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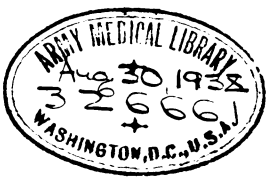

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The Importance of Vitamins in Dietetics

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Presidential Address, Ulster Medical Society,
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IT is my intention this evening to give you a brief survey of the work which led to the discovery of vitamins, and of the important part they play in nutrition and dietetics.

The whole subject is reviewed at length in the report published by the Medical Research Council in 1932, and it is largely from this report that the subject matter of my address has been compiled.

Vitamins perform very important nutritional functions in life, yet only minute amounts are necessary for the adequate fulfilment of these functions. In ordinary diets they are present in quantities far too small to yield any appreciable contribution to the energy supply of the body, or to furnish structural elements for the tissues.

Since a supply of vitamins is essential for the animal body, these are generally present in the natural foods which are instinctively consumed by men and animals.

Vitamins are primarily formed during the synthetic activities of the green plant on land, or of algæ or other organisms in the sea. From these they are transferred to the tissues of animals.

The distribution of vitamins in vegetable and animal foods may be partial and irregular, but, broadly speaking, it is safe to say that the adult individual finds a sufficient supply of vitamins in his food, so long as that food is reasonably varied.

Yet should the natural foods be specially purified and fractioned for the sake of taste or appearance or, for convenience, be preserved in various ways, it frequently happens that the vitamins, owing to their partial distribution, may be removed or, owing to their relative instability, destroyed.

It was from the rice-eating countries, especially in the East, where the diet is

not sufficiently varied, that we first had evidence of the ill-effects which might arise from the artificial treatment of food.

When modern milling machinery was introduced, the rice thus treated was deprived of vitamins which were present only in the cortex. The consumption of this decorticated, or polished, rice led to the development of beri-beri.

It was long before the importance of food factors was recognized, as disease was always considered to be due to some positive agent, microbic or toxic, and it was difficult to conceive that it could also be caused by a negative agent, that is, by the absence of some apparently unimportant factor. But when this fact became clearly established, we were able to supplement clinical and sociological observation by controlled experiments on animals.

Although it was known for centuries that scurvy was due to a diet containing an inadequate supply of green vegetables and fruit, yet it was not till 1881 that evidence of the existence of vitamins, based on animal experiments, was furnished by Lunin, one of the workers from the school of Bunge at Basle. Lunin was investigating the rôle played by the inorganic salts in nutrition. He fed mice on an artificial mixture of the individual constituents of milk, namely, protein, fats, salts, and carbohydrates, and found that the animals failed to survive. He came to the conclusion that a natural food, such as milk, must therefore contain, besides these known ingredients, small quantities of unknown substances essential to life.

Ten years later, in 1891, Socin, another of Bunge's assistants, working on the same lines, arrived at the conclusion that some unknown substances must be present in food, substances which, he stated, must be present in whole milk and in egg yolk.

In 1897, Dr. Christian Eijkman, a military doctor in the Dutch East Indies, and later Professor of Hygiene at Utrecht, proved that beri-beri in man was due to the use of polished or decorticated rice as a staple food.

He also observed that birds (fowls, pigeons, and ducks), when fed on polished rice, developed a disease similar to beri-beri, which he called *polyneuritis gallinarum*, and that the disease failed to develop when the birds were fed on whole rice, or on rice grains still containing the pericarp or silver skin.

About 1901 another Dutch scientist, Grijns, put forward the view that beri-beri, whether in birds or man, was due to a deficiency, to the absence of an essential nutrient from the food. This in rice happens to be confined to the cortical part of the grain which is removed by polishing.

To Grijns belongs the credit of first picturing clearly what is now called a deficiency disease, and also of first investigating the properties and distribution of a vitamin.

In 1905 Professor Pekelharing, probably because he was well aware of these researches which were not generally known outside Holland, carried out similar experiments with milk, and referring to this unknown substance, stated: "If this substance is absent, the organism loses the power properly to assimilate the well-known principal part of food, the appetite is lost, and with apparent abundance the animals die of want. Undoubtedly this substance occurs not only in milk but in all sorts of foodstuffs, both of vegetable and of animal origin."

Hopkins at this time was carrying out experiments in England, and in 1906 published a paper confirming these findings. He claimed that scurvy and rickets were both due to the absence of some unknown dietetic factor, also that nutritive errors affecting the health of individuals depended on unsuspected dietetic factors.

In 1907 two Norwegian scientists, Holst and Frölich, showed that typical scurvy could be produced in guinea-pigs by deficient diets, and could be as easily cured by suitable additions to the diets.

1912 Casimir Funk, as the result of work carried out at the Lister Institute, published a paper entitled "The Etiology of the Deficiency Diseases." He reviewed the literature concerning beri-beri, scurvy, and pellagra, and advanced the opinion that all three were deficiency diseases. In this paper the term 'vitamin' was used for the first time.

In 1913 McCollum and Davis in America discovered the importance of the fat soluble vitamin contained in butter, and in 1915 they published a paper proving that at least two accessory diet factors were essential for normal growth, the one being present in butter fat, and the other being widely spread in natural food materials such as wheat-germ, etc. They suggested that these two vitamins should be called fat soluble A and water soluble B. The anti-scorbutic vitamin C was also included about this time. Up till 1918 these were the only vitamins recognized.

Between 1918 and 1921 E. Mellanby established the fact that rickets was also a deficiency disease, and could be produced in puppies by withholding from the diet a substance, the anti-rachitic vitamin, which appeared to be similar as regards distribution and properties to the fat soluble vitamin A.

Between 1922 and 1925 it was proved by many workers that the original vitamin A, contained in cod-liver oil, was composed of two different vitamins. On treating the cod-liver oil by heat and oxidation the anti-rachitic factor was unaffected, while the anti-xerophthalmic or growth factor was destroyed. The anti-rachitic factor was now named vitamin D.

It was further discovered that vitamin D, but not vitamin A, could be produced by the action of certain radiations upon the animal organism, or upon natural foodstuffs composing the diet.

It is now well known that vitamin A and vitamin D are distinct fat-soluble dietary factors, both of which are required by animals for satisfactory growth and nutrition.

About 1923 vitamin E was discovered.

Vitamin A.

Deficiency is generally associated with the following pathological conditions :—

1. Cessation of growth.
2. Xerophthalmic and infective conditions of eye.
3. Night-blindness or hemeralopia.
4. Various tissue changes.
5. Increased susceptibility to infection.

Xerophthalmia.—Bloch studied the incidence of xerophthalmia in children in Copenhagen over a number of years, and proved that most of the cases were due to vitamin A deficiency.

He says that the eye disease showed every stage of severity from xerosis of conjunctiva to hardening of the cornea leading to ulceration, necrosis, and even ultimate blindness. Local treatment of the eye condition in the ophthalmic department of the hospital gave little relief and no permanent improvement, but on supplying the patients with an adequate diet containing whole milk and *ol. morrhuæ* the improvement was rapid.

A critical examination of 434 cases of keratomalacia in children and of nineteen cases in adults, which occurred in Denmark from 1909 till 1920, has shown that these were due chiefly to lack of vitamin A in the diet, and in the case of children to the increased requirement of this vitamin involved in rapid growth. The greatest number of cases occurred in winter and spring. This was attributed to the seasonal variation in the vitamin content of milk.

Night-blindness has also been shown by many European and foreign investigators to be due to vitamin A deficiency. Aykroyd, reporting on cases of night-blindness occurring in Newfoundland and Labrador, states that the Newfoundlanders themselves know how to treat the disease by fresh cod's liver or by cod-liver oil. Discussing the antiquity of treatment by liver, he points out that Hippocrates recommended that for night-blindness the patient should eat as large an ox-liver as possible, raw and dipped in honey.

Night-blindness has been stated to be due to a subnormal amount of visual purple in the retina.

Tissue Changes.—Hort, Miller, and McCollum in 1916 described changes in the anterior horn cells of the spinal cords of pigs caused by diet deficiency.

In 1926 E. Mellanby noted the production in dogs of a condition resembling combined sclerosis by the use of diets rich in cereals, especially in wheat-germ, and deficient in fat-soluble vitamins. In 1929 the same observer found that the experimental production of subacute combined degeneration of the cord could be hastened and intensified by adding a small quantity of ergot to the diet. The addition of vitamin A substances such as cod-liver oil or cabbages prevented the degeneration of the cord, or arrested its development if present.

It has been shown by McCarrison that in rats, renal and vesical calculi are produced when the diet has a low vitamin A content.

He also mentions that stone is commoner among wheat-eaters than among rice-eaters in India, and that whole wheat flour is much more productive of calculi in rats than rice flour.

Increased Susceptibility to Infection.—Green and Mellanby in 1928 reported the results of experiments on rats.

In ninety-four rats fed on a diet deficient in vitamin A they found the following percentages of infection :—

Xerophthalmia, thirty-eight per cent.; abscess at base of tongue, seventy-two per cent.; infection of lungs, nine per cent.; infection of genito-urinary tract,

including renal and vesical calculi, forty-four per cent.; septic middle ear and nasal sinuses, twenty per cent.

In fifty control rats on the same diet with the addition of some source of vitamin A, there was no evidence of any septic infection.

It is still doubtful whether the administration of vitamin A is really of direct benefit in the treatment of bacterial infections in man. It is probable that animals deprived of vitamin A have less vitality and resistance to infection than animals with adequate nourishment.

Animal organisms possess the property of storing reserves of vitamin A which have been obtained directly or indirectly from vegetable sources. The amounts of vitamin present in the tissues will depend therefore not only on the power of the tissues to store the vitamin, but also on the previous dietary. The reserve amounts in the tissues of a grass-fed animal are much higher than in those of a stall-fed animal. This is important in considering the vitamin A content of milk and butter.

Most of the reserve is contained in the liver. The liver fats of grass-fed animals, such as the sheep and ox, are among the richest sources of vitamin A known.

Vitamin D, the Anti-rachitic Calcifying Vitamin.

This is a fat-soluble substance having the specific function of controlling the deposition of calcium and phosphorus in the tissues.

As bones and teeth are largely composed of calcium phosphate, it is obvious that the structure of these tissues is largely determined by the adequacy of the supply of vitamin D to the body during the period of their active development.

The extent of defective bone formation as seen in the great prevalence of rickets in the temperate zone, the widespread defect in the structure of teeth and the high incidence of dental caries, suggest that a deficient intake of vitamin D may be the most important dietetic defect at present known.

About 1922 it was discovered that if a diet deficient in vitamin D were exposed to irradiation it acquired the property of preventing rickets. Later, in 1924, it was found that various foodstuffs, incapable in themselves of preventing or curing rickets, became endowed with anti-rachitic power after exposure to ultra-violet rays, and it was further shown that the foodstuffs which possessed this property were the fats.

These researches explained the effects of both sunlight and diet in preventing rickets; sunlight, by its action on the skin, generating vitamin D from cholesterol, and diet, by its containing adequate amounts of vitamin D.

It is probable that vitamin D is produced in the skin itself, or in the blood circulating immediately below the surface of the skin, by the activation of a precursor already present, probably cholesterol. The light waves which exert this action are confined to that part of the spectrum having wave-lengths of three hundred mille-microns or lower. This accounts for the negative effect of sunlight which is filtered through glass, as ordinary glass is opaque to these radiations.

It has been shown that dark-skinned races require more exposure to sunlight to generate vitamin D than white people. This accounts for the greater susceptibility of negro children to rickets when living in northern climates.

The only natural foods which are known to be rich in vitamin D are egg yolk, cod-liver oil and other similar fish-liver oils. Cream and butter contain small amounts. Fresh vegetables, fruit, and meat have no apparent anti-rachitic effect on laboratory animals, and cereals may actually favour the development of rickets.

The anti-rachitic potency of cow's milk is a variable quantity depending on the environment and diet of the cow. In summer, when the cows are in the fields and exposed to sunlight, the content is much higher than in winter. The vitamin D content can be increased by including cod-liver oil or irradiated yeast in the animals' diet.

Milk is at no time a rich source of the vitamin; skim milk contains mere traces.

Children who, on account of poverty, cannot be supplied with adequate amounts of dairy produce, including eggs, and who consume vegetable fat in the form of margarine, are obviously liable to suffer from a defect of this vitamin unless its supply is assured in some special way, as by administering cod-liver oil or by exposure to natural or artificial ultra-violet radiation. Light and diet should be regarded as factors which supplement each other in the supply of vitamin D. Where there is much sunshine, less is required in the diet, but in the polar regions where the sunlight is less intense and the body more completely clothed, the function of protection passes from the light to the diet.

If the Eskimos who, on their natural diet of meat, fish, and oil, are healthy and have good teeth, change to civilized diet while living in the same latitudes, the health deteriorates, teeth decay, and the children develop rickets.

In Britain at the present day the adaptation of diet to climate is incomplete. Osteomalacia is rare, but bad teeth are almost universal and rickets is a common disease.

Experiments were carried out in Vienna in 1922 and 1923 by Chick and others on the relation between vitamin D and sunlight. Observations were made upon young infants receiving two types of diet.

Diet No. 1 consisted of undiluted milk with added sugar; diet No. 2 consisted of full cream, dried milk, and cod-liver oil.

Between May and October no case of rickets developed among a total of forty-two infants. Between November and April, thirteen out of fifty-one developed rickets; all these occurred among the twenty-five infants on diet No. 1.

During the summer the infants spent a great part of their time out of doors in the sun. Further observations showed that active rickets could be cured in the summer by exposure to sunlight, no matter what diet they were receiving. In winter rickets could be cured by diet No. 2, but progressed on diet No. 1.

The outbreak of osteomalacia which occurred in Vienna as a sequel of the Great War shows clearly that in winter we depend on our diet for the provision of this vitamin. It is quite certain that famine was the cause of the disease in Vienna. It was truly called hunger-osteomalacia, but it was equally truly cured by summer sunshine, and could have been cured by ultra-violet radiation from an artificial source.

Thus, while failure of diet was the cause of the disease in Vienna, the custom of

purdah is the factor which determines the development of osteomalacia in India. *Purdah* confines women to the house and prevents their exposure to sunlight. For the same reason the disease is very common in parts of China. In these countries men on the same diet are not affected.

A study of ancient skeletons suggests that osteomalacia, which through the deformities caused in the pelvis has a crippling effect on reproduction, was the cause of the extinction, about the end of the fifteenth century, of the Norse colony founded in A.D. 985 by Eric the Red in Greenland. This prevalence of osteomalacia was probably due to failure to adapt the diet so as to supplement the lack of ultra-violet rays from the sun in these high latitudes.

A deficiency of calcium or phosphorus, or a faulty balance of these elements, in a diet containing inadequate amounts of vitamin D, will intensify the rickets-producing effects of the diet.

Relation to Cereals.—Where vitamin D is deficient, rickets develops more strongly in those animals which eat more cereals.

Of the cereals studied, oatmeal produced more severe rickets than maize, barley, or rice. Wheat-flour interfered less with bone calcification. (Mellanby: experimental work on puppies, 1922-5.)

Oatmeal contains plenty of calcium and phosphorus, so the effect cannot be due to deficiency of these elements. This occurs only when vitamin D is deficient.

Mellanby also showed that if the mothers receive an adequate supply of vitamin D during pregnancy and lactation, their offspring are much more resistant to rickets than puppies whose mothers have received no cod-liver oil during pregnancy.

Premature children are notoriously liable to develop rickets, and it is believed that the normal infant receives from its mother during the last few weeks of pregnancy important stores of vitamin D which help to protect it from rickets during its post-natal career.

Relation of Vitamin D to the Parathyroids.—The effect of the parathyroid secretion is apparently to maintain or raise the calcium and phosphorus excretion at the expense of the bones, while vitamin D brings about the incorporation of calcium and phosphorus in the bones, so that their actions are in opposite directions.

In tetany, which is frequently associated with rickets in infancy, vitamin D seems to raise to normal the blood-calcium by increasing the retention in the body of calcium present in the food. Parathyroid raises the blood-calcium by withdrawing it from the bones.

Briefly, in treating rickets, tetany, and osteomalacia, it is important to supply plenty of vitamin D and to cut down the cereals. Green vegetables also are useful. In addition, when possible the available sunshine should be used, or artificial sources of ultra-violet radiation employed.

Vitamins and Dental Tissues.

Two types of dental defect are commonly found in civilized man: 1, Dental caries; 2, periodontal disease, including pyorrhœa alveolaris. The first of these concerns the tooth itself. The second involves the soft structures adjacent to the tooth and also the hard alveolar bone.

Vitamin D is concerned with the structure of the teeth and of the alveolar bone.

Vitamin A is concerned with the structure of the marginal epithelium of the gums.

The important investigations carried out by Mrs. Mellanby, 1918 till 1930, have definitely proved the importance of vitamin D as a factor in the normal development of the teeth and jaws. If the teeth are badly formed, and the dentine and enamel deficient, caries tends to develop at an early age.

Young puppies fed on a diet deficient in vitamin D showed the following defects in the development of the teeth and jaws :—

1. Delay in eruption of the permanent teeth.
2. Thickening of the jaw-bones and irregularity in the arrangement of the teeth.
3. Irregularly formed and poorly calcified enamel, the surface of which is pitted and grooved and frequently pigmented.
4. Defective development and irregular calcification of the dentine.
5. Abnormal development of the calcified tissues at the gingival margin, and hence irregularity of the periodontal membrane.

When an adequate supply of cod-liver oil was given, the surface was smooth, white, and shiny, and much thicker layers of enamel and dentine were produced, the dentine exhibiting a perfectly uniform structure with complete absence of interglobular spaces.

Vitamin E.

It is only within the last fifteen years that the existence of a specific vitamin essential for reproduction, at any rate in the case of rats and mice, has been established. The view previously held was that a diet which would satisfy the animal's needs for growth and health would also be adequate for reproduction.

In 1920 Mattell and Conklin found that rats reared on whole milk, though growing well and appearing in good health, were usually sterile.

In 1922 Evans and Scott found that rats receiving a diet containing adequate amounts of protein, salts, and all the known vitamins were partially sterile in the first generation and wholly so in the second generation. This sterility was corrected by an unknown substance X present in certain natural foods, such as fresh lettuce leaves, wheat embryo, and dried alfalfa.

In 1923 Evans and Bishop showed that the X factor was fat soluble and not identical with any of the known vitamins.

