report gives the results of treating painters who suffered from chronic lead poisoning with supplements of vitamin C. Those who suffered from chronic lead poisoning were found to improve clinically when they received such supplements. By means of test-tube experiments it was shown that vitamin C reacts with lead ions to form poorly ionized compounds of lead which are much less toxic than the metal itself. It is believed that painters who constantly absorb lead may have their stores of vitamin C exhausted by this detoxifying mechanism, and therefore require additional amounts of vitamin C in the diet. It is suggested that this may be supplied in the form of daily doses of ascorbic acid of 50 milligrams added to a diet rich in natural forms of the vitamin. Indications for this simple precaution are so strongly shown by the present work that this preliminary report is published to enable those exposed to the lead hazard to take advantage of it at once.

USE OF VITAMIN C IN TREATMENT OF HEMATURIA ESSENTIAL

By C. E. BURKLAND

J. Urol., 41: 401, 1939

The author believes that the chief anatomical defect in essential hematuria is an abnormal permeability of the glomerular capillaries, which allows red cells to escape from their normal position inside the capillary loops. One possible cause for such an abnormal permeability is a wakening of the intercellular cement

which is thought to seal the interstices of all cells in the body. This defect in intercellular cement substance is characteristic of vitamin C deficiency, and accounts for some of the hæmorrhagic phenomena observed in scurvy. Accordingly, Burkland gave vitamin C in the form of its sodium salt once or twice daily in doses of 100 milligrams to four patients who were suffering from essential hematuria. In every case the bleeding stopped a few days after the treatment had been started and did not recur during the follow-up period. The cases showed no other definite signs or symptoms which might have led one to make a diagnosis of vitamin C deficiency.

JAUNDICE, EXPERIENCE WITH VITAMIN K PRE-OPERATIVELY

By H. R. BUTT, A. M. SNELL AND A. E. OSTERBERG

J.A.M.A., 113: 383, 1939

Vitamin K concentrate obtained from alfalfa has been administered to a total of 127 patients, of whom 75 per cent were jaundiced. Only one patient failed to respond to the medication. The extract was given in doses varying from 0.2 to 8.0 gm. As much as 20 gm. have been administered by mouth for a period of 7 days without the appearance of any untoward reactions. In certain special cases where the patient did not seem able to absorb this material by mouth, this same extract has been given intramuscularly. Though no damage resulted to the tissues from the intramuscular administration of 13 gm. of the material for a period of four days, the improvement obtained in the prothrombin content of the blood was slow and not very satisfactory. Vitamin K is poorly stored in the body, and is not found in abundance in the ordinary low-fat diet.

ESTRONE, CLINICAL USE IN AMENORRHŒA AND MENSTRUAL HEADACHE

By E. NOVAK

Endocrinology, 25: 423, 1939

In a general discussion of the application of various hormones to clinical practice, the author points out that some hope for effective treatment in amenorrhœa is held out by estrogenic substances. It has always been held that there could be little rational basis for the use of estrone in treating amenorrhœa due to ovarian deficiency because estrone does not stimulate ovarian function, but merely replaces one part of it. However, it does seem that in some cases a quantitative deficiency in the patient's own estrogen may be filled by the administration of estrone and thus an approximately normal interplay between the hypophysis and the ovary initiated. Furthermore, it is logical to believe that in some cases an underdeveloped endometrium may be sensitized by the administered estrone to become responsive to the patient's own hormones. Estrogenic substances frequently are successful in the treatment of headaches definitely associated with the menstrual period.

UNRECOGNIZED PREVALENCE OF VITAMIN C DEFICIENCY

By T. MCGOVERN, C. F. GANNON AND I. S. WRIGHT

Am. J. Med. Sc., 197: 310, 1939

Scurvy and allied conditions have been written about exhaustively for the past five years and it therefore seems appalling that the disease should be as prevalent as it is today. The fact that scurvy is actually being precipitated by diets prescribed by physicians causes the author to believe that many doctors are failing to recognize the possibility, believing that scurvy never occurs in modern times except in connection with extreme grades of poverty and malnutrition. The author states that exactly the converse is true: Scurvy is very commonly found among the higher economic groups if the physician is alert to the possibility of finding it. Avitaminosis may be produced by a variety of causes, including a poor dietary, increased destruction of the vitamin, deficient absorption or increased elimination, as is said to occur with the injudicious use of salicylates. Scurvy may masquerade as rheumatism, erythema nodosum, lupus erythematosus, hæmorrhagic nephritis, and many others.