Sure, working independently, had come to the same conclusion, and suggested that this factor should be named vitamin E.

In 1927 Evans and Burr stated that in male rats and mice deprivation of vitamin E led to complete and incurable sterility in eighty-five to one hundred and fifty days, and that this was due to degeneration of the testes.

The richest natural sources of vitamin E are green leaves and the embryo of seeds. It is also present in animal tissues, especially muscle and fat, and to a lesser extent in milk and butter.

This work is being studied in relation to stock-breeding, by giving intramuscular injections of wheat-germ oil, and successful results have been reported in sterile

cows. A number of workers are also investigating the part played by vitamin E in cases of human sterility. In these cases wheat-germ oil has also been used with success in some instances.

Vitamin B Complex.

In 1915 McCollum and Davis reported that young rats fed on a purified synthetic diet, containing butter fat to supply the fat-soluble vitamins already discovered by them in 1913, required for normal growth an additional factor, which in 1916 was named water-soluble vitamin B. This was considered by McCollum and his co-workers to be identical with the anti-neuritic vitamin discovered by Eijkman in 1897.

The fact that the distribution and properties of the water-soluble B factor, as ascertained by experiments on rats, closely agreed with those of the anti-neuritic factor established by experiments on pigeons, coupled with the similarity of the symptoms exhibited by rats and pigeons suffering from deficiency of this factor, led to the supposition that these substances were identical. Later it was found that the rat needed for normal growth two water-soluble vitamins—B_1 and B_2—both of which were contained in vitamin B. (B_1—the heat labile anti-neuritic vitamin discovered by Eijkman in 1897; B_2—more heat stable, the pellagra preventive factor discovered by Goldberger and others in 1926, and necessary to prevent dermatitis in rats.)

Further research has shown that there are other factors present in the B complex, and that all of these are present in fresh yeast.

Vitamin B_1, the Anti-neuritic or Beri-Beri Preventive Vitamin.—Beri-beri occurs principally among rice-eating populations in Japan, India, Malay Peninsula, Dutch East Indies, and the Phillipine Islands. It is also endemic in Labrador and Newfoundland, where the inhabitants subsist largely on a diet of white wheaten flour.

In one case an outbreak amongst the laboratory fowl in Batavia was found to be due to the use, by the laboratory assistant, of boiled rice from the hospital kitchen for feeding the fowl. The disease lasted five months, and disappeared when a new chef was appointed who refused to supply the good military rice for fowl which were under the civil administration of the laboratory.

McCarrison pointed out that the milling of rice is not the sole cause of beri-beri, as long before the introduction of machine milling beri-beri was endemic in India.

He believes that the supplemental foods in a diet are important in determining the development of this disease whatever may be the kind of rice consumed.

Outbreaks of beri-beri are not common among wheat-eating populations, as people who eat white wheaten bread generally belong to the more highly civilized and richer countries where the diet is more varied and this vitamin is obtained from other sources.

In Newfoundland and Labrador the population subsists largely on bread during the winter and spring. Formerly when the bread was baked from brown flour, beri-beri was unknown, but later when pure white wheaten flour was introduced, beri-beri became common.

Beri-beri was rare in Norwegian ships prior to 1894. In that year improvements were instituted in the diet supplied to the sailors; one of these was that bread was to be baked from white wheaten flour instead of from rye flour. After this beri-beri frequently occurred in these ships.

Beri-beri also occurred among our troops in the Dardanelles and in Mesopotamia during the Great War, due to the consumption of white wheaten bread and to the absence of a suitable mixed diet; as a supplement to the bread, chiefly canned and preserved foods were being used.

In Mesopotamia the disease was confined to the British troops, and did not occur among the Indian soldiers. The reason for this was that the latter received *atta*, a coarsely-ground whole-wheat flour, and also a daily ration of dried pulses of various kinds which are rich in anti-beri-beri vitamin.

During the siege of Kut-el-Amara in 1916, beri-beri appeared early among the British troops, but later ceased when the white flour was finished and the troops received part of their flour ration in the form of barley-flour or *atta*. The Indian troops were not affected.

During the latter half of the siege the Indian troops suffered greatly from scurvy, while the British troops were not affected. The diet of the former was largely cereal, while the latter were protected by a large ration of meat, including horse-flesh. They consumed from eight to twenty ounces daily, and this apparently protected them from scurvy. No fresh vegetables were available.

Vitamin B_2, the Anti-dermatitis Vitamin or Anti-pellagra Vitamin (Vitamin G of some American writers).—Sufferers from pellagra get dermatitis on the face and hands and on those parts of the body exposed to sunlight, accompanied by disorders of the digestive system, and later by lesions in the nervous system with mental symptoms.

Pellagra was first described by the Spaniard Casal in 1735. Some time later it was recognized, and received its name, in Italy, where it has since been prevalent.

Early in the nineteenth century it was observed in France, and subsquently spread eastward across Europe to Hungary, Roumania, Turkey, and Greece.

In the United States pellagra first became seriously evident about 1909. In 1917, 170,000 cases were recorded among the negroes and poor whites in the southern states, with a high mortality.

Before the germ theory of disease became established (and fashionable) as the cause of certain diseases, many physicians recognized that pellagra and beri-beri were due to dietary deficiencies, but when the bacterial origin of disease was established by Pasteur, it was believed that these diseases must also be due to microbic infection.

Between 1843 and 1866 the French physician Roussel pointed out the very important fact that the history of the spread of pellagra in Europe is the history of the introduction of maize as a staple food.

Brought from America, maize reached first Spain, then France, and thence its use spread gradually eastward, and pellagra followed it across Europe into Africa.

At one time it was believed that pellagra was due to a poison contained in maize.

Cases have been reported among people on other diets—rice, millet and wheat-flour. These are exceptional, and pellagra should be regarded as almost exclusively a maize-eaters' disease.

It was found that the addition of meat and milk to the diet prevented and cured pellagra, and later in 1926 the value of yeast as preventive factor was proved by Goldberger and Tanner, who accidentally discovered that yeast was effective in preventing experimental black-tongue in dogs—a condition similar to pellagra in man.

Subsequently Goldberger and his colleagues were able to identify the pellagra-preventive factor with a vitamin contained in yeast, and differing from the anti-neuritis vitamin in its stability to heat and in its distribution in foodstuffs. This is now definitely known as vitamin B_2.

Vitamin C, the Anti-scorbutic Vitamin.

Scurvy has for many centuries been regarded as a disease due to dietetic deficiency. It was common knowledge in olden times among seafaring folk that scurvy occurred after deprivation, for long periods, of fresh foodstuffs, and that it could be prevented and cured by the use of fresh vegetables and fruits.

Lind in 1757 published "A Treatise on the Scurvy." In this he states: "On the 20th May, 1747, I took twelve patients in the scurvy on board the "Salisbury" at sea. Their cases were as similar as I could have them. They all in general had putrid gums, the spots, and lassitude, with weakness of their knees. They lay together in one place, being a proper apartment for the sick in the forehold, and had one diet common to all, viz., water-gruel sweetened with sugar in the morning, fresh mutton broth oftentimes for dinner, at other times light puddings; boiled biscuits with sugar, etc., and for the supper barley and raisins, rice and currants, sago and wine or the like.

"Two of them were ordered each a quart of cyder a day. Two others took twenty-five drops of elixir vitriol three times a day on an empty stomach, using a gargle strongly acidulated with it for their mouths. Two others took two spoonfuls of vinegar three times a day upon an empty stomach, having their gruels and their other food well acidulated with it, as also the gargle for their mouths. Two of the worst patients, with the tendons under the ham rigid (a symptom none of the rest had), were put under a course of sea-water. Of this they drank half a pint every day, and sometimes more or less, as it operated by way of a gentle physic. Two others had each two oranges and one lemon given them each day. These they ate with greediness at different times upon an empty stomach. They continued but six days under this course, having consumed the quantity that could be spared. The two remaining patients took the bigness of a nutmeg three times a day of an electary recommended by a hospital surgeon, made of garlic, mustard seed, rad-saphan, balsam of Peru, and gum myrhh, using for common drink barley-water well acidulated by tamarinds, by a decoction of which with the addition of cremor tartar they were gently purged three or four times during the course.

"The consequence was that the most sudden and visible good effects were perceived from the use of oranges and lemons, one of those that had taken them being

at the end of six days fit for duty. The spots were not indeed quite off his body, nor his gums sound, but without any other medicine than a gargarism of elixir vitriol, he became quite healthy before we came into Plymouth, which was on the 16th June.

"The other was the best recovered of any in his condition, and being now pretty well, was appointed nurse to the rest of the sick.

"Next to the oranges, I thought that the cyder had the best effects. It was, indeed, not very sound, being inclined to be aigre or pricked. However, those who had taken it were in a fairer way of recovery than the others. The putrefaction of the gums, but especially their lassitude and weakness, were somewhat abated, and their appetite increased by it.

"As to the elixir vitriol, I observed that the mouths of those who had used it by way of gargarism were in much cleaner and better condition than any of the rest, especially those who used the vinegar, but perceived otherwise no good effects from its internal use upon the symptoms.

"There was no remarkable alteration upon those who took the electary and tamarind decoction, the sea-water, or vinegar, upon comparing the condition at the end of the fortnight with others who had taken nothing but a little lenitive electary, and cremor tartar at times in order to keep their belly open, or a gentle pectoral in the evening for the relief of their breast."

Apparently the anti-scorbutic factor is found in nature, associated primarily with living plant tissues in which the active metabolic processes are still proceeding. When the active processes cease or are greatly reduced, as in seeds, this vitamin disappears. In the case of seeds it is created anew during germination.

Although present in the animal body in muscle, it does not appear to be stored there to the same extent as vitamin A, and it has been shown by experiments on guinea-pigs that previous administration of large amounts of vitamin C to the animals does not increase the time necessary for the development of scurvy.

Vitamins and Human Diets.

So far as this country is concerned, the rareness of well-marked deficiency diseases such as pellagra, beri-beri, xerophthalmia, and scurvy indicates that an absolute deficiency of vitamins rarely exists in the individual diet, but it is probable that much sub-normal health, under-development, and liability to infection may be associated with a partial deficiency of one or more of the vitamins. The influence of these deficiencies may be serious when they occur in early life, and judging from animal experiments an adequate supply of these vitamins in later life may fail to make good the damage caused by deficiency in infancy and childhood. There is also a danger that partial or latent deficiency may persist as a chronic condition in adult life, as many diets are deficient in vitamin supply, especially among the poor. Cereals are said to form sixty per cent. of the total food consumed in this country, and in the diet of the poor this percentage is higher on account of the relative cheapness of cereals. Cereal food, although it provides sufficient energy, is almost devoid of vitamins A, C, and D, and has been shown to have an antagonizing action on vitamin D.

In planning restricted diets which may require to be taken for prolonged periods, sight should never be lost of the vitamin content of the diet. This applies especially to the dietary of patients suffering from gastric and duodenal ulcers, colitis, diabetes, and nephritis, when patients are frequently kept for a long time on a totally inadequate diet as regards vitamins. In many cases, as a result of this, they become anæmic and debilitated, their resistance is lowered, and their power of recovery is lessened. The same difficulty occurs commonly in the case of children, who are frequently capricious and faddy about their food, and refuse to take certain articles of diet containing vitamins which are absolutely essential for their proper development.

In such cases it is the duty of the physician to secure the provision of these factors from other sources, including the artificially prepared substitutes which are now available.

VITAMIN CONTENT OF THE MORE COMMON FOODSTUFFS.

Vitamins	*A*	*B*	*C*	*D*	*E*
FOODSTUFFS.					
Cod-liver oil	+ + +	—	—	+ + +	—
Butter	+ +	—	—	+ +	0 to +
White bread	—	0 to +	—	—	—
Wholemeal wheaten bread	+	+ +	—	—	—
Wheat germ oil	+	—	—	—	+ + +
Oatmeal	0 to +	+	—	—	—
Potato (cooked)	+	—	+ +	—	—
Green peas	+ +	+ +	+ +	—	—
Cabbage, fresh, green	+ +	+ +	+ + +	—	+
Cabbage, cooked	+	—	+	—	—
Carrot, raw	+	+ +	+ +	—	—
Carrot, cooked	—	—	+	—	—
Lettuce	+ +	+	+ + +	—	+ +
Spinach	+ +	+	+ +	—	—
Apple	+	+	+	—	—
Orange	+	+	+ + +	—	—
Banana	+	+	+ +	—	+ +
Grape fruit	+	—	+ +	—	—
Lemon	—	+	+ + +	—	—
Tomato	+ +	+ +	+ + +	—	—
Beef	—	+ +	0 to +	—	—
Ox-liver	+ + +	+ +	—	—	+ +
Eggs	+ +	+	0	+ +	+
Cow's milk, whole, fresh	+	+	+	0 to +	+
Yeast	0 to +	+ + +	0	0	0 to +

Royal Victoria Hospital, Belfast

By Robert Marshall, M.D., F.R.C.P.I., D.P.H.

Opening Address of the Winter Session, 1935-6

It is now exactly a hundred years since the Belfast Medical School was formally opened as a department of the Royal Belfast Academical Institution, and surely it is a happy coincidence that one hundred years after its foundation the chairman of the Board of Governors of the Institution should be chairman of the honorary staff of the Royal Victoria Hospital.

It is over 108 years since Dr. James McDonnell, who should be for ever honoured as the founder of this charity, gave the first clinical lecture within its walls, and for many years it has been our custom that each member of its honorary staff should, in turn, give an address at the commencement of the winter session. The subjects of these addresses have varied at the discretion of the speakers, but all have these in common, first, that they have referred to the outstanding events and achievements of the preceding year, and, secondly, that each orator in turn has extended, as I do now, a very warm welcome to those who are commencing their clinical studies.

During this year the Hospital has lost its greatest friend: it was a fitting thing that the Viscountess Pirrie should have been our Lady President, for it is largely owing to her own inspiring leadership that 'the Royal' exists in its present form. Those of us who were privileged to know her will not soon forget the singular charm of her smile, and the compelling beauty and grace of her spoken word and gesture, while those who knew her best knew what a wise head she had, how kind a heart, and what pride and love were hers for the Royal Victoria Hospital.

Time brings changes, and some of these seem most untimely: in 1896, a young man named Thomas Sinclair Kirk was elected an assistant surgeon; in 1935, a young man named Thomas Sinclair Kirk has been elected a consulting surgeon. We still find it a little difficult to imagine Wards 9 and 10 without him after all these years of untiring and devoted service. We wish him many happy years as a consulting surgeon. On Mr. Kirk's retirement, Mr. Henry Price Malcolm was promoted surgeon, and, as his successor, we welcome Mr. Cecil Armstrong Calvert. Mr. Calvert entered the Medical School in 1917, and has served a happy, if laborious, apprenticeship as pupil, houseman, and surgical registrar: we wish for him that he too may become a consulting surgeon.

The Board of Management of this Hospital has long been noteworthy for its courage and enterprise, and during this past year has made three notable achievements: last October work was commenced on a new Nurses' Home to cost £72,500, in April of this year work was commenced on a pavilion for private patients, at a cost of £43,510; and last, but to my mind far from least, a superannuation scheme was instituted to which the nurses will not have to contribute, but

which will provide each with a pension of thirty shillings per week on reaching the age of retirement. I feel that staff and students alike will join us in congratulating the Board on a deed so generous and so well deserved.

The second part of my traditional duty presents much greater difficulty than the first—not that I am lacking in enthusiasm or warmth of welcome for our neophytes, but because I have made the astounding discovery that no first-year hospital student ever attends this opening lecture. I have made inquiries, and everyone I have asked is in the same position as myself, and does not think he attended the lecture, or, if he did, he cannot remember what it was about. This discovery appalled me, and I felt a wave of sympathy for my predecessors in this office, who had addressed wise counsel intended for the guidance of youth to Miss Mussen, Dr. Morrow, and the rest of us. But I have found a solution to the difficulty: I have brought my audience with me. I am not referring to any relative of my own who may have gate-crashed into this assembly, nor have I bribed any flesh-and-blood medical student to attend. It is much simpler than this, and not even original. I have simply copied Sir James Barrie, who invented Macconaghie to make his speeches for him: I have invented some one to listen to this one, which is perhaps more difficult. His name is MacPatrick, and he has passed his second medical in June. He is rather an elusive person; sometimes I feel that I know him very well, and sometimes I do not understand him at all. He has a good deal to say for himself about things that do not matter very much, but it is not so easy to find out what he is really thinking. For example, if you were to ask him why he "went in for medicine"—not that you would dream of asking him that: this is a question that no medical man ever asks another, although there are bitter moments when he asks it of himself. But if you were to ask MacPatrick, you would probably get an answer that was unsatisfactory or even impolite. It is not that medicine runs in the family, for his father is a farmer or a shopkeeper; and MacPatrick does not know that the answer to your question is written in Greek on the Robert Campbell Medal in words which Hippocrates used two thousand years ago: "Where there is love of humanity there is love of the art." MacPatrick does not discuss love of humanity, but nevertheless this is the reason why he is a student of medicine. As I have said, he gives unsatisfactory answers to questions. When I asked him what he thought of "The Northman's" statement last January that Queen's has no tradition, he thought that I was referring to a member of a football team, and said Queen's would win the Senior Cup next year. I explained that "The Northman" was a literary organ published in connection with his university, and that the issue with this statement had probably been sent to many other universities. He gave me the impression that it did not matter very much anyhow.

So I propose to address the remainder of my remarks to him, and I heartily wish that I could reverse what one so often does with the wireless, and quietly fade out those visible members of my audience to whom what I am about to say will seem an oft-told tale. It will at least be short, for how can I, even by "jumping o'er times, turn the accomplishment of many years into an hour-glass"?

I do not propose to try to tell you the story of 'the Royal,' but I should like to try

to tell you what manner of house this is into which you have come to serve, and how it comes to be here like a great tree grown from a tiny seed; and I should like, if I am able, to tell you something of the men who planted the seed, little dreaming what would come of it. If only I can tell you this, as clearly and plainly as I could find it in my heart to do, you would learn something this morning of the tradition of 'the Royal,' just as a recruit in a British regiment learns in his first year the history of the regiment, in order that he may share in its pride and its tradition. Tradition is still one of the most powerful things in the world, and one of the most difficult to define. The Oxford Dictionary defines it as "that which is handed down, a statement, belief, or practice handed down, especially orally, from generation to generation." This is a good definition, but perhaps the greatest traditions are those which are passed on from one generation to another by something which is not even talked about, by a way of doing things, or of not doing things.

In 1792, which marked the beginning of our history, Belfast presented a very different aspect from the city as we know it, and, at first glance, was a much prettier and more romantic place. It was then described as "uncommonly picturesque and beautiful—the pleasantest spot in the North of Ireland." It was a small place then, and, looking at its map, one wonders how it housed its eighteen thousand inhabitants. Its northern limit was the Charitable Society's "Poor House," which still overlooks Donegall Street, and on the southern side of the White Linen Hall, which your father remembers on the site of the City Hall, a new street called Linenhall Street strayed out towards the Pass Loaning, still fringed with trees. The Long Bridge, which had been damaged by Schomberg's artillery, led to the rural delights of Ballymacarrett, and on the western side the site of the Institution was described as "almost a waste and desolate spot." There were some fine houses and pleasant old-world gardens in the town : the Marquess of Donegall lived at one corner of Donegall Place, and the Massereene family at the other; the Earl of Westmeath had a house in Castle Lane, and the first Lord Londonderry had a residence in High Street. Our founder, Dr. James McDonnell, practised medicine at 13 Donegall Place. It was a busy and prosperous town, and rapidly growing in size and importance. No fewer than twenty-five ships traded between here and the West Indies, and one can picture High Street, and Skipper Street and Pottinger's Entry and Winetavern Entry, full of their merchandise : cargoes of mahogany, tobacco, sugar, rum, spices, cotton, dyestuffs, oil-hemp, dried fish, wines, fruits, and soap-ash were discharged, and the ships were loaded with beef, corn, hides, salmon, herring, tallow, butter, and cheese. Think of their mingled odours ascending with the peatsmoke of a thousand chimneys! The surroundings of the town must have been very beautiful—there was no ribbon development in those days, and the countryside was dotted by gentlemen's residences with familiar names : Malone House and Macedon, Maryville and Myrtlefield, Belvoir Park and Ballydrain, and Purdysburn and Parkmount. It was an exciting place to live too : Thurot's landing at Carrickfergus was within living memory, and the recent French Revolution was eagerly debated. Theological

differences of opinion were just as sharply defined then as now, and drew much larger congregations. For those of lighter mind, the new theatre had its attractions and was, in the course of a few years, to be "celebrated throughout Britain." There were no football matches, but there were cock-fighting and bull-baiting for the poor, and fox-hunting for the rich, and much card-playing by the ladies in the late afternoon and by the gentlemen in the very early morning. It was a period of great desire for knowledge, for culture, and for social betterment. The middle classes were thrifty and prosperous, and formed societies for their mutual improvement: Dr. James McDonnell was founder and first president of the Belfast Literary Society in 1801, and of the Irish Harp Society in 1807. Dr. S. M. Stephenson, one of our first physicians, was the father of the Belfast Reading Society, later the Belfast Library and Society for Promoting Knowledge. Another, Dr. S. S. Thomson, was president of the musical society known as the Anacreontic, found in 1814, a predecessor of the Philharmonic Society. The Galvanic Society of 1806 became the Philosophic Society of 1808, with Dr. Robert McGee as its first president. The first school for the blind was commenced by Dr. Alexander McDonnell, our founder's brother, in 1801, and afterwards joined with an institution for the deaf and dumb which has been housed for many years on the Lisburn Road. Our own Ulster Medical Society, founded in 1805, with Dr. S. S. Thomson as its first president, and Dr. Andrew Marshall, a surgeon of this Hospital, whose portrait may be seen in the Boardroom, as its first honorary secretary.

A further proof of its commercial prosperity may be inferred from the fact that there were two banks in Belfast in those days, with many good shops and stores; little linen was made in the town itself, but there were twelve bleach-greens within the parish boundary, and the docks were repeatedly being made wider and deeper to accommodate larger ships.

There is, however, another side to this attractive picture. I can perhaps best sketch it for you by reading you an extract from the prospectus which was issued by thirty-nine representative citizens on 13th April, 1792, appealing for funds to found a general dispensary for the sick poor (and this was the planting of the seed) :—

"The importance and utility of the industrious poor to a civilized and commercial nation are indispensable, yet little attention has been paid in this country to the preservation of their lives and healths. Besides the misfortunes to which labourers and artists are liable in common with the rest of mankind, there are many peculiar to themselves—exposed to the inclemency of the seasons, living upon unwholesome food, and crowded into narrow habitations, they become a prey to various diseases; and supporting the existence of to-day by the scanty produce of yesterday's labour, a short sickness reduces them to uttermost misery. . . . If the numbers of lives annually lost by the ravages of smallpox did not of itself point out the necessity of some association for the inoculation of the children of the poor, yet another inducement of the most urgent nature would be found in the frequent occurrence of blindness from the same cause among the lower classes. How many

of our fellow-creatures are compelled, by this cruel malady, to wander over and disfigure the face of this flourishing country, whose useful labours might otherwise contribute to the support of families and the public good."

The appeal went on to say that "as soon as subscriptions have amounted to fifty pounds, the subscribers shall proceed to nominate an apothecary, two physicians, and two surgeons, and also such other officers as may tend to secure order, permanency, and utility to so laudable an undertaking."

The sum of fifty pounds was rapidly subscribed, and a meeting of subscribers was held on 16th May, when no fewer than forty-eight laws and regulations were passed—almost one for every pound subscribed. It always amazes me that this Institution, which runs smoothly on the "simple little rules and few" of common sense and kindness, should have been born with a cord of red tape round its neck.

The first honorary staff consisted of Dr. Halliday and Dr. Mattear as consulting physicians, Dr. McDonnell and Dr. White as attending physicians, Mr. Fuller and Mr. McClelland as attending surgeons. It is interesting to note that, pending the election of Mr. Hull as apothecary at forty pounds a year, the surgeons were expected to dispense medicines for the physicians. The Belfast Charitable Society kindly provided rooms, and, thus launched on its career, the work of the dispensary appears to have proceeded smoothly enough for some five years; rough waters were ahead, however, for, in 1797, financial support had so diminished as to be almost non-existent, and a committee of five met on 5th January to inquire into the possibility of keeping afloat. It was felt that a dispensary was not enough, and that the increase of fever alone demanded a hospital for in-patients. (Perhaps I should say that in those days no distinction had been made between typhus and typhoid fevers.)

After several meetings, public interest was sufficiently roused to justify the taking, at an annual rent of twenty pounds, of the house of a Mr. Pollard in Factory Row, Smithfield, in which a nurse and six bedsteads were installed. On 4th May, 1797, Dr. S. M. Stephenson and Dr. McDonnell, as physicians, with Messrs. McClelland, Bankhead, and McCluney as surgeons, entered upon their duties. Sad to relate, by October of that year the slender capital was exhausted, and although sixty patients had been treated, with only one death, it seems that the hospital had to close its doors. After a lapse of two years, in 1799 the following members, afterwards described by Dr. A. G. Malcolm as "the bone and sinew of the charity"— Rev. Wm. Bristow, Vicar and Sovereign; Dr. McDonnell, Mr. Clark, Mr. R. Bradshaw, and Mr. Valentine Jones—met in the coffee-room of the Exchange for the purpose of reviving the hospital. The last-named was honorary secretary and for a time-treasurer, the first of a distinguished line to hold such offices, and as enthusiastic as Dr. McDonnell himself. With funds (about £113) principally derived from the proceeds of a special sermon by Mr. Bristow, a fresh start was made. Three houses in Smithfield were rented, and Dr. McDonnell and Mr. Fuller appointed as physician and surgeon respectively. In 1803, however, finances again ebbed, and at a special meeting of Committee "a subscription of

five guineas each was raised on the spot, rather than permit the Institution again to sink into oblivion." So the hospital kept its doors open and steadily gained the appreciation of the public, and the year 1810 marked a new phase of the story.

Dr. McDonnell and his colleagues of the committee and staff, made bold by the continued success of their efforts, waited on the Marquess of Donegall and obtained promise of a plot of ground for building purposes. The place chosen was in Frederick Street, and the plot was let for grazing until required. It was in 1815 (Waterloo Year) that the plans of Mr. Blair, an architect, were approved, and the foundation stone laid with considerable ceremony by the Marquess of Donegall. The account of this may interest you. In the centre of the stone were placed various articles, emblematic of the civilization of the period. A piece of pottery of exquisite workmanship, several silver and copper George III coins, a copper Jubilee medal, a Belfast almanac and a map of the town, a small quantity of linen yarn of one hundred hanks to the pound, impressions of the seal of the town and of the Academical Institution, a small Bible about two inches square, a specimen of letterpress printing, a manuscript in Irish character, and an inscription in Latin, which I have freely translated as follows :—

"This Hospital, dedicated to the sick and to the art of medicine, for the public health, for the cure of diseases, for the solace of suffering, and for the practice of medicine and surgery, the citizens have here erected under favourable auspices, amid the great goodwill and approval of the people and of the medical faculty, the first stone of the building having been laid by that most noble George Augustus Marquess of Donegall on the 5th of June, in the year of our Lord, 1815, and in the thirty-fifth year of the reign of King George the Third."

You may think me one of those tiresome people who cannot resist the obvious when I direct your attention especially to the following words: "This hospital, dedicated to the sick and to the art of medicine," and when I tell you that though the stone with those words enclosed in it lies buried in the derelict hospital in Frederick Street, they remain the guiding principle of this house, and I would further have you note that the sick man is first and the art of medicine second.

We can well imagine with what pride James McDonnell and Valentine Jones watched the completion of the building at a cost of five thousand pounds, and we read that its walls were wet and its staircases scarcely secure when its first patients were admitted on 1st August, 1817. During this year a resolution was passed by the staff: "That the physicians and surgeons of Belfast should be invited to place their pupils there to acquire experience by observing its practice, and in the course of a few years it might become a school of physic and surgery of no trifling importance to the young medical students of this neighbourhood and the province of Ulster." It was not until 1820 that the admission of pupils was authorized—each physician or surgeon to the Hospital to be allowed to introduce one pupil to assist in the care of his own patients, and each to be responsible for the conduct of his pupil. The first such pupil was Mr. W. Bingham, who afterwards practised in Downpatrick. When *you* become a resident pupil, if any houseman speaks harshly to you, you can comfort your soul by remembering that *you* belong to the senior

service, for there was no house surgeon until Dr. W. Johnston was appointed in 1838, while house physicians are relatively upstarts! It was not until 1882 that James Alexander Lindsay was appointed the first house physician. (He was, as you ought to know, the great little man who taught us medicine.) This system of resident pupilship has been for over a century the distinctive feature of Irish medical teaching, and it is interesting to note that the General Medical Council now apparently wishes to introduce it into the English and Scottish schools. You *must* become a pupil: it is the most important part of your course. You will learn without knowing that you are learning—by a sort of osmosis—in the wards and in the externs, and in the east wing too; and I hope that by the time you are resident, this present separation of pupils' and housemen's dining-rooms will be over, and that you will all dine together, as your predecessors have done for ten decades.

1827 marks another stage in our history, for it was in that year that Dr. McDonnell, then sixty-five years of age, gave the first formal clinical lecture. His subject was Systematic Medicine, and surely this was a good title for our first "clinique." The need for a medical school was even then keenly felt. Ulster students went in considerable numbers to Dublin and to Edinburgh, and it was sad to read in a letter written by one of them in Edinburgh that "to be a student of medicine is a term of contempt, but to be an Irish student of medicine is the very highest complication of disgrace." So they must have been pleased when the Royal Belfast Academical Institution, founded in 1810, of which you yourself may be an alumnus, decided to form a medical department. It was in the autumn of 1835 that this was opened, and the following gentlemen were appointed to their various chairs:—Anatomy: Dr. James L. Drummond. (Professor Drummond had been teaching anatomy in "Inst" since 1818. He also taught botany, but in 1836 Dr. William Mateer was appointed professor of this subject.) Midwifery and Diseases of Children: Dr. Robert Little; Materia Medica and Pharmacy: Dr. J. D. Marshall; Chemistry: Dr. Thomas Andrews; Surgery: Dr. John McDonnell; Medicine: Dr. Henry McCormac. The new Medical School was fortunate in its choice of professors, and that good fortune has never deserted it. Of the original "team" whose names I have read to you, the most distinguished were Thomas Andrews and Henry McCormac. The former was born in Donegall Square in 1813, and was himself an Instonian. He published his first scientific paper, "On the Use of the Blow-pipe on Flames," at the age of fifteen, had already studied in Dublin, Paris, and Edinburgh, and practised as a surgeon in Belfast, before finally deserting medicine for pure science on his election to the chair of chemistry at the age of twenty-three. When a medical student he wrote the following in a letter:—"There is one great source of pleasure in the medical profession which few other pursuits afford to the same degree—the great and intense interest in the subject which affords one so much excitement; and although this is too often a cause for great anxiety, yet I believe there are few medical men who would willingly exchange their pursuit for any other." It was fortunate for science that he personally did make the exchange, and his researches gained for him enduring fame, and, incidentally, the fellowship of the Royal Society.

Dr. Henry McCormac, the first Professor of Medicine, is chiefly remembered because he was the first to insist on fresh air in the treatment of tuberculosis. It is said that he had to appear in the police court for breaking his patient's windows with his umbrella. It is not so widely known that he was the first to recognize that phthisis and "surgical" tuberculosis were one and the same disease. He was a man of great erudition, and conversant with twenty languages. His son William was for a time surgeon to the Hospital; he went to London, where he became Sir William McCormac, Baronet, President of the Royal College of Surgeons of England. This is the only Hospital which has given Presidents to both the English and Irish Colleges of Surgeons—for Professor Andrew Fullerton was elected President of the Irish College in 1926. Henry McCormac worked so hard for the sick poor during the great cholera epidemic of 1832 that he was made the recipient of a public testimonial. The story of that epidemic is worthy of a paper of its own; briefly it is this: In 1830 the Hospital Committee and staff, even then in the midst of a typhus epidemic, and with smallpox an ever-present menace, were faced with a new terror: the dreaded Asiatic cholera had crossed the Russian frontier and had commenced its march across Europe. When its approach seemed imminent, in November, 1830, the sum of seven hundred pounds was raised, a special building erected as a cholera hospital at the rear of the Frederick Street Hospital, and shortly afterwards a large building in Lancaster Street was rented for the quarantine of contacts. Two cholera stations for night medical attendance and a supply of palanquins to take patients to hospital were also established in different parts of the town. Four months elapsed before the first case appeared in the person of one Bernard Murtagh of Quay Lane. His condition was correctly diagnosed by Surgeon McBurney, and it is noteworthy that he was visited by a number of other practitioners anxious to be able to recognize the disease. Before the end of 1832, 2,870 persons had been attacked, with 480 deaths. The second cholera epidemic in 1849 gave rise to 2,051 cases with a death-rate of one in three. In the annual report of the Hospital for 1847 we read that "seven dispensary doctors contracted typhus fever, but all recovered, a fact peculiarly gratifying to your Committee when it is considered that the mortality from fever among the medical profession in Ireland during the past year has been considerably greater than that of the British officers engaged in the Peninsular War." The dispensary doctors were paid fifty pounds per annum at that time; the Hospital staff was then, as always, honorary.

In 1845 James McDonnell died at the age of 82 years. Few men could look back on lives of greater honour or usefulness. He was born near Cushendall, and qualified in Edinburgh in 1784. His thesis was entitled "On the Drowned," and in it he discussed various methods of resuscitation, including, in the last resort, transfusion of blood. When he commenced practice in Belfast the population was approximately fourteen thousand persons, and we know that some few years later there were nine doctors in medical practice. He lived to see the population grow to some eighty-five thousand, with some seventy medical practitioners, and during that lifetime he had, largely by his own enthusiasm, created the Hospital which

you have now entered, and the medical school of which it is a part. I should like to read for you two references to him. The first was written in a private letter in 1788, when he had been some two or three years in practice: "There is little doubt of his getting fast forward . . . he is said to be sensible and modest, but these are not qualifications which generally gain the middling or lower sort of people—smart, impudent fellows who rail at their seniors and their systems oftenest succeed. This McDonnell avoided."

The second is from Dr. A. G. Malcolm's History of the Hospital, published in 1851: "Friends flocked around him in admiration of his talent, and long before the ordinary period of professional fame he became celebrated as one of the first physicians, not alone in Belfast, but in the whole country around. . . . He gathered around him the great spirits of the age, and no contemporary of any note in Britain was ignorant of his profound learning and distinguished name. It would seem, indeed, that so great and varied was his intellectual capacity, that he was enabled, almost single-handed, to stamp a literary face upon the entire locality . . . he spared neither his time, his pocket, nor his labour in his devotion to the charitable institutions of the town; and to the very latest period of his protracted life, his heart was filled with that love that wearies not in well-doing. The Dispensary and Fever Hospital were peculiarly the objects of his unceasing care. So long as health permitted, he was to be seen working in the districts like a very slave, or toiling in the wards for hours. It is recorded that his devotion to the poor occasionally interfered with his attentions to the solicitations of the rich; but, however this may be, while he gained the gratitude of the one, he lost not the respect nor admiration of the other." He accumulated a considerable library, and, in his spare time, loved to obtain specimens for his natural history museum. For many years it was his custom to pay a fortnightly visit to his mother at Cushendall: he left Belfast on horseback at midnight, changing horses at Glenarm, and after a few hours in his own home, rode back again, completing the double journey in twenty-four hours. One of his sons became the first professor of surgery in the Medical School, but soon resigned his chair, as he went to practise in Dublin; another was a distinguished scholar of Oxford University. When he (Dr. McDonnell) became a consulting physician to the Hospital, after some forty years of work for it, he was presented with a service of plate valued at seven hundred pounds, "by the nobility, ladies, and gentlemen of Belfast and its vicinity."

When next you are at Cushendall, perhaps you will walk a mile to the little churchyard of Layde overhanging the sea: James McDonnell is buried there, his family's burial place since 1647; his grave is marked by a Celtic cross beautifully carved with scenes from the life of our Lord, but in this Hospital you will seek in vain for any memorial to him except that which, all unknowing, he commenced himself in 1792.