TRANSFUSION, SUGGESTED METHOD OF PREVENTING ACCIDENTAL SYPHILIS

By C. C. KAST, C. W. PETERSON AND J. A. KOLMER

Am. J. Syph., Gonor. and Ven. Dis., 23:150, 1939

The authors conceived the idea that arsphenamine or neoarsphenamine might be added to citrated blood in small amounts to kill any spirachetes which might be present due to undetected syphilis in the donor. Preliminary tests indicated that a 1:10,000 concentration of disodium arsphenamine or neoarsphenamine could be relied upon to kill completely all spirochetes if the blood to which it was added was allowed to stand for fifteen minutes at room temperature. No destructive effect upon blood cells was observed from the addition of the arsenical compounds during this short period, and human subjects have received 300 cc. of blood containing a 1:1,000 to 1:3,000 concentration of neoarsphenamine without demonstrating any toxic effect. 300 to 400 cc. of blood containing disodium arsphenamine or neoarsphenamine have likewise been given as transfusions without producing any detectable deleterious effect upon the subjects who had volunteered to act as recipients.

USE OF POWDERED SULPHANILAMIDE IN COMPOUND FRACTURES

By N. K. JENSEN, L. W. JOHNSRUD AND M. C. NELSON

Surgery, 6:1, 1939

The idea of packing infected wounds with antiseptics can be traced back to Lister's famous carbolic acid dressings, but in modern times antiseptics have not been generally used in wounds because of the realization that any agent which was likely to prove toxic to bacteria would also prove toxic to traumatized tissue. Sulphanilamide, however, is an agent which may be present throughout the body in concentrations sufficient to prove detrimental to bacteria, yet does not harm the tissues. The first case treated by the authors was a compound fracture in which mud had been driven into the ends of the bones. After careful cleansing and debridement, 5 gm. of powdered sulphanilamide were placed in the wound which was closed tightly. The wound healed without drainage, and a bone graft took six weeks later. 39 compound fractures have been thus treated since and 37 were healed without infection. Two cases were re-compounded and only then did they become infected.

Editorial

THE JOURNAL, in its ten years of existence, has attempted to give the students a medium through which they may gain experience in writing and publishing medical papers. The students apparently do not appreciate this opportunity, as is apparent by the appalling lack of student articles in each issue.

The art of writing a scientific paper suitable for publication is not easily acquired, and where can the student better gain experience than by publishing in his own undergraduate journal? The writer should remember that his efforts are noticed and appreciated by others, as well as being of great value to himself. In the past, letters have been received by THE JOURNAL staff commenting favourably on the calibre of the articles published by the students. It is hardly necessary to point out how valuable such an article can be to the writer. It is the very best type of recommendation when seeking a hospital appointment.

Our alumni and the staff of the School give THE JOURNAL their support. The Board of Advisors give a great deal of their valuable time in aiding the Editorial Staff with the preparation of each issue. We urge the students to show their appreciation by giving THE JOURNAL their fullest co-operation.—J. D. A.

* * * *

The Editor wishes to thank W. F. Maguire of the Department of Anatomy and John C. Clark '41 for their assistance in preparing the illustrations in this issue of THE JOURNAL.

DISEASES OF THE FOOT

By ERNIE D. W. HAUSER, M.S.M.D.

(472 pp., 263 illustrations. Published by W. B. Saunders Co., 1939. Price, $6.75.)

Dr. Hauser has prepared a comprehensive volume on a subject that is usually inadequately presented to medical students. The author begins with a rather detailed study of the anatomy and physiology of the foot and subsequent pathological conditions, in so far as possible are described in terms of altered physiology and anatomy. The list of diseases affecting the foot that are discussed is most complete, ranging from such a common condition as Flat Foot to such rare tumors as Subungunal Glomus Tumors and Calcinosis of the Skin. There are also chapters on applications of plaster casts, adhesive strapping for sprained ankle and orthopœdic appliances for the foot. What the reader particularly liked was the discussion of the hygiene and general care of the feet, the proper fitting of shoes and the care of the feet during pregnancy.

—D. STATE.

CLINICAL GASTRO ENTEROLOGY

By HORACE WENDEL SOPER

St. Louis, Miss.

(Published by C. V. Mosby Co., 1939)

In the preface the author states that he is attempting in this book to clarify a subject which has become too complex. That he has attained this object is doubtful, but he has presented us with a book on Gastro Enterology which can be read in one evening. The book consists of 300 pages but only 180 pages of large type are in the text; the other 120 pages are devoted to illustrations with their accompanying descriptions. In such a small book all subjects are covered rather sketchily, cancer

of the stomach and other gastric tumors being dealt with in three pages. The author devotes a larger section to the discussion of milk. On this subject he has some rather unorthodox opinions, and says that Bacterial Soup is a good synonym for it. He also states that "Research into the habits of the people of ancient, as well as modern civilization reveals that they all were consumers of milk and all suffered from dental caries." Another subject to which he devotes more space than appears to be warranted is that of Indicanuria, which he believes to be of great importance. He states that he has examined the urine of 18,000 patients for indican. From this large number of examinations he, however, fails to present any data of much practical value.