It was in this same year, 1845, that Andrew George Malcolm became a physician to the Hospital. He was not only a great clinical teacher, but a pioneer of sanitary reform. He was the first to advocate the medical examination and supervision of factory workers. He was only 38 when he died, and I cannot think that anyone

ever had a greater love for his Hospital. It was he who wrote in 1851 the History of the Belfast General Hospital, from which I have quoted repeatedly this morning. The copies of this book are now very scarce, but I wish that I could give one to you, and to every first-year hospital student, so that you could discover for yourself the quaint, old-fashioned charm of his style, and his love for humanity and love of his art. You may compete very soon for the Malcolm Scholarship established by his widow. I should like to read you one more passage from his book, this time from the preface:

"How many of the few hundreds who give their annual mite to the support of the Belfast General Hospital are aware of the immense amount of relief which this charity has afforded since the period of its foundation—of the existing invaluable benefits which are freely bestowed upon the town through its incessant operations—of the numbers of hard-working artizans and toiling labourers whose descent into the abyss of irreclaimable poverty its friendly hand has timely prevented? 'Few and far between,' we fear are those who can appreciate the almost boundless extent of its charity. Those who, like ourselves, have almost lived about it, may possess a fair idea of its never-ceasing utility; but the mass who may know at the most that there is such an institution, how can they conceive of its paramount importance?"

I think that if the editor of "The Northman" had read this book before stating in print that Queen's had no tradition, he might have realized that when the college was opened in 1849 Queen's had already a birthright, an endowment, a tradition handed down to her from Factory Row and Frederick Street as well as from College Square.

The sand slips through the hour-glass, and very reluctantly I must leave it to others to tell you the later developments of the story of 'the Royal': of the Charters and Mulholland wings, added in 1865: of the operating-theatre designed by Sir Charles Lanyon, and of the gift of the Throne Hospital in 1874, and how in 1903 this present Hospital was opened at a cost of £120,000; of the subsequent addition of the King Edward Memorial Building, of the additional wards and laboratories, and of how the X-ray department, once the Cinderella of the Hospital, met her Prince Charming and grew to be rich and powerful.

I should have liked to try to tell you something of James Cuming, scholar and physician, and of Alexander Gordon, "the master-surgeon." Most of all, I regret that I cannot this morning tell you of the great ones who were our teachers—Sir William Whitla, Sir John Byers, Sir John Walton Browne, Dr. Lindsay, Dr. McQuitty, Dr. McKisack, Dr. MacIlwaine, Mr. Robert Campbell, and Mr. Andrew Fullerton. I should be a graceless fellow if I were to say no word of the matrons, sisters, and nurses, on whose loyal co-operation all advance depends; or of the men and women who, as members of the Board, as life-governors and as donors and collectors of money, have made the story possible, and of what has impressed me, and will impress you most of all in your work here—the amazing courage and fortitude in the face of suffering and adversity which you will see every day within its walls.

Many possible careers open out for you once you have passed your 'final': whichever you choose I wish you well. I have no need to ask you never to forget 'the Royal': you cannot realize this morning what a place it will make in your life. I cannot wish you greater happiness that that you should continue to serve it—and, if you do, I can address to you the words which Barrie gave to the students of St. Andrews:

"Despite the imperfections of your betters, we leave you a great inheritance for which others will one day call you to account."

REVIEWS

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It is many years since a general textbook of anæsthetic agents and their administration has been published, and Dr. Nosworthy's book is very opportune. In it the older anæsthetics are considered in some detail, as it has been recognized that in spite of the great advances in new drugs and apparatus, chloroform and ether still have large fields of usefulness, and that a sound knowledge and experience of these two drugs is essential for any person giving anæsthetics. No mention is made, however, of the use of chloroform capsules in midwifery, or of that useful piece of apparatus, Pincin's bomb, for giving warmed ether vapour. Super-heated ether is of such recent introduction that its omission from a textbook is understandable.

The revival of interest in nitrous oxide and oxygen has produced many machines for their accurate and easy administration. These are dealt with adequately. The basal hypnotic agents are dealt with in a pleasing and balanced manner, but no mention is made of the fact that avertin in expert hands has been shown to be a useful "complete" anæsthetic.

Spinal anæsthesia is also well treated, and the advantages and limitations of the various preparations clearly indicated. We can confidently recommend this book to every medical student, who should read and study it before and during his practical training in anæsthetics, and also to those already qualified, as there are many valuable aids to better and safer anæsthesia which should be useful to them.

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The scope and object of the present edition remain as before—the methods how best to demonstrate physical signs, and to explain clearly the inferences which may be deduced from them. The author has wisely avoided the temptation to enlarge the book, and though there appears to have been a complete revision of the text, and several new illustrations added, it has not been lengthened to any appreciable extent.

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The Ante-Natal Care of the Expectant Mother, with Reference to the Prevention and Treatment of the Toxæmias of Pregnancy

By H. L. HARDY GREER, M.B., F.R.C.S.EDIN.,
from the Royal Maternity Hospital, Belfast

NUMEROUS articles in the medical journals and the daily newspapers have recently called our attention to the high maternal mortality and the question of anæsthesia in labour. How large a part the toxæmias of pregnancy play in producing our present high maternal mortality is not fully realized. Professor Stander, of the department of obstetrics of Johns Hopkins University, says: "By the term 'toxæmias of pregnancy' is usually understood a group of disorders associated with gestation which account for about twenty-six per cent. of the total maternal mortality incident to childbirth. To correctly classify, determine the etiology of, and successfully treat these disorders, has been and still is one of the most important problems in obstetrics." In the final report of the departmental committee on maternal mortality and morbidity, 17.6 per cent. of the deaths were recorded as due to eclampsia and the toxæmias.

INCIDENCE.—Cruickshank, Hewitt, and Couper, in their report to the Medical Research Council on a study of 23,630 cases of pregnancy in Glasgow, found 6.6 per cent. of cases of toxæmia, i.e., albuminuria, pre-eclamptic toxæmia, eclampsia, and nephritis—in other words, an incidence of one in fifteen cases.

From the reports of various English hospitals, I found that out of 11,458 ante-natal cases there were 678 cases of toxæmia requiring admission to hospital—an incidence of one in seventeen.

In the years 1930 and 1931, out of 2,551 cases attending our ante-natal clinic at Townsend Street, there were 164 cases of toxæmia admitted for treatment—an incidence of one in sixteen.

CLASSIFICATION OF CASES.—Stander's classification is :—

1. Vomiting of pregnancy.
2. Low reserve kidney.
3. Nephritis complicating pregnancy.
4. Pre-eclampsia.
5. Eclampsia.
6. Acute yellow atrophy of the liver.

Cruickshank, Hewitt, and Couper classify cases into four groups :—

1. Albuminuria, which corresponds with Stander's low reserve kidney.
2. Pre-eclamptic toxæmia, which corresponds with Stander's pre-eclampsia.
3. Nephritic toxæmia, which corresponds with Stander's nephritis complicating pregnancy.
4. Eclampsia.

The latter classification is a useful clinical one :—Group 1, albuminuria; group 2, pre-eclamptic toxæmia; and group 4, eclampsia forming a series of increasing degrees of severity of the same type of toxæmia.

Etiology.—Many differing views have been put forward regarding the etiology of the toxæmias of pregnancy. Excluding chronic nephritis complicating pregnancy, the chief of these are (C. H. C.) :—

1. That the toxæmias are due to a failure on the part of the mother to deal with the large amounts of normal waste products which arise from the fœtal and maternal metabolism during pregnancy.
2. That the fœtus produces some abnormal substance or substances which, on entering the maternal circulation, give rise to intoxication.
3. That the cause of the toxæmias of the second half of pregnancy is to be found in the placenta.

No explanation of the condition meeting with general acceptance being forthcoming, the practising obstetrician is forced to adopt some simple working rules to guide his treatment, which should preferably be prophylactic.

As a student I was taught to test the urine for albumen, in order to prevent the onset of eclampsia. At the present day obstetricians should have as their aim, by ante-natal supervision, the prevention, if possible, of the onset of even the milder form of toxæmia as shown by the appearance of raised blood-pressure and albumen in the urine. In order to see how far this is possible, I have analyzed my last hundred consecutive private midwifery cases. By private midwifery cases I mean those which I have had under my care during pregnancy and labour.

Before giving you the results of my analysis, I shall enumerate the factors which, in my opinion, predispose to the onset of toxæmia in the pregnant woman. These are :—

1. Poor general hygiene—lack of fresh air and exercise, late hours, especially in stuffy, overcrowded atmospheres, excessive smoking, and alcohol.
2. Unsuitable diet, especially overfeeding and a diet either poor in vitamins or predisposing to acidosis.
3. Constipation.
4. Chronic focal sepsis, especially of the teeth, tonsils, or cervix uteri.
5. Occurrence of acute infections such as colds, influenza, and sore throat, and pyelitis of pregnancy.

Accordingly, to avoid these unfavourable factors, I insist on the following simple rules being carried out :—

Hygiene—proper ventilation in the home, with open window in bedroom.

Daily exercise in the open air, taking the form of walking, preferably twice a day, for an hour each time, but in the later weeks of pregnancy stopping short of fatigue.

Retire to bed at about 10.30 p.m.

Rationing of cigarettes to not more than five per day.

Avoidance of alcohol.

Diet.—Plenty of fruit, vegetables, and salad, butter to taste, moderation as

regards eggs, meat once a day, and avoidance of rich dishes, fries, pastries, and cream. One or two glasses of buttermilk daily. Patients are warned against eating to excess. Constipation is generally corrected by the regular daily exercise, the diet, and encouragement to drink water in the morning and at night. Where an aperient is necessary, syrup of figs or some of the paraffin emulsions are advised. A salt-free diet is a useful preventative of œdema.

Sepsis.—The teeth are examined and visits to the dentist arranged. Any infected teeth are removed, one at a time, under local anæsthesia. The tonsils are examined and the help of a throat specialist and or a bacteriologist sought.

Infections of the cervix uteri are treated with five per cent. or ten per cent. silver nitrate or brilliant green.

Acute Infections.—Undoubtedly the occurrence of a bad cold or a sore throat may precipitate the onset of well-marked albuminuric toxæmia, while an attack of influenza or a septic throat frequently precipitates labour, often with disastrous consequences to mother and child. Patients should, therefore, be warned to avoid close contact with anyone suffering from cold or sore throat or influenza.

Skin and Kidneys.—Free elimination by the skin and kidneys should be promoted by daily baths and an adequate amount of fluid.

Prevention of Acidosis.—As is well known, in pregnancy there is an increased tendency to acidosis. In 1922 I began to give patients attending the ante-natal clinic a simple alkaline powder for the relief of heartburn. I noticed, as time went on, that the urine of these patients was usually alkaline in reaction and that the occurrence of albuminuria was infrequent amongst them. I therefore began to give the powder as a routine in the second half of pregnancy. Since then papers have been published by Rivett of Queen Charlotte's Hospital, Cameron and Thompson of Glasgow, and others, advocating alkalies in the prevention and treatment of toxæmia. The powder I have used for some time is:—Mocol, mag. carb. pond., calc. carb., sod. cit.—1 oz. of each. *Dose:* Drs. 1 t.i.d., p.c., ex. aq. Cameron and Thompson give a tablet of:—Calc. sod. lactate, grs. 7½; pot. cit., grs. 40; sod. bicarb., grs. 20. *Dose:* 3 or 4 per diem.

Analysis of One Hundred Cases.—Of the hundred cases 57 were primigravida, 31 were two-gravida, 7 were three-gravida, 3 were four-gravida, and 2 were five-gravida.

Age.—Fifteen were between 20 and 25, 38 were between 25 and 30, 26 were between 30 and 35, 16 were between 35 and 40, while 2 were over 40, the elder being 45.

Ante-Natal Visits.—The hundred cases were seen and examined 415 times, an average of slightly over four visits per patient.

Blood-pressure.—The highest recorded systolic blood-pressures were as follows:—One case did not rise above 110 mm., 16 did not rise above 120 mm., 47 did not rise above 130 mm., 25 did not rise above 140 mm., and 8 did not rise above 150 mm. Two cases were above 150 mm., while one case passed 170 mm.

Age and Blood-pressure.—Of the eighteen cases over 35 years of age, in nine, or fifty per cent., the blood-pressure did not rise above 130 mm.; in six, or thirty-three

per cent., the blood-pressure did not rise above 140 mm.; while in three, or seventeen per cent., the blood-pressure rose above 140 mm. In the whole group, in sixty-four per cent. the blood-pressure did not rise above 130 mm., in twenty-five per cent. the blood-pressure was not above 140 mm., while in eleven per cent. the blood-pressure was above 140 mm. The tendency is, therefore, for rather high blood-pressure to be recorded at the older ages.

Maturity.—Fifty-four cases were delivered in the fortieth week, eight cases were post-mature; eighteen cases came into labour during the thirty-ninth week, six during the thirty-eighth, six during the thirty-seventh, three during the thirty-sixth, two during the thirty-fifth, one during the thirty-third, and two during the thirty-second week.

Results to Mother.—There was one maternal death. This was a case of ulcerative colitis complicated by pregnancy. I was asked to see her when she was four months pregnant. The question of induction was debated by the consulting physician in charge and myself, and finally it was decided that interruption of pregnancy would be as risky as non-interference. She continued to keep fairly well until about the thirty-first week of pregnancy, when she had a relapse, developed a peri-rectal abscess which resulted in a recto-vaginal fistula. In the thirty-third week she came into premature labour and was delivered of twins. Post-partum haemorrhage and retained placenta completed the tragedy, and she died in a few hours.

Results to Infants.—Ninety-seven infants were born alive, ninety-five survived, while two premature twins died during the first week. There were four premature still-births; one of these was a macerated fœtus at thirty-second week, associated with placental infarcts in a primigravida aged 39. One child was still-born at the thirty-second week with the cord tightly twisted round its own axis from umbilicus to placenta. Another child was still-born at six months, cause unknown, whilst a fourth was a macerated anencephalic at the thirty-fifth week.

Cæsarean Sections.—There were eleven Cæsarean sections. Two of these were repeat Cæsareans, one for contracted pelvis. The others were as follows:—Three for mitral stenosis, two for contracted pelvis, two for fibroids (one showing red degen., aged 42), one for placenta previa, one for a primigravida aged 15, married some years.

Albuminuria of Pregnancy and Eclampsia.—There was no case of eclampsia. Only one case developed albuminuria. She was an Italian woman of 21, pregnant for the first time. In spite of all I could say, she continued to do all those things she should not have done—stayed indoors in a stuffy atmosphere all day, ate large meals of rich food, innumerable chocolates, and stayed up until one and two o'clock in the morning, and omitted to take her alkaline powder. Her pressure slowly increased to 140 mm., but the urine remained free from albumen, until at the thirty-sixth week her pressure suddenly jumped to 172/98 mm., and albumen appeared in the urine for the first time. I sent her into the nursing-home at once and commenced treatment. On the third day she came into labour spontaneously and was delivered of a living baby weighing four and a half pounds. Both did well, and the albumen rapidly disappeared and pressure became normal.

Pyelitis of Pregnancy.—Two cases developed B coli pyelitis. The first was a mild case beginning about the fourth month. It cleared up under treatment in a few weeks and did not recur. The second was a more severe case with rigors and high temperature, beginning about the thirty-seventh week. She improved under treatment, but was still febrile when she came into labour in the thirty-ninth week. She delivered herself spontaneously, and was afebrile in forty-eight hours. Both she and her baby did well.

External Version in Breech Cases.—I am a firm believer in the usefulness of this manœuvre. One patient had a breech with each of her three pregnancies. I had to turn once the first time, twice during the second pregnancy, and four times in the third pregnancy. Each time she was safely delivered of a living child by the vertex.

Established Toxæmia.—Taking the classification of Cruickshank, Hewitt, and Couper as a basis, I propose to consider the first three groups—albuminuria, pre-eclamptic toxæmia, and nephritic toxæmia, leaving eclampsia out of consideration, as this paper does not purport to deal with it. The first two groups differing merely in degree, I shall refer to briefly as albuminuria, mild or severe, and the third group I shall refer to simply as nephritis.

SYMPTOMS. C.H.C.

	Group 1	Group 2	Group 3 (N)	Group 4 (E)
Oedema	25%	90%	90%	70%
Headache	50%	70%	60% (severe)	20% (severe)
Vomiting	Seldom	50%	33% (severe)	Nearly all, 25% severe
Visual disturbances	20%	50%	50%	20%
Giddiness	10%	25%	25%	10%
Drowsiness	Few	33%	20%	Few
Epigastric pain	—	5%	5%	20%
Jaundice	Few	Few	Few	Few
Mental symptoms	Nil	14%	Nil	Amnesia in 20%
Blood-pressure	Av. 125 mm.	Av. 155 mm.	Av. 164 mm	Av. 168 mm.
Amount of albumen	0.1%	0.6%	+ + + when B.P. high	+ + + +
Pulse	Seldom up	Seldom up	Seldom up	Raised (120 in 45%)
Respiration	—	+ in severe cases	+ in severe case	+
Temperature	Nil	Nil	Nil	Pyrexia in 60%
Coma	—	—	—	+
Convulsions	—	—	—	+

SYMPTOMATOLOGY.

The symptomatology of the two conditions is very similar, yet it is very important to distinguissh chronic nephritis complicating pregnancy from albuminuria of pregnancy, as, when there are definite signs of chronic nephritis, it is unwise to allow the occurrence of further pregnancies, as each subsequent pregnancy leads to more permanent damage of the renal tissue.

Stander states that chronic nephritis constitutes about twenty-five per cent. of all gestation toxæmias. Stander and Peckham give the following as outstanding characteristics of chronic nephritis complicating pregnancies :—

1. The last pregnancy shows more renal involvement than the one preceding it, as shown by the fact that a rising blood-pressure and albuminuria are noted far earlier than was the case in the previous pregnancy.
2. Nitrogen partition in the urine is often disturbed, the ammonia nitrogen increasing and the urea nitrogen being relatively less in amount.
3. In some cases nitrogenous retention in the blood becomes quite appreciable, as is shown by a rise in the non-protein nitrogen, as well as in the urea nitrogen.
4. Oedema is quite marked in a large percentage of cases, and sometimes persists throughout the puerperium.
5. At the end of the puerperium following the last pregnancy, the blood-pressure, especially the diastolic, has not returned to the normal level, and there is usually some albumen in the urine.

Cruickshank, Hewitt, and Couper, in discussing the results of their investigation, emphasize the following points as distinguishing chronic nephritis from albuminuria :—

1. Tendency for the blood-pressure to remain high, or fall but slowly after labour, and for similar behaviour on the part of the albuminuria when this was large in amount.
2. Less sudden onset of symptoms, facial œdema as an isolated phenomenon, visual disturbance early in pregnancy, and the fact that blindness might cause the patient to consult an oculist in the first instance.
3. High degree of albuminuria out of all proportion to the severity of the other symptoms.
4. Large daily variations in the amount of albumen in the urine.
5. Nephritic patients are more prone to miscarry.
6. Ninety per cent. of the albuminuric and eclamptic patients had a systolic blood-pressure of 140 mm. or less by the fourteenth day post-partum; only eighteen per cent. of the nephritic patients showed a similar fall.

The report of the White House Conference on maternal morbidity and mortality says : "According to Miller, Massey, and Keith, Cheney, Kruckman, and others, typical albuminuric retinitis is found only in those patients with primarily damaged kidneys. This finding is not to be confused with retinal œdema, which is frequently present in pre-eclampsia and eclampsia. The absence of this change in the eye-grounds by no means rules out the possibility of nephritis." The same report says that women with chronic nephritis should not marry, or if they do, that pregnancy should be prohibited.

In the interests of both mother and infant, the differential diagnosis between chronic nephritis and albuminuria of pregnancy is of the greatest importance. In all but the most severe cases of albuminuria of pregnancy, the chance of the mother being able to continue the pregnancy sufficiently long to secure a living baby,

without permanent impairment of her kidney function, is reasonably good, whereas in cases of chronic nephritis the risk of miscarriage or premature still-birth is very high, and in all but the mildest cases the chance of securing a living baby is remote. Added to this is the knowledge that in any event the mother's kidney function is almost certain to suffer further and possibly greater impairment.

I have been greatly indebted to Dr. J. A. Smyth for his help, both clinically and from the biochemical side, in arriving at a differential diagnosis and in conducting the treatment in cases of chronic nephritis. Guided by him, I have been accustomed to rely on the following in arriving at a diagnosis:—

History—General.—History of scarlatina, diphtheria, tonsillitis, or any hæmolytic streptococcal infection. Polyuria, especially nocturia, œdema, or albuminuria predating pregnancy.

Obstetric.—History of previous miscarriages or premature still-births.

Clinical Findings.—Abnormal nocturia, arterio-sclerosis, retinal changes, onset of albuminuria relatively early in pregnancy, i.e., before twenty-six weeks.

Urinary Findings.—Reduction in variation of specific gravity. Casts and epithelial debris. Red blood-cells. Range of urea concentration test giving a maximum figure of less than two per cent. and a minimum figure of greater than one per cent.

Blood Examination.—Raised blood-urea (normally low in pregnancy).

Once the diagnosis of chronic nephritis has been made, it is my practice to advise termination of pregnancy, except in cases without a bad obstetric history of previous miscarriage or still-birth, of a clinically mild character with satisfactory renal function tests. These cases are kept under close supervision by Dr. Smyth and myself, their renal function frequently tested, and induction of labour carried out as soon as there is reasonable hope of a viable child (thirty-fifth or thirty-sixth week), or sooner if their condition begins to deteriorate.

In this connection Stander writes: "From a consideration of the prognosis in nephritis, it is clear that one assumes a grave responsibility by allowing gestation to proceed in the face of an underlying nephritis. If the nephritic condition is severe, immediate termination of pregnancy becomes imperative. In the milder types of chronic nephritis, rest in bed and dietetic treatment occasionally enable us to carry the patient to term without any serious harm to the mother, but it is well to remember that such an outcome is the exception rather than the rule. I strongly advocate the termination of pregnancy in all cases of nephritis, unless marked and rapid improvement follows the conservative treatment of rest in bed with restricted low protein, and in some instances salt-free diet and plenty of fluids."

Albuminuria of Pregnancy.—Coming now to cases of albuminuria of pregnancy—I have already spoken of etiology and prophylaxis—early diagnosis is important if treatment is to be effective, for in my view only time and response to treatment and final result enable one to really distinguish between mild and severe cases. The early symptoms of headache, nausea, œdema of the ankles, and vomiting are well known, but by careful ante-natal supervision it is frequently possible for diagnosis to precede any complaint made by the patient. The urine should be tested every four

weeks during the first eight lunar months, every fortnight during the ninth lunar month, and every week during the last four weeks of gestation. The onset is rarely before the twenty-eighth week, and is usually somewhat later. The blood-pressure should be carefully taken at each visit. In my experience the earliest physical sign is a rise of ten or more points in the systolic blood-pressure above the individual patient's normal. This usually precedes the appearance of albumen in the urine by a week or more. Close inquiry from the patient, on the occurrence of this rise in pressure, will usually show that some of the rules of hygiene and diet are being neglected, or examination reveal some focus of sepsis. Suitable treatment, such as reduction and modification of diet, treatment of constipation or sepsis, instituted at once, will usually result in a fall in pressure to normal, and albumen will not appear in the urine.

If the condition is not discovered until albuminuria and raised blood-pressure are present, the patient should be put to bed on the routine treatment. No solid food, fluids only—water, glucose, and lemon drink. Mist. alb. in the morning, alkaline powder four-hourly until the urine is alkaline, when the dose should be reduced. If the pressure is very high—over 170 mm.—sweating should be encouraged by diaphoretics or hot packs. Early mild cases will clear up in a few days, and the diet may be rapidly increased. In all cases the amount of urine passed in twenty-four hours should be charted, the amount of albumen noted, and the blood-pressure recorded daily.

In severe cases with greatly diminished urinary output, intravenous glucose should be given. The addition of intravenous calcium gluconate, as recommended by Cameron, has been of service in some cases. Marked increase in the urinary output, fall in the blood-pressure, and diminution in the amount of albumen passed, with lessening of œdema and amelioration of symptoms, are signs of improvement. If these signs are delayed more than a few days, termination of pregnancy should be considered.

The following I regard as calling for induction of labour :—

Immediate Induction:

1. Systolic blood-pressure of 200 mm. Hg.
2. Blindness or marked diminution of vision.
3. Severe epigastric pain.
4. Uncontrollable vomiting.
5. Onset of jaundice.
6. Increase of blood-pressure and amount of albumen in the urine, with diminished output of urine in spite of adequate treatment.
7. In severe cases, failure to improve in these respects in spite of treatment.

Methods of Induction of Labour.—In cases of albuminuria of pregnancy and chronic nephritis, the methods employed for induction of premature labour are :—

1. By rubber stomach tube.
2. Rubber balloon distended by sterile saline.
3. Puncture of the membranes.

Tube induction is most commonly employed for cases induced after the twenty-eighth week, while balloon induction is usually employed in cases induced before the twenty-eighth week.

Puncture of the membranes is a very old method which has been recently re-introduced, and has been employed largely in America. Reports on its use from Johns Hopkins Hospital are favourable, as the following quotation from the White House Conference report shows: "Castor oil and quinine, followed (four hours later) by artificial rupture of the membranes, is superior to the other methods, because it is the most successful, shortens labour, and does not affect unfavourably the likelihood of spontaneous delivery, the neo-natal mortality, or the maternal morbidity. It is equally satisfactory in primiparas and most multiparas, but a strong contra-indication to this method is great multi-parity, i.e., women who have had four or more children. This, we think, is the only condition in which the bougie is preferable to rupture of membranes."

In their comparison of the three methods—bougie, bag, and rupture of membranes, fœtal mortality was 18.7 per cent. with the bag, 3.6 per cent. with the bougie, and 2.9 per cent. with rupture of the membranes. Prolapsed cord occurred in 24.3 per cent. with the bag, 5.5 per cent. with the bougie, and 0.6 per cent. with rupture of the membranes. Maternal morbidity was 37.2 per cent. with the bag, 23 3 per cent. with the bougie, and 18.2 per cent. with rupture of the membranes.

At the Royal Maternity Hospital we have been trying this method of induction recently.

Results of Treatment of Cases of Albuminuria and Nephritis.—During the years 1930, 1931, and 1932, 334 cases were treated in the Maternity Hospital.

Maternal mortality—3, or 0.9 per cent.

Fœtal mortality—28, or 8.5 per cent.

93, or 28 per cent., of the deliveries were premature.

63 cases (19 per cent.) were induced, 47 by tubes and 16 by balloons.

52 of the inductions were albuminuric cases, and 11 were nephritics.

There were two maternal deaths amongst the induced cases—one albuminuric and one nephritic.

Hyperemesis Gravidarum.—This form of pregnancy toxæmia has been divided into three types:—

1. Reflex.
2. Neurotic.
3. Toxæmic.

In my experience all the cases have been primarily neurotic. I have not, as yet, seen any case which convinced me that it was either reflex or primarily toxæmic. Reflex cases are supposed to have their origin in such lesions as retroversion, or erosion of the cervix. I have had cases of hyperemesis with one or both of these lesions get better on routine treatment without any treatment of the retroversion or erosion, and we have all seen countless cases of retroverted gravid uterus, or erosion associated with pregnancy, which have not suffered from excessive vomiting.

Many of these cases fall into one or other of two groups :—

1. The young, highly-strung, introspective girl, pregnant for the first time, who is openly or secretly terrified by her ideas of the ordeal of pregnancy and labour, even though she may at the same time earnestly desire to have a baby.
2. The woman who has had one or more babies, but is most reluctant to have, or terrified by the prospect of having, any more.

Diagnosis.—It is necessary, of course, to exclude other causes for the vomiting. Also, it is well not to take the history of excessive vomiting at its face value, but to seek confirmation by testing the urine for acetone and diacetic acid.

Treatment.—Every uncomplicated case will respond to suitable treatment if this is begun early. Mild cases clear up readily by reassurance, correction of constipation, and giving of a light, mainly carbohydrate, diet. All other cases must be removed from home and over-anxious relatives to either nursing-home or hospital where the co-operation of a trustworthy, well trained nurse is of the utmost importance in securing the patient's confidence.

The confidence of the patient in the ability of her medical attendant to cure her vomiting is of the utmost importance. No visitors should be allowed until the vomiting is under control.

The bedroom should be light and well ventilated. In hospital these patients should be in a single-bed ward. All except the gravely ill cases should be encouraged to occupy themselves with light reading or needlework.

On admission, the rectum and colon should be emptied by an enema. Neither fluid nor food should be given by the mouth for twenty-four to forty-eight hours. Rectal feeding with six or eight ounces of five per cent. glucose saline every three hours should be carried out during this period. In very nervous patients thirty grs. of bromide may be added to the glucose two or three times daily. The twenty-four-hour urinary output should be measured and charted each day, and the urine examined daily for acetone and diacetic acid and albumen. The ketones are always present in large amounts, and disappear as the condition improves.

Frequent cleansing of the mouth with glycerine and borax is helpful, as the tongue is red and raw, and the gums spongy and bleeding.

In many cases the vomiting ceases in twenty-four or forty-eight hours, or is infrequent, and the scanty urinary output increases.

Glucose and lemon, or glucose and orange drinks, are then given by mouth, and in a day or two a light, mainly carbohydrate, diet, free from fats, can be given.

In severe cases, as shown by harsh, dry skin, dry brown tongue, emaciation, rapid pulse, drowsiness, and very scanty urine, glucose should be given in large amounts intravenously—one or two ampoules of 50 c.c. of fifty per cent. strength plus a pint of the five per cent. strength.

Danger signals are rise of temperature and pulse-rate, increasing apathy and drowsiness, with diminishing urinary output and the appearance of bile and albumen in the urine, and an icteric tinge in the skin, and conjunctiva. Intensive

intravenous glucose therapy is called for. In rare cases where these measures fail, abortion has to be induced. Anæsthesia is very dangerous in these cases. Gas and oxygen should be chosen.

Results of Treatment.—Out of 790 patients admitted to my wards at the Royal Maternity Hospital from August, 1933, till the end of 1934, thirteen cases were admitted as hyperemesis. Of these four did not vomit after admission, and the urine was free from acetone and diacetic acid. They are therefore excluded, leaving nine cases of hyperemesis—an incidence of one in eighty-eight of admissions. Of the nine cases, four were primigravida.

Seven were between seven and ten weeks pregnant. One was twenty-one weeks pregnant, and one was twenty-seven weeks pregnant. On admission all had acetone and diacetic acid in the urine, and the average systolic blood-pressure was 110 mm.

The average duration of symptoms was three weeks, and the average stay in hospital was seventeen days. All were discharged free from symptoms and ketonuria and on ordinary diet.

REVIEW

ANTE-NATAL AND POST-NATAL CARE. By F. J. Browne, M.D., D.Sc., F.R.C.S.Ed. London: J. & A. Churchill, Ltd., 1935. Pp. 479; figs. 58. Price 15s. net.

Professor Browne's recently published book, "Ante-Natal and Post-Natal Care," condenses much useful information into small bounds. It is interesting to note in it that the earliest patients to receive the benefits of ante-natal care were unmarried mothers, and that it was not for a very long period that these benefits were extended to their married sisters. Professor Browne also points out that the comparative failure of ante-natal care to reduce the maternal death-rate is not due to something inherently wrong with it, but to inefficiency in the carrying out of ante-natal examinations, or to neglect of the earliest danger signals. He points out that the earliest sign of toxæmia is usually a slight rise in blood-pressure, but he does not state clearly whether there is any significance in a rising diastolic pressure, with the systolic remaining constant, or vice versa. The subject is treated from the point of view that rise in systolic pressure always synchronizes with a rise in diastolic.

A useful chapter of this book is devoted to the dietetic requirements of pregnancy.

There is an excellent chapter on the "influence of the emotions upon pregnancy and parturition." The theory of the cause of labour pains is discussed in a clear and readily understood manner, but one would doubt whether the author's method for abolishing pain in normal labours without the use of any sedative would always be successful.

In the chapter dealing with multiple pregnancies, Professor Browne quotes the case of a Russian peasant who by two wives was the father of eighty-seven children, and of another Russian who by two wives was the father of seventy-two children, figures that far outstrip the man from Ballymena, whose one wife was the mother of thirty-six children.

Although this book is entitled "Ante-Natal and Post-Natal Care," there are less than seven pages out of 479 devoted to post-natal care. It is also to be regretted that in such an excellent book more care was not taken in correcting proofs, as the occasional running together of words prevents easy reading. Then, too, in chapter v. the index mentions as one of its sub-headings "Marital Intercourse," yet no mention is made of this subject in the chapter named.

In spite of these minor faults, the book can be recommended to every thoughtful medical practitioner and student. It is on the whole easy to read, and should prove of very great value to everyone interested in the practice of obstetrics.

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Diagnosis and Treatment of Gonorrhœa in the Female

By H. I. McCLURE, M.B., B.SC., F.R.C.S., M.C.O.G.

THIS article is based on work on forty cases of gonorrhœa in the Royal Victoria and Ulster Hospitals, Belfast.

To establish a diagnosis of gonorrhœa, Thomson[1] gives the following points :—

1. History of frequent scalding micturition.
2. History of vaginal discharge subsequent to this.
3. Clinical signs of past or present inflammation in Bartholin's ducts or glands, urethra, vulva, and cervix.
4. Bacteriological examination of discharge from these structures, repeated if necessary after menstruation, or twenty-four to forty-eight hours after a provocative dose of gonococcal vaccine.
5. Complement fixation test.

Opinions on the complement fixation test vary: Abraham[2] states that it is useless in the diagnosis of acute gonorrhœa; Lailey and Cruikshank[3] found a positive result in only 116 cases out of 217 cases of clinical gonorrhœa.

The diagnosis in my series was made on satisfaction of Thomson's first three criteria. Each case showed redness and œdema of the labia with profuse vaginal discharge. Signs of inflammation of Bartholin's ducts or glands were present in all cases. The urethral orifice was always reddened and œdematous, and pus could be milked from the peri-urethral glands. Twelve patients complained of irritation of the vulva, probably the result of excoriation by leucorrhœal discharge. Each patient complained of, or gave a recent history of, painful frequent micturition and profuse vaginal discharge.

In every case the cervix was inflamed, being enlarged, œdematous, and tender, with a profuse secretion from its surface and the canal. Erosion, due to desquamation of the epithelium, was present in each case, while almost invariably small purulent spots were to be seen on the surface of the cervix.

I am satisfied that these points are sufficient to make a diagnosis, and I think the most reliable sign is the squeezing of pus from the urethra. I am supported in this by T. H. Cherry,[4] who states that a reliable history is the best guide, and that laboratory tests, including complement-fixation tests, are not of great value in diagnosis.

Recently we have been trying out the CO_2 cultural method[5] as an aid to diagnosis, and results have been satisfactory.

Infection of the cervix was as frequent as urethritis, and is probably the most important factor in chronicity of infection and causation of metastatic complications. These were present in twelve, or thirty per cent. of my cases. Infection here almost always begins in the endocervix, the squamous epithelium of the portio vaginalis being more resistant to infection than the palisade epithelium of the canal. The gonococcus possesses the power of penetrating uninjured epithelium to set up an acute inflammatory process in the subjacent tissues by the power of an

endotoxin liberated at its death. The racemose nature of the cervical glands tends to render this process chronic, and for this reason infection of the cervix is the most important feature of gonococcal infection.

Thirty of the patients were married; seventeen had not borne children, six had had one child each, and seven had each three children.

Six patients were under 20 years, twenty were between 20 and 30 years, thirteen were between 30 and 40 years, and one patient was over 40 years of age.

Treatment.

Ten patients were treated with bi-weekly applications of silver nitrate, five per cent. solution for the urethra and twenty per cent. for the cervix, after cleansing with five per cent. dettol in water. Following each application, a woollen lampon of glycerine and ichthyol, or a gelatine pessary of acriflavine, was inserted against the cervix. After removal, the patient was instructed to douche the vagina, using a solution of boric acid, one teaspoonful to the pint.

Cure was considered satisfactory when no physical signs were present, and all symptoms had disappeared. The average number of treatments before this state was reached was twenty-one.

I am satisfied that acriflavine is better than glycerine and ichthyol in the treatment of gonorrhœa.