It is not a book that could be recommended as a reference work for either the student or practitioner. The X-ray plates of different gastro intestinal diseases, however, are particularly fine.

—J. H. GEDDES, M.D.

MENSTRUAL DISORDERS: PATHOLOGY, DIAGNOSIS AND TREATMENT

By C. FREDERIC FLUHMANN, B.A., M.D., C.M.

Fellow of the American Gynecological Society

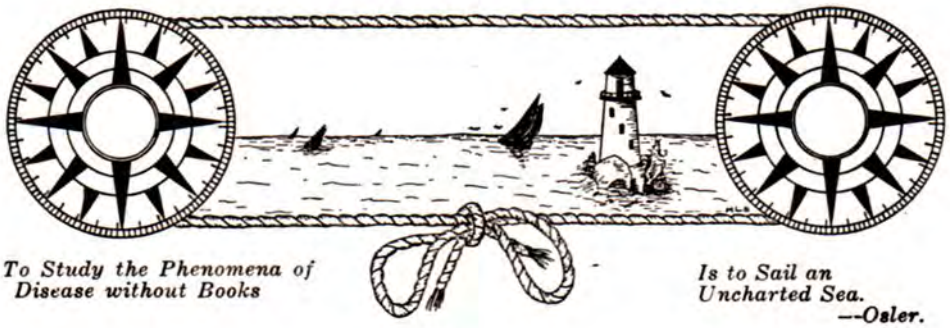
(329 pp., illustrated, indexed, $5.00; W. B. Saunders Co., 1939.)

This book begins with an interesting historical review of the concepts of menstruation. The present concepts of this phenomenon with their experimental foundation are described. The author's purpose has been to present the various disorders of the physiology of the menstrual cycle which may occur under the influence of local or systemic disease. Special emphasis is placed on the endocrine factors. The experimental data on this phase of the subject is reported and criticized. The multitude of references listed in the bibliography at the end of each chapter is evidence of the great amount of literature that the author reviews.

The book is written for the practitioner of medicine as a guide in determining the possible causative factors of certain symptoms of unknown ætiology. It also outlines the therapeutic measures and agents which recent study has determined to be of value in treating these factors and in providing symptomatic relief.

This is a collection into one volume of the more recent theories and experimental work in this subject. The modern methods of research and investigation into this field are presented but the author states that the book is written for the physician and certain aspects of the subject are left to larger works in gynecology. The student will regard it as a reference book which is easy to read.

—R. B. PALMER, '41.



To Study the Phenomena of Disease without Books

Is to Sail an Uncharted Sea.
—Osler.

RECENT ACCESSIONS TO THE MEDICAL SCHOOL LIBRARY

American Foundation—American Medicine, in 2 vols. 1937.
Armstrong—Principles and Practice of Aviation Medicine. 1939.
Bourne—Recent Advances in Obstetrics and Gynecology. 4th ed. 1939.
Bramwell and Longson—Heart Disease and Pregnancy. 1938.
Brickel—Surgical Treatment of Hand and Forearm Infections. 1939.
Bucher und Hofflin—Die biologische reaktion. 1939.
Clark—The Tissues of the Body. 1939.
Conference on Psychiatric Education—Proceedings. V. 2-4. 1935-38.
Conybeare—Text-book of Medicine. 4th ed. 1939.
Crothers—A Pediatrician in Search of Mental Hygiene. 1937.
Eisendrath—Urology. 4th ed. 1938.
Gardiner—Handbook of Skin Diseases. 4th ed., rev. by John Kinnear. 1939.
Gerling—Short Stature and Height Increase. 1939.
Johnstone—A Text-book of Midwifery. 10th ed. 1939.
Jones and Chamberlain—Electrocardiograms; an elementary atlas for students and practitioners. 1939.
Kerr—Combined Text-book of Obstetrics and Gynecology. 3rd ed. 1939.
League of Nations—Health Organization. Report on the Physiological Bases of Nutrition. 1935.
Miles—Rectal Surgery. 1939.
Roffo—Lo que debe saberse sobre el cáncer. 1934.
Rolleston and Moncrieff—Modern Anæsthetic Practice. 1938.
Samuels—Der zyklus der frau, reform des ehelebens. 1938.
Shanks, Kerley and Twining—A Text-book of X-ray Diagnosis. V. 3. 1939.
Vaughan—Practice of Allergy. 1939.
NEW SUBSCRIPTIONS:—
British Journal of Rheumatism.
Journal of Endocrinology. (British.)
Journal of Mental Science.
New York Academy of Medicine. Bulletin.
Psychosomatic Medicine.