Thirty patients were treated with diathermy to the urethra and cervix. The optimum temperature for culture of the gonococcus is from 95 to 98° F., and above this the growth of the organism is checked. Experimentally it has been shown that at temperatures from 102 to 113° F. the organism is killed in non-living culture media. On these experiments, and on the fact that, in patients with gonorrhœa and pyrexia due to other causes, the gonococcal infection has abated, it was thought that an increase in temperature in living tissues would be prejudicial to the growth of this organism.

Diathermy current is a sustained alternating high-frequency current, and by means of it the temperature of various parts of the body can be raised by heat generated in the tissues.

The temperature of the cervix uteri may be raised sufficiently high to injure organisms growing therein, without causing harm to the tissues.

While the temperature so induced may not be high enough to kill the organisms, it is at least sufficiently high to render possible their destruction by factors in the tissues. It may be that protective measures against infection are increased, and in support of this is the fact that the increased heat causes a hyperæmia of the part, resulting in an increase of protective substances.

The diathermy current traverses the tissues by means of two electrodes. The directing or body electrode is a thin sheet of lead, three inches wide, placed round the body at the level of the hips, and attached to the diathermy machine. The active electrode, or thermophere, is a metal case of tubular metal, three-sixteenths of an inch in diameter, containing a thermometer, and it is placed in the urethra. For the cervical canal, the electrode is a metal case twelve inches long, with its lower end

curved at an angle of 130° to admit of entry into the cervical canal. In each case the electrode is insulated with rubber tubing, split longitudinally to admit of easy application and removal; this stops short of the distal end of the electrode, where the casing is absent on one side to permit viewing of the thermometer scale.

By means of the active electrode placed in the urethra, the temperature is raised to 110° F., and maintained for ten minutes, and with the cervical thermophere, maintained in the cervical canal at 115° F. for the same period. The length of electrode actually placed in the cervical canal is three-quarters of an inch, and to maintain the above temperature I have found an amperage 0.5 to be sufficient.

The temperature in the urethra is maintained readily, but a close watch must be kept in the case of the cervix, for here the temperature is apt to fall suddenly, probably due to heat being carried away by the excess blood supply.

By this method thirty of the forty cases have been treated. Treatment was given at weekly intervals for ten minutes in the cervical canal at 115° F., at 110° F. in the urethra for the same period. The average number of treatments before disappearance of signs and symptoms was six.

The effects of treatment were soon apparent: such symptoms as dysuria and irritation were invariably relieved within forty-eight hours of the first application. Treatment was always continued, not only till all symptoms had disappeared, but all evidence of infection, such as pus in the urethra and palpability of Bartholin's glands, had disappeared. Particular attention was paid to the cervix, and before cure was considered complete the cervix showed neither erosion nor leucorrhœa.

This method of treatment is undoubtedly the best yet devised, not only for gonococcal infection of the urethra, and more particularly of the cervix, but also for metastatic manifestations such as arthritis.

Twelve cases showed metastatic complications—six were suffering from arthritis of the knee-joint with pyrexia, two had multiple arthritis also with pyrexia, corneal ulcer was present in two cases, irido-cyclitis in one, while one patient was suffering from severe teno-vaginitis of the forearm. In every case there was definite evidence of gonococcal infection of the urethra, and more particularly of the cervix.

In all cases of arthritis the results of treatment to the cervix were dramatic; in every case of monarticular arthritis the pain was almost completely relieved within twenty-four hours, and heat and swelling of the joint began to subside almost immediately. Attempts at passive movements of the joint before treatment made the patients scream, but by the end of the fifth day after the first treatment, joint movements had returned to normal. In each case the temperature was over 101°, and within twenty-four hours commenced to fall, and was normal in four days.

Two patients who had been treated unsuccessfully with sodium salicylate, had multiple arthritis with pyrexia. Definite evidence of gonococcal infection was present in each, and to the cervix and urethra diathermy was applied. Previously these patients had had several applications of the diathermy current to the larger joints, with relief for a few hours only, but immediate and permanent relief was given within twelve hours of the first application to the cervix and urethra. Not only was there a decrease in the pain, but joint movements became much easier and

the temperature began to fall. Within seventy-two hours it returned to normal, although in one of these patients it had risen to 105° two hours after treatment.

Three patients with ocular manifestations—two with corneal ulcer and one with irido-cyclitis—showed definite evidence of gonorrhœa in the urethra and cervix. Each had received appropriate local treatment for the eye conditions for some time before diathermy treatment of the cervix and urethra was instituted. Till then little improvement was evident, but by the end of fourteen days after the first diathermy application, the eye conditions were cured. Treatment was, however, continued for six weeks.

The patient with the teno-vaginitis of the forearm had marked swelling, œdema, and tenderness of the flexor aspect of the forearm, with contraction of the fingers. Attempts at opening the fingers failed, and caused the most excruciating pain. There was evidence of gonococcal infection of cervix and urethra, and diathermy treatment was instituted immediately. In forty-eight hours slight movements of the fingers were possible, and by the end of the fifteenth day movements had returned to normal without any local treatment.

I have followed up each of these twelve cases, and, with one exception, each is apparently cured of local and metastatic complications of gonorrhœa. The exception is a case with arthritis of the knee, who, after eight weekly treatments, has a mass on each side of the uterus. She has, however, neither pain nor limitation of movement in her joint, and feels well save for occasional attacks of abdominal pain.

With diathermy treatment the cervix is usually much improved after the second application, and it has regained its normal features in all cases after six applications.

From the patient's point of view—the relief of symptoms—the effect of diathermy treatment is almost instantaneous, urinary symptoms disappearing within forty-eight hours after the primary application. The only disadvantage of the treatment is the uncomfortable position which the patient must maintain during application.

All cases, with one exception, were found to be cured after six applications, spread over six weeks, while with treatment of silver nitrate, twenty-one was the average number of treatments required, spread over a period of eleven weeks.

Treatment with silver nitrate makes no appreciable difference in any respect on metastatic manifestations.

The results of other workers with diathermy treatment to the cervix and urethra in gonococcal infections are all good. Cumberbatch and Robinson,[6] pioneers in this method of treatment, give excellent results in acute, subacute, and chronic gonorrhœa, and particularly in metastatic complications. According to Milner and Maclachlan,[7] there is only one disadvantage in this method, namely, the possibility of stricture of the urethra following burning; and they place their active electrode outside the urethra, but against it in the vagina. My experience of urethral diathermy is that patients will not stand temperatures above 110° F. in the urethra, and it is hardly likely that stricture will follow this degree of heat.

If results of treatment by diathermy continue to be as uniformly good as those already published, and as in my series, then gonococcal infection will be no longer the dreaded danger it has hitherto been, and Osler's statement that in many

respects arthritis is the most damaging, disabling, and serious of all the complications of gonorrhœa will no longer hold.

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An Ancient Treatise on Embryology

By MAURICE J. BOYD, B.A.,

Department of Latin, Queen's University, Belfast

MINOIDES MYNAS, in the course of a visit to the monasteries of Mount Athos, undertaken on the instructions of Villemain, Minister of Education in France from 1840 till 1845, found a number of hitherto unknown Greek manuscripts. Among these was one which contained the conclusion of Galen's "On Decline," the whole of Galen's "Introduction to Logic," and a treatise under the title "Galen to Gaurus on How Embrya Become Living Beings." The last of these works, which is that with which we are concerned, is seriously mutilated at the end.

Mynas himself believed the *ad Gaurum* to be a genuine work of Galen, but since then Kalbfleisch, in his edition of it (*Anhang zu den Abhandlungen der Akademie der Wissenschaft zu Berlin*, 1895), has produced very convincing proof that it is not a work of Galen, but of Porphyry, the Neoplatonic philosopher. Here we have space for only a brief summary of Kalbfleisch's arguments. First, the arguments to show that the treatise is not by Galen :—

(i) It is not mentioned in Galen's own indices of his works.

(ii) It is not referred to in any of the works which we know to be by Galen, though these are full of quotations from his other works, nor does it refer to any other work on embryology by its author.

(iii) Galen as a rule left aside all metaphysical questions, confining himself to the empirical, but this treatise frequently refers to metaphysics.

(iv) The views expressed in the *ad Gaurum* are very seriously different from those expressed in the works which deal with embryology which are

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(iv) The views expressed in the *ad Gaurum* are very seriously different from those expressed in the works which deal with embryology which are

known to be by Galen. The author of the *ad Gaurum* insists throughout the treatise that the fœtus has no animal life until the moment of birth, but Galen holds that the animal life of the fœtus begins with its first heart-beat, and insists that it is an error to suppose that it has no voluntary movement of its own. It is not inconceivable that this may represent a change of view on the part of Galen, but it would be most peculiar that he should not call attention to the change.

Secondly, the arguments to show that the treatise is by Porphyry :—

(i) It is obvious throughout that the author of the treatise is a keen Platonist.

(ii) Certain remarks make it clear that he is a Neoplatonist.

(iii) The style reminds us of that of Porphyry.

(iv) There are striking parallels both in thought and in language between the *ad Gaurum* and the known works of Porphyry.

(v) Later writers speak of Porphyry as having held the views on embryology which are expressed in the *ad Gaurum*. Iamblichus says : "According to Porphyry, the first real creation of life and presence of the soul takes place at the birth of the child." And Michael Psellos gives an account of the views of Porphyry which might be a summary of the *ad Gaurum*.

The fact that the treatise has been handed down under the name of Galen may be due to a desire to father it on the man who was, after Hippocrates, the doctor *par excellence*, or to a copyist's careless confusion of the name 'Malchus' (which was Porphyry's original name) with the name 'Galen' (in Greek script this would be possible), or to a combination of the two.

The *ad Gaurum*, then, is probably a work of Porphyry, the Neoplatonist. This Porphyry was born in Syria, probably in the year A.D. 234. For a time he studied at Athens under Longinus (afterwards minister of Zenobia at Palmyra), and later at Rome under Plotinus, the head of the Neoplatonic school. His death should probably be placed in the early years of the fourth century.

The title of the treatise is, as we saw, "How Embrya Become Living Beings." What Porphyry wishes to prove is that the soul comes to the embryon from outside, that it is not a part of the father's soul nor of the mother's, nor a combination of parts from both of these. This, he held, could be most easily proved by showing that the embryon is not a living-being till after the moment of birth. Accordingly, most of the treatise, as it is preserved, is taken up with the proof that the embryon is not a living being while it is in the womb.

The problem is stated in the first chapter : Scientists and practically all doctors are in doubt whether we ought to consider embrya to be already living-beings or merely to have the same sort of life as plants have, the specific character of a living-being consisting in cognition and appetition, and that of a plant being seen in its receiving of nourishment and its growth. In addition, those who hold that embrya possess the souls of living-beings dispute whether we ought to consider them to be living-beings actually or merely potentially. The word 'potentially,' of course, may be used either of things which do not yet possess a certain power but are capable of possessing it, or of things which do possess that power but which

are not at the moment exercising it. It is clearly in the latter sense that the word is used when people speak of embrya being living-beings potentially.

Then chapter two goes on: If it were shown that the embryon is not a living-being, either actually or potentially (in the second of the two senses of the word), then it would be easy to show that the soul must come to the child from outside, and to show at what time it comes. For it is obvious that its arrival will be at the moment when the fœtus first receives the qualities of a living-being, that is, after leaving the womb. But if the embryon is a living-being either actually or potentially (in the second sense of that word), then it will be very difficult to define the moment of the soul's arrival: one will say that it is when the sperm is deposited; another that it is when the embryon first takes on its human shape, that is, after thirty days in the case of males, after forty-two in the case of females; another that it is when the embryon first moves (of the movement of the embryon Hippocrates says: "When nails and hair first take root in the extremities of the child's body, then its first movement takes place: in the case of the male this is after three months, in the case of the female after four months").

Chapter three: If we consider the differentiæ both of plants and of animals, we shall be able to see to which of these two classes embrya are most similar. Plants are fed, not through mouths, but through the power which is in their roots that draws up the nourishing moisture surrounding them in the earth. Animals, on the other hands, receive their nourishment through mouths and digest it in the organs set apart for this purpose by nature. Moreover, some animals breathe through nostrils, but plants breathe only through their pith and, in particular, fruit receives nourishment and air only through the stalk from which it hangs and from which it falls when ripe. Those animals which live on land perish if surrounded by moisture, but it is only by being surrounded by moisture and by drawing it in from the earth that seeds are able to grow. If, then, embrya were nourished through mouths and not through the power within their seeds which, like plants drawing in moisture from the ground, draws in the blood which surrounds them in the womb; or if they breathed through nostrils and not through the umbilical cord, to which they are attached in the middle as if to a root or a stalk, and from which like fruit they fall when ripe; or if they were able to survive even for a short time without being surrounded by moisture (after birth, on the other hand, land-animals cannot survive if they are surrounded by moisture); if, in fact, the life of the embrya in the womb was similar to that of living-beings, then we might admit that they were living-beings. But since their life is practically the opposite of that which they live when they have left the womb, we must conclude that they are not living-beings.

Chapter five: Against this it is objected by some that embrya must be able to move and to be aware of heat, for they leap about when hot air strikes the mother's womb in the baths; others hold that the peculiar desires which pregnant women feel at no other time but during pregnancy are really desires of the embryon, and in support of this they say that, if these desires are not satisfied, the children bear on their bodies the mark of this lack of satisfaction; they say that a strong proof that embrya possess appetitive souls is seen in the process of birth, for dead

children are difficult to bring forth since they have no desire to come out, and female children are slow in coming out since females are naturally slow in movement. If we must agree to this nonsense, we might go on to say that embrya share the perceptions and opinions of their mothers. For it is admitted that many living-beings, and in particular women, produce offspring which resemble that member of their own species whose appearance they have in mind at the moment of coitus. For that reason we place before mares and bitches and pigeons, and even before women, beautiful pictures in order that they may remember them and produce offspring like them. This, they say, would surely not be so unless the sperms possessed souls capable of perceiving the pictures.

Chapter six : To reply to the last point first : men are unable to model their bodies in accordance with their perceptions, and it is therefore unreasonable to assume that there is in the embryon a soul capable of doing this. But if we agree with Plato that the lower parts of the soul, though they themselves do not share in the functions of the higher parts, are yet capable of being controlled by them, then it would not be strange if that part of the mother's soul which is concerned with growth, in being united to the power in the sperm, should bring with it obedience to the cognitive part of the mother's soul. If this is so, it would explain why children resemble whatever picture the mother had in mind at the moment of coitus.

Chapter seven : Secondly, the movements of the embryon are not the result of its possessing faculties of appetition and cognition, but rather are like those movements which take place in all our bodies, like the process of digestion, which clearly has no connection with cognition or with appetition.

Chapter eight : Finally, the desires which it was said that the mother derived from the embryon are really derived from the womb. According to Plato, the womb is controlled by appetition of its own, and has a function almost equal to that of the sperm in producing the child. He says that the womb is a living-being desirous of producing children, and that, if it remains barren for long after reaching maturity, it is troubled and wanders about everywhere through the body, blocking up the air-passages and causing all kinds of diseases, until desire brings the two people together and sows in the womb living-beings shapeless and invisible, which it afterward separates and develops and finally brings forth into the light, and then forms into complete living-beings.

Chapter nine : When Plato here compares the depositing of the sperm in the womb to the sowing of a seed, he clearly shows that he believed that the life of the embryon was like that of a plant. And again, when he says that the embryon comes forth into light before it is formed into a complete living-being, he clearly shows that he believed that it gets its soul after birth.

Chapter ten : So far we have been basing our discussion mainly on the statements of Plato. We must now consider the facts in themselves. We must ask whether the whole coming-to-be of the embryon is not exceedingly like that of a plant, the father sowing the seed and the mother taking part, not merely like the earth, which is the medium through which the plant gets its food, nor merely by supplying the embryon with milk, but rather like what we see in the grafting of

plants : for in the womb a power is added to the sperm by which, though that which is grafted and that on which it is grafted both retain their separate natures, yet they combine to produce another entity, the engrafted whole. The life of the embryon is indeed very like that of a plant, for the power which is contained in the sperm becomes attached to the body of the mother, and connected with it by a fine tube like a root attached to its middle, from which the embryon hangs and through which it breathes and receives nourishment—in fact, the umbilical cord; the spherical covering of the sperm stretches out on all sides and produces an external membrane which protects the embryon from all damage from outside.

Chapter eleven : But if the life of the embryon is like that of a plant, the soul clearly cannot enter the body till after the moment of birth. The theologian of the Hebrews seems to refer to this when he says that when the body of man had been completely formed, God breathed on it and made it a living soul. (Genesis ii, 7 : "And the Lord God formed man of the dust of the ground, and breathed into his nostrils the breath of life; and man became a living soul.") The soul does not enter into the different parts of the body in turn, but rather illumines the whole body at once. It does not enter the body under compulsion, but naturally, through the agreement of the harmoniously organized body with that which can harmoniously fit into it, i.e., the soul, without will or choice having anything to do with its entry, just as neither of these things can keep it in the body once the harmony has been broken. The reason why one soul is fitted to one body and not to another may perhaps be found in the previous life of the soul.

Chapter twelve : If indeed it were possible to prove that the embryon is already a harmoniously organized whole, then we should have to suppose that the soul which is to control this harmoniously organized whole is already present in it. But since the embryon is not harmoniously organized, the soul cannot be present in it. Nor is it surprising that the soul should only enter the body after birth, for it is clear that intelligence arrives even later. The cognitive soul, if it were present, would in fact impede the processes of growth and nourishment in the embryon, for we notice that it is in sleep, when the cognitive faculties are least active, that growth and nourishment are most active, and the deeper the sleep the more active they are.

Chapter thirteen : We have shown that the embryon is not a living-being in actuality; we must now show that it is not a living-being even in potentiality, using potentiality in the sense of a thing which possesses a quality but is not at the moment using it. Until the organs of the body are perfected, the functions which manifest themselves in those organs cannot be present : for example, until the organs of perception are perfected, perception cannot be present. Since, then, the organs of the body are not perfected until the moment of birth (for, just as acorns fall from the tree as soon as they are ripe, so the embryon leaves the womb as soon as it is mature), the functions which manifest themselves in these organs, that is, the soul, cannot be present.

Chapter fourteen : Some people claim that, just as the sperm in some way contains within itself teeth and beard and all the other parts of the body which only develop

after birth, so it possesses the faculties of appetition and cognition, though these faculties only develop after birth. But this is to contradict the metaphysical principle that that which is lower in the scale of values is derived from that which is higher, not the higher from the lower. The possession of a quality or function in actuality is of higher value than the possession of it merely in potentiality, and therefore the former cannot be derived from the latter. Besides, to suppose that the soul is already present in the embryon in the same way as teeth are would involve us in supposing that the surrounding air or something equally ridiculous is the cause of the soul's appearance out of whatever it was that existed before.

Chapter sixteen : If, however, anyone wishes to call the plant-like power, which is in the sperm, soul, then we might grant that in that sense the sperm possesses a soul, and that this soul is either broken off from the father's soul or produced by it, and that the soul of the sperm gets from the mother nourishment or even the co-operation with it of this same plant-like power in the mother; but what we cannot grant is that the sperm possesses soul in the strict use of that word. That this is the common opinion of mankind can be seen from what we do when we wish to ensure that parents shall produce fine children : it is not their souls that we train, but their bodies.

Chapter seventeen : Even if you believe that the embryon does already possess a soul, yet you will have to admit that, at whatever time this soul may enter the embryon, it must come from outside it. For the cognitive soul cannot be divided, and therefore the soul of the embryon cannot be a part broken off from the souls of the parents.

The remainder of the treatise is in a very fragmentary condition, and the nature of its contents can only be conjectured.

BRITISH CONGRESS OF OBSTETRICS AND GYNÆCOLOGY

BELFAST MEETING IN APRIL, 1936

THE next meeting of the British Congress of Obstetrics and Gynæcology will be held in Belfast on April, 1, 2, and 3, 1936, under the presidency of Professor R. J. Johnstone, F.R.C.S., M.P.

The principal subject for discussion will be the conservative treatment, by operation or otherwise, of pathological conditions of the ovaries, tubes, and uterus, with special reference to functional results.

The openers of the discussion will be Prof. Hendry (Glasgow), Prof. Leyland Robinson (Liverpool), and Dr. Bethel Solomons (Dublin).

The foreign guests will be Dr. Heymann (Stockholm) and Dr. Gray Ward (New York), both of whom will contribute papers.

A provisional programme will be published in the April number of this Journal.

Any member of the Ulster Medical Society who wishes to be enrolled as a member of the Congress should communicate with the hon. secretary, Mr. C. H. G. Macafee, 18 University Square, Belfast.

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A HISTORY OF THE ULSTER MEDICAL SOCIETY

THE editor is at present engaged in writing a history of the Ulster Medical Society, and would be glad of any help that members of the Society can give him. He would be particularly grateful for the loan of, and opportunity to study, any notices, papers, abstracts, proceedings, or other matter concerning the Society. Every possible care would be taken of any printed matter loaned, which would be returned with grateful thanks. Any of our readers who have material of the above nature, or know where it would be available, will they please communicate direct to Dr. R. H. Hunter, Department of Anatomy, Queen's University, Belfast.

"THE BLOODLESS PHLEBOTOMIST"

WE have just received an advance copy of "The Bloodless Phlebotomist," Vol. 8, No. 3. This little journal, published by the Denver Chemical Manufacturing Company of New York, is replete with interesting articles written by physicians who are located in many different countries; and while the purpose of the publication is to acquaint its medical readers with Antiphlogistine, the physicians will find a number of items and illustrations which will excite their curiosity and interest. Altogether this little journal is well worth reading, and we note that 1,450,500 copies are printed in nine languages and distributed to every doctor in the world with a known address, excepting in the countries of Russia, Latvia, and Bulgaria.

If you do not receive a copy, write to the Denver Chemical Manufacturing Company, New York, who will place your name on their list. The journal will be supplied you free of all charges.

ULSTER MEDICAL SOCIETY

THE opening meeting of the session 1935-6 was held in the Whitla Medical Institute on Thursday, 24th October, 1935. Dr. S. R. Hunter introduced the incoming president, Dr. Foster Coates, and placed the chain of office around his neck. Before doing so, Dr. Hunter offered his thanks to the officers of the Society for the assistance they had given him during his term as president. He then paid a special tribute to Dr. Montgomery, the hon. secretary, for his help and assistance, and especially for the very excellent and well balanced programme which he had arranged. The task of introducing Dr. Coates, he said, was simple; as one of our foremost consultants he was well known, and because of the well-earned reputation which he had made for himself by the papers which he had contributed to the Society since becoming a member in 1907, and lastly because he was the son of Dr. Stanley Coates, who had done so much for the advancement of the Ulster Medical Society in the earlier days of its history.

Dr. Foster Coates then arose, and before delivering his presidential address, "The Importance of Vitamins in Dietetics" (published elsewhere in this number

of the Journal), he referred to the loss the Society had sustained by the death of the following members and fellows :—

This is a melancholy duty at all times, he said, but this year the Society had been singularly unfortunate, and it deplores the deaths of Dr. Picken, Dr. Loughridge, and Dr. Gibson, three younger members who might confidently have been expected to remain for many years. The Society deeply regrets the loss of these talented and popular young men.

Dr. O'Connor of Newry, who passed away in his prime, will be missed far beyond the area in which his practice lay. A great sportsman, he was deservedly popular among a large circle of friends. His kindly nature and wide professional knowledge had earned him the affection and respect of numerous patients.

Dr. Cahill had a large practice in this city, and was an old member of this Society. He took a keen interest in all medical matters, frequently taking part in debate, where his clear-sightedness, knowledge, and sound judgment were highly valued.

Dr. Tait of Downpatrick and Dr. McDonald of Portaferry were prominent figures in County Down, and highly esteemed not only for their professional skill, but also for the public services which they rendered to the community. It was a pleasing thought that men who held such important and respected positions in the county should have been members of the honourable profession of medicine.

The second meeting of the session was held in the Whitla Medical Institute on Thursday, 7th November, 1935, at 8.30 p.m. The president, Dr. Foster Coates, was in the chair. A number of short papers were read and discussed. These are published elsewhere in this number of the Journal. The authors were:—Dr. F. M. B. Allen, "A Case of Polyserositis"; Dr. J. T. Lewis, "A Case of Acute Hæmolytic Anæmia"; Dr. Hilton Stewart, "A Case of Advanced Rickets with Pathological Findings," with radiological notes by Dr. F. P. Montgomery and pathological notes by Professor J. S. Young; and Mr. C. J. A. Woodside, "A Case of Carcinomatosis of Glands of Unknown Origin."

The third meeting of the session was held in the Whitla Medical Institute on Thursday, 21st November, 1935, at 8.30 p.m. Dr. Coates, the president, occupied the chair. An interesting series of medical cinematograph films was shown. These included the following :—

(*a*) Mechanism of the normal heart.
(*b*) Cardiac irregularities.
(*c*) Typical gaits.
(*d*) Treatment of fractures of the spine (Bohler).
(*e*) Treatment of fractures of the finger (Bohler).

The president referred to the value of the cinema in the teaching of medical students, and its possible application to the study of disease. Dr. J. S. Morrow strongly supported the president's remarks, giving examples of possible application to industrial medicine.

The annual dinner was held in the Whitla Medical Institute on the 5th December. The president, Dr. Coates, was in the chair. A number of distinguished guests were

present. The toast of the Society was proposed by Prof. W. B. Morton, and responded to by the president. "The Guests" was given by Dr. Robert Marshall, and responded to by Mr. F. W. Ogilvie, Mr. Seton Pringle, and Mr. E. Warnock, K.C.

H. Hilton Stewart, *Hon. Editorial Secretary.*

18 Malone Road, Belfast.

LONDONDERRY MEDICAL SOCIETY

The inaugural meeting of the session 1935-6 was held in the City and County Infirmary, Londonderry, at 8.15 p.m. on Friday, 1st November, 1935.

The following office-bearers were elected for the ensuing session:—President, Dr. A. Milseed; hon. treasurer, Dr. J. Watson; hon. secretary, Dr. J. A. L. Johnston; Committee: Dr. J. McCormick, Dr. W. G. McKinney, and Dr. W. S. Watson.

A proposal that the Londonderry Medical Society should merge with the Londonderry and District Division of the British Medical Association met with no encouragement from the members of the Society. It was felt that it would be a mistake for what is an independent Society to sink its identity in this manner. It was recognized that there was a need for a strong active branch of the B.M.A., and that there was no objection to this running parallel with our own Society. It was pointed out that owing to the peculiar geographical position of Londonderry, we have members in our Society from no less than three different Divisions of the B.M.A., viz., Londonderry and District, the North-Eastern Division, and the North Tyrone Division, and also a considerable number from the Donegal Division of the Irish Medical Society, and that this in itself would make any attempt at merging with the local B.M.A. Division quite hopeless. In this connection it is worth recording that one of our Free State members made the interesting suggestion that, leaving aside all question of merging our own Society with the B.M.A., it would be worth while making representation to have a branch formed with headquarters in Derry, to deal with business arising from the four divisions named, including the Donegal Division.

J. A. L. Johnston, *Hon. Secretary.*

19 Clarendon Street, Londonderry.

BRITISH MEDICAL ASSOCIATION
BELFAST DIVISION

The opening meeting of the session was held in the Whitla Medical Institute on 31st October, 1935, when Dr. S. J. Killen, the outgoing chairman, introduced his successor, Dr. S. B. Boyd Campbell.

The latter took as his subject, "The Influence of Gall-bladder and Other Infections on the Incidence of Coronary Thrombosis." After commenting on the increasing incidence of coronary thrombosis, Dr. Boyd Campbell reminded members how

similar the symptoms of acute cholecystitis and coronary thrombosis might be. He went on to describe a large series of cases where there seemed to be a connection between a focus of infection and an attack of coronary thrombosis. In most of these a cholecystitis was the associated condition. It was remarkable how often a gall-bladder infection was, or had been, present in cases of coronary occlusion. He believed that if these patients would submit to operation—too often they refused—a further attack would often be prevented or postponed. Furthermore, these cases stood operation remarkably well.

Dr. Boyd Campbell also quoted cases to show that coronary thrombosis might occur during an attack of influenza, or in connection with a phlebitis, a sinusitis, or septic teeth. His cases were illustrated with slides of excellent electro-cardiograms and X-rays.

A vote of thanks to the speaker was proposed by Sir Thomas Houston, and seconded by Dr. S. R. Hunter.

J. C. C. Crawford, *Hon. Secretary.*

360 Lisburn Road, Belfast.

BRITISH MEDICAL ASSOCIATION
NORTHERN IRELAND BRANCH

The opening meeting of the session 1935-6 was held in the Whitla Medical Institute on 28th November, 1935. In the unavoidable absence of the president, Professor P. T. Crymble, Dr. H. J. Ritchie occupied the chair. The incoming president, Dr. William Lyle (Newtown Stewart), was introduced to the members by Dr. Ritchie, who conveyed to him the best wishes for a most successful year of office.

Dr. Lyle thanked the members for electing him to a very high office, which had been occupied by many distinguished and eminent members before him. He promised to do all he could to uphold the strength of the Branch, and, if possible, to increase its usefulness. Having referred in suitable terms to the exceedingly heavy obituary list of the past year, he proceeded to deliver his presidential address on "The Decadence of the Medical Profession, and the Remedy." In this he referred to the misdemeanours, intentional and otherwise, of certain members, and how powerless the profession was in censuring such an erring member. The disciplinary powers of the General Medical Council were not always applicable, and the offender avoided the ethical committee of the B.M.A. by resigning his membership. Dr. Lyle appealed for the strengthening of the powers of the profession in exercising penal powers, and suggested that the B.M.A. ought to have facilities for reprimand and punishment. His suggestion was that a doctor who was not a member of the Association should be virtually ostracised. Reference was also made to the declining influence of the medical profession, especially in relations with Government departments, and he appealed for a stand towards making the profession fully worthy of its highest traditions, especially in relations with the general public.

Professor W. W. D. Thomson proposed a very hearty vote of thanks to the president, and this was seconded by Dr. Lagan and passed with acclamation.

BRITISH MEDICAL ASSOCIATION
ANNUAL MEETING IN BELFAST, 1937

THE machinery for making the arrangements for the 1937 annual meeting is now beginning to move, and various sub-committees are being formed. At the meeting of the General Committee held some weeks ago, a chairman and convener were appointed for each sub-committee, and within the past few weeks members of the British Medical Association have been asked to indicate on which committees they would be willing to help. It is hoped that these names will all be utilized shortly and the real work soon begin. Mr. W. M. Fullerton has consented to act as honorary treasurer, and Mr. S. T. Irwin is to be the chairman of the Finance Committee, with Drs. Foster Coates, Eileen Hickey, S. R. Hunter, T. B. Pedlow, and Professor W. J. Wilson, Mr. David Strain, and Mr. J. R. Wheeler as members. At a meeting of the Executive Committee held on 3rd December, Professor R. J. Johnstone outlined the scope of the meeting and the necessary arrangements. It has been decided to establish the offices of the meeting in the Whitla Medical Institute, and the British Medical Association is duly grateful to the Ulster Medical Society for their courtesy in extending this valuable offer.

73 University Road, Belfast.

F. M. B. ALLEN, *Hon. Secretary.*

BRITISH MEDICAL ASSOCIATION
NORTH-EAST ULSTER DIVISION

THE Division met in the Cottage Hospital, Coleraine, on Monday, 29th October, 1935. The chairman, Dr. J. C. M. Martin, presided, and there were fourteen members present. Before the meeting, the matron and her staff kindly entertained those present to tea. The main business was the exhibition of a cinematograph film entitled "Sodium Evipan Intravenous Anæsthesia."

Before the film was shown, the chairman returned thanks for the honour done him in electing him chairman of the Division. The film, which was lent to the chairman for the day by Messrs. Bayer & Co., was seen by him in the Gordon Hospital in London some time ago, and he immediately wrote to the hon. secretary and asked him to procure it. The subject, "Sodium Evipan Intravenous Anæsthesia," is not new to many, but the technique certainly is different in parts from the original method. Dr. Martin said he thought this was the greatest advance in medicine for over thirty years. He said he had used evipan for the past two years in 167 cases, and never had the least anxiety. Up to now, he had never used premedication; the book which he had used was strongly against any type of opiate; but now it is known that it can be used with safety, and even doses up to 40 c.c. of sodium evipan can be given to a patient for a prolonged operation, provided that attention is paid to the technique shown in this film, and that during the operation intravenous injections of glucose are given to fortify the liver. The many advantages of evipan are :—

Wide margin of safety; no psychic shock; pleasant to take, no feeling of suffocation; ideal for chest cases, where inhalation anæsthesia is contra-indicated; does not aggravate any pathological condition present (liver excepted); accidental leak outside the vein does not cause damage to surrounding tissues; no sickness or headache; amnesia is the most striking feature of the drug.

J. M. HUNTER, Hon. Secretary.

36 Eglinton Terrace, Portrush.

REVIEWS

A PRACTICAL HANDBOOK OF MIDWIFERY AND GYNÆCOLOGY. By W. F. T. Haultain and C. Kennedy. Second Edition. Edinburgh: E. & S. Livingstone, 1935. Pp. 356; figs. 44; plate 1. Price 15s. net.

This very excellent handbook has now reached its second edition. It has been brought thoroughly up to date by the revision of the subject matter and the addition of several new chapters.

The book is written in a very concise and practical manner, and the text, if not illustrated as profusely as some books, is easily read and understood. In these days when most authorities regard ante-natal care as essential, not only for the well-being of the mother, but also the good health of the child, it is pleasing to see this chapter so admirably treated. It is also refreshing to see prognosis and treatment given such a prominent place, the latter in such a manner as to be practical for the general practitioner and yet including the most modern methods. The section on Gynæcology deals with the commoner diseases, and is treated in the same practical and concise manner.

The book should prove invaluable not only to the medical student, but also to the general practitioner, and once on the bookshelf will be often used as a book of reference.

AN INTRODUCTION TO GENERAL THERAPEUTICS. By H. K. Fry, M.B., B.S., D.P.H. First Edition. London: Cassell & Co., 1935. Pp. 223. Price 6s. net.

The novel approach to the subject and the attractive way in which it is set forth are one important features of this little book.

In approximately two hundred pages, the author has dealt not only with the chemotherapy found in the many handbooks of therapeutics, but with several more specialized and more recent branches of modern methods of treatment: thus about one-half of the book is divided equally between chemotherapy and physiotherapy, while the remainder includes chapters on subjects, important but often neglected, such as climatology, psychotherapy, organotherapy, and dietetics. The chapters on medical electricity, massage, medical gymnastics, and muscle re-education are especially valuable, as too often these subjects are omitted from otherwise good textbooks. The section on chemotherapy is disappointing and somewhat inaccurate, as, for example, the statement that salicylates are specific therapy in rheumatism.

In so far as the book is a concise summary of modern methods of treatment, it has fulfilled the author's purpose. It is not intended to take the place of the larger textbooks of therapeutics, but rather to outline the principles underlying modern treatment.

The book is written in an easy, straightforward style, and makes enjoyable reading. It may confidently be recommended to both students and practitioners as an interesting and helpful introduction to the study of general therapeutics.

CASE REPORTS

A CASE OF POLYSEROSITIS

By F. M. B. ALLEN, M.D., M.R.C.P.Lond.

Assistant Physician, Belfast Hospital for Sick Children;

Physician in Charge of Infants, Royal Maternity Hospital, Belfast;

Lecturer in Infant Hygiene and Diseases of Children, Queen's University, Belfast.

THE case I have to record is that of a boy of twelve years who enjoyed good health, apart from an attack of whooping-cough, until October, 1934, when he was kicked by a horse. This injury consisted of an abrasion of the third finger of the left hand, and possibly a bruise on the chest. The injury was not regarded as serious at first, but his hand became swollen, and eventually he had to go to bed, being very seriously ill. The history of this illness is rather indifferent, but there is no doubt that he had a pericardial effusion, but the character of the fluid or its certain cause is unknown. The boy was kept in bed for several weeks, and during this time the wound in his finger "broke down," and did not make any attempt to heal until two pieces of bone were extruded. This was probably in December of 1934.

His progress from this time was steady, up to a point, but his mother thinks that he never really recovered, and that his health has been indifferent since then. She thinks he has become "delicate," and is not "strong."

The physical examination on admission to hospital in July, 1935, showed that he was pale and somewhat under-nourished, his weight being seventy-six pounds. The cardiac dullness was increased outward and upwards, but not to the right. The heart-sounds were distant, no murmurs were heard, and the rhythm was regular. Pulmonary resonance was impaired on the left, and Traube's space was dull. The outline of the abdomen was full, and there was some shifting dullness. On palpation it was felt to be "doughy." The Mantoux skin tuberculin test was positive. The temperature was normal.

July 27.—An X-ray of the chest showed a large pericardial effusion, with a sharp outline of the left border in the middle zone being continuous with the aortic arch and the base of the heart (fig. 1). The left cardiophrenic angle was obscured by a pleural effusion.

July 28.—The chest was explored, and 30 c.c. of fluid were withdrawn from the pleural cavity. This fluid was blood-stained and contained some pus cells, but no organisms were seen. Diphtheroid organisms were reported on culture. No tubercle bacilli were seen.

August 1.—The pericardium was tapped, and 30 c.c. of a greenish fluid were obtained. No organisms were seen in this fluid, and a culture was sterile. The aspiration of this amount of fluid made no difference to the X-ray appearance of the cardiac shadow.

August 8.—The pericardium was again aspirated, and 350 c.c. of fluid obtained without causing any cardiac distress. This fluid was similar in character to that previously reported.

August 9.—An X-ray of the chest still showed a considerable quantity of fluid in the pericardium. The fluid level was indicative of a pneumo-pericardium, with evidence of a pleural effusion (fig. 2). This film shows a considerable degree of thickening of the pericardium. A film taken the next day with the patient in the prone position showed that the fluid was quite free within the pericardial sac.

The boy's physical condition remained much the same. There was no dyspnœa, no circulatory œdema, and no evidence of cardiac distress. His weight remained constant, and he took his food well. Examination at this time showed his apex beat to be four inches from the middle line. The heart-sounds were still faint. Deep inspiration showed indrawing of the lower intercostal spaces, but there were no abnormal pulsations. There was no clubbing of the fingers.

August 13.—It was noticed that he had a network of veins over the front of the chest. When he was placed in the prone position, the cervical veins were noticed to fill up to the level of one inch above the manubrium. The abdomen was tense and distended.

September 2.—It was noted that the pericardial effusion was apparently as marked as before. The abdomen was becoming progressively more distended, and there was evidence of free fluid within the pericardial cavity. No œdma of the extremities was noted. His weight had increased by eight pounds.

September 5.—The peritoneal cavity was explored, but only a few drops of mucoid fluid were obtained. A few days later the evidence pointed to a considerable quantity of fluid being present, and the peritoneal cavity was again explored, but only a few drops of blood-stained fluid were obtained. A rectal examination made at this time revealed a rounded mass about the size and shape of a small egg, and the possibility of the condition being malignant was considered.

An attempt was now made to elucidate the problem of the cause of the recurring pericardial effusion associated with the presence of fluid in the pleural and peritoneal cavities. The provisional diagnosis at this time was one of polyserositis, but it was felt that there might be some other underlying condition. A number of clinical and laboratory investigations were made. A blood-count showed red cells 4,500,000, with hæmoglobin 86 per cent., and white cells 11,200. The differential count was as follows: polymorphonuclears 73 per cent., eosinophiles 2 per cent., basophiles 1 per cent., large lymphocytes 6 per cent., small lymphocytes 11 per cent., large mononuclears 4 per cent., and transitionals 3 per cent. The Wassermann reaction was negative, and the blood-calcium was 18.1 mgms. per 100 c.c. of blood. An intravenous pyelogram absolved the kidney from malignant changes by showing normal shadows. A barium enema showed no signs of obstruction from the rectum to the cæcum, there being only slight evidence of colitis. A microscopical examination of the urine revealed a few red and white blood cells, but no tubercle bacilli.

The only abnormality that was found was the rather high blood-calcium figure, and this may bear some relation to the histological report received later. The abdomen could not be properly palpated, and the condition therein was very uncertain, so that an exploratory laparotomy was performed on September 27. The peritoneum showed, on the parietal and visceral surfaces, numerous nodules varying in size from a pinhead to a small marble. The cavity was practically obliterated

by adhesions which formed largish plaques of proliferative tissue. It was impossible to examine the liver on account of large masses of adherent peritoneum. The kidneys and other abdominal organs were apparently normal. Some tissue was removed for examination, as was also a lymph-gland.The pericardium was aspirated previous to the operation, and 410 c.c. of fluid obtained. A guinea-pig was inoculated with a specimen of the fluid.

The pathologist's report was that the mesenteric gland and nodules were the seat of chronic caseous tuberculosis. In the lymph-gland the tuberculous lesion tends to conform to the proliferative type in the respect that caseation was relatively slight and tissue reaction is considerable.

October 24.—The pericardium was again aspirated, and 850 c.c. of fluid were withdrawn. Air was excluded from the pericardial sac, and an X-ray revealed that the pericardial membrane was collapsible and apparently not adherent to structures either lateral or anterior. The axis of the enlarged heart-shadow is, however, oblique, and suggests that there may be some adhesions with the structures of the posterior mediastinum.

The guinea-pig which had been injected with pericardial fluid was reported to be suffering from tuberculosis.

The significant features of this case are: (1) The trivial nature of the initial illness which led to pericarditis. (2) The character of the pericardial effusion and its non-absorption and persistent recurrence. (3) The presence of tuberculous infection of at least two serous membranes, as proved by the result of injection of pericardial fluid into the guinea-pig, and the pathological report on the tissues removed from the peritoneum. (4) The history of previous good health.

Attention is drawn to fig. 1, which shows the thickening of the pericardium, indicative of the involvement of all serous sacs, and possibly related to the high blood-calcium figure. It is also noted that the heart has remained normal throughout, and is not the victim of a constrictive adhesion, which would, in turn, result in ascites and œdema of the extremities, as in Pick's disease.

The disease known as polyserositis is sometimes called polyorrhomenitis, chronic hyperplastic peritonitis, Concato's disease, etc. Examples are not common, but they would seem to fall into three groups: (1) Those associated with varying degrees of chronic inflammation of the pericardium, pleuræ, and peritoneum. The commonest sac in which it may originate is the pericardium. In such cases one must presuppose a very much attenuated infection, and in this case now reported, one does not know if the tuberculous condition has persisted throughout or whether it has been imposed upon a pathological condition produced by some other organism. In this connection it is unfortunate that the character of the fluid in the original pericarditis is unknown. (2) In another group a relation exists between a perihepatitis with ascites, arterio-sclerosis, and granular contracted kidneys. In such cases the kidney is regarded as the organ primarily at fault, and the involvement of the various sacs is secondary. (3) The third group includes granulomatous conditions such as tumour, growth, or a proliferative type of tuberculosis. The present case seems to be related to the first and third groups in its characteristics and clinical features.

The diagnosis from Pick's disease (chronic constrictive pericarditis) is relatively

simple in this case, as there are no signs of cardiac distress, nor is ascites a prominent feature. White, in a recent description of Pick's disease, states: "Polyserositis is due to tuberculosis, associated with pneumonia, or, most commonly, of unknown origin. The pleuræ and pericardium are the serous cavities generally involved, but sometimes the peritoneum is also affected. The infection begins as an acute process, sometimes insidious and obscure, with little clinical evidence, and sometimes severe and easily diagnosed." White admits that polyserositis may precede Pick's disease, and that the two conditions may coincide. Other possibilities of diagnosis were considered and excluded. Malignancy was eliminated, in view of the histological report. Rheumatic pericarditis is usually followed by dense adhesions accompanied by hypertrophy of the heart. In this boy the heart is not hypertrophied, and there are no endocardial murmurs. Portal cirrhosis is scarcely worth consideration, on account of the absence of ascites, which is such a prominent feature of this condition.

In expressing my thanks to Professor Young for the pathological report, to Dr. Douglas Boyd for the radiograms, and to Drs. Fisher and Galbraith for the clinical notes, I must not omit the patient. He has been very interested in every procedure carried out, and most co-operative in all the investigations to which he has been subjected.

A CASE OF CARCINOMATOSIS OF GLANDS OF UNKNOWN ORIGIN

By C. J. A. Woodside, F.R.C.S.I.,
from the Royal Victoria Hospital, Belfast.

A married woman, 62 years old, was sent to the out-patient department by Dr. Nicholson of Bangor. Her sole complaint was a swelling of the upper part of the left side of the neck, first noticed three weeks before. It was painless, and she had the impression that it was subsiding. She declared that she was in good health, and had had no recent illness. Twenty-five years ago she was operated on for a strangulated hernia and an ovary was removed, and ten years ago she had severe "neuritis."

She was a plump and cheerful little woman, rather pale and slightly anæmic. Her teeth were false, her mouth and pharynx healthy.

On the left side of the neck, behind and below the angle of the jaw, was a swelling the size of a half lemon, consisting of enlarged and discrete upper deep cervical lymph-glands. The skin was just perceptibly thickened over them, and possibly a little adherent. The occipital glands were also enlarged, although there was no scalp lesion. The lower group of glands on this side were not enlarged, but a couple of small supraclavicular nodes could be felt. The right side of the neck was normal. Both axillæ were filled with masses of large and perfectly discrete glands; both breasts then felt normal. The glands in the groin were palpable, but not grossly enlarged. The abdomen revealed no abnormality. An X-ray of her chest was normal.

On clinical grounds the condition strongly suggested Hodgkin's disease, with the alternative diagnosis of a lymphoid leukæmia.

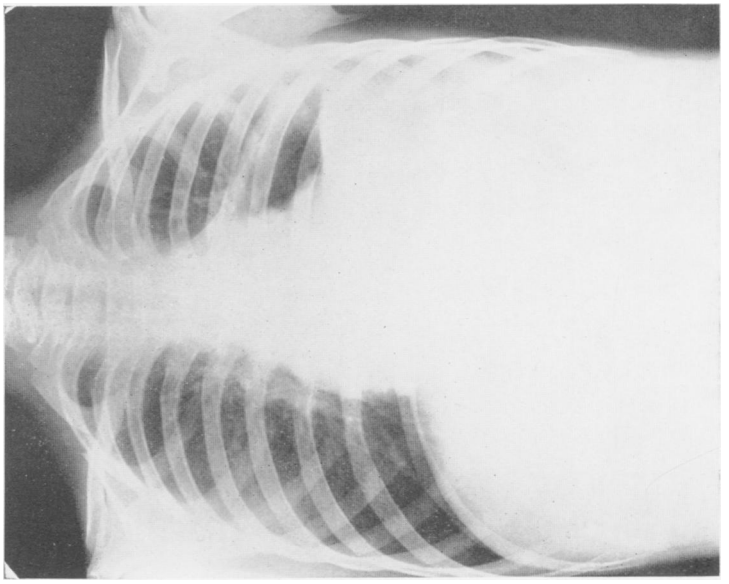
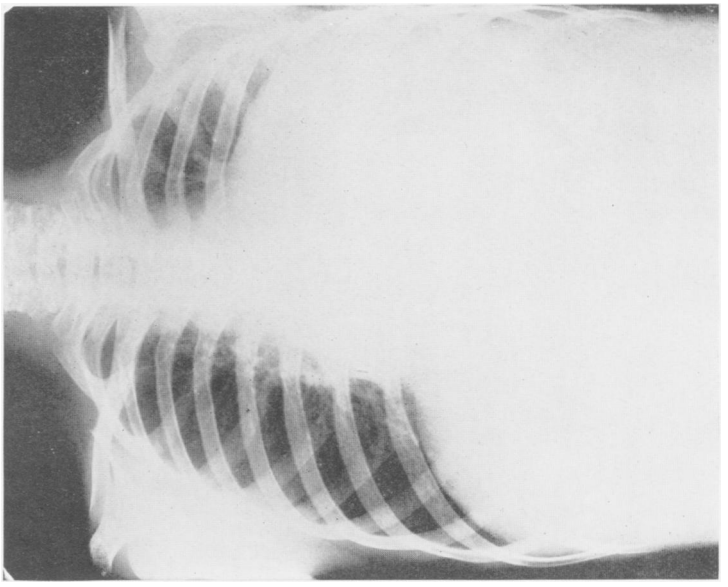


Fig. 2



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On clinical grounds the condition strongly suggested Hodgkin's disease, with the alternative diagnosis of a lymphoid leukæmia.

The blood-count revealed a moderate anæmia and a moderate lymphocytosis, but no increase in the total white cells. I then persuaded her with some difficulty to allow me to remove a gland for section. I excised one from her right axilla, and to my surprise Professor Young reported that it was invaded and almost entirely destroyed by a highly cellular spheroidal cell carcinoma with very numerous mitotic figures.

Since first seen the progress of the disease has been very rapid, as the glands in the left axilla have coalesced, and œdema of that breast developed from lymphatic blockage. The initial focus is still unknown.

The chief points of interest in the case are the "silence" of a primary focus giving rise to such glandular extensive invasion, and the discontinuity of the spread, so resembling on clinical evidence very closely, Hodgkin's disease.

A CASE OF ADVANCED RICKETS

By H. HILTON STEWART, M.D., M.R.C.P.Lond.,
Hon. Physician, with charge of Out-Patients,
Ulster Hospital for Children and Women, Belfast.

RICKETS has been described by Still as "one of the commonest disorders of the poorer population of large cities." In spite of all advances in child welfare in the last decade, cases of rickets are still frequent. Cases, however, of very advanced rickets are comparatively rare, and while the intention is not to report any new features of the disease, an opportunity is afforded to revise our knowledge of the clinical and radiological aspects of an advanced case.

R. C. T., a male child aged two years, was admitted to the Ulster Hospital on 26th August, 1935. He was said to be an adopted child without previous illness. He was said to have been fed on cow's milk and biscuits. No report is available as to whether there was any breast-feeding, or, if so, for how long it was continued.

The presenting complaint was that the child could not sit up. He had always lain on his side. The appetite was poor, and diarrhœa was present. The child was said to sleep badly, and frequently woke up screaming.

Examination showed a very pale and hypotonic child, quite unable to sit up or stand. The heart was normal and the lungs showed no abnormal physical signs; the abdomen was distended, tympanitic, and the liver was palpable but not tender. The bony changes were striking. The head showed frontal bossing. There was a marked pigeon chest. Harrison's sulcus was marked, and the rickety rosary was more than usually prominent. The epiphyses at the wrists were markedly thickened, and kyphosis and slight scoliosis were noted. Only twelve teeth were present instead of the normal twenty. The temperature on admission was 100° F., and remained raised throughout the illness. The motions continued to be loose in character. The urine was normal to the ordinary clinical tests, and the anæmia was of the secondary type, the hæmoglobin being low in proportion to the numbers of the red cells.

X-ray examination was made, and Dr. Montgomery's report is appended.

The blood calcium was estimated a week after admission, and this was found to

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The blood calcium was estimated a week after admission, and this was found to

be unusually high. It was 13.8 mgm. per cent. The blood phosphorus, however, was only 1.8 mgm. per cent., so that the ratio between calcium and phosphorus, instead of being the normal two to one, was eight to one. While it is more usual to find both the blood calcium and phosphorus lower than normal, it is this alteration in the calcium-phosphorus ratio that is typical of rachitic blood chemistry.

In spite of treatment which included fresh cow's milk in the diet, haliverol five drops three times a day, and some orange juice, the child developed broncho-pneumonia, and died on the twentieth day after admission.

Clinically the case was one of advanced active rickets, with marked changes in the bones and mucous membranes. While the bony changes were perhaps most marked, the poor resistance of the mucous membranes to infection was evidenced by the enteritis and terminal broncho-pneumonia.

DR. F. P. MONTGOMERY'S REPORT.

The case under review shows the typical changes which are seen in advanced cases of rickets. There is a marked degree of osteo-porosis, with diminution of the compact cortex and increased coarseness of the cancellous trabeculation. The extremities present marked irregular cupped deformity, while there is considerable bowing of the femora, and much periosteal thickening along the inner margin to compensate for the outward bowing. Radius and ulna on one side show pathological fractures. The slight convexity of the normal diaphysis is markedly altered, and presents an irregular and ill-defined concave appearance which is characteristic of the disease. The ribs on both sides show typical changes.

A CASE OF ACUTE HÆMOLYTIC ANÆMIA WITH SPONTANEOUS RECOVERY

By J. T. LEWIS, M.D., M.R.C.P.Lond.,
Assistant Physician, Royal Victoria Hospital, Belfast.

PATIENT A. D., female, aged 19, was admitted to the Belfast Infirmary on 28th August, 1933. She stated that she had been quite well until one week before admission. She then began to complain of generalized pains and "lightness in the head." This was followed by a severe fainting attack, after which she was admitted to hospital. She would not admit that she had noticed any pallor until about three days before admission.

There was no history of hæmorrhage or of the administration of any drug. Apparently she had been a normal healthy girl, without any previous illnesses of note. There was no history of anæmia or jaundice in the family.

On admission, the patient was seen to be a small under-nourished girl, profoundly anæmic with a distinct icteric tinge, especially marked in the conjunctivæ; temperature 99° F., pulse 120.

There was no ulceration of the mouth or throat, no enlarged glands, and no enlargement of the liver or spleen.

There was a generalized systolic murmur heard over the præcordium. Urine was

be unusually high. It was 13.8 mgm. per cent. The blood phosphorus, however, was only 1.8 mgm. per cent., so that the ratio between calcium and phosphorus, instead of being the normal two to one, was eight to one. While it is more usual to find both the blood calcium and phosphorus lower than normal, it is this alteration in the calcium-phosphorus ratio that is typical of rachitic blood chemistry.

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There was a generalized systolic murmur heard over the præcordium. Urine was

normal, except for a marked excess of urobilin. For a few days after admission there was mild pyrexia and vomiting; these symptoms gradually subsided, and except for marked weakness the patient had no complaint.

Blood Examinations :—

2/9/33—Hb., 23 per cent. Red cells, 1,100,000 per cmm.; white cells, 65,000 per cmm.; colour index, 1.05; reticulocytes, 52 per cent.

Film : Red cells show general megalocytosis. There were a very large number of normoblasts present (42 per cent. of total red cells). Many of the normoblasts were reticulated.

Differential count : Polymorphonuclears, 52 per cent.; lymphocytes, 9 per cent.; monocytes, 2 per cent.; myelocytes, 28 per cent.; myeloblasts, 9 per cent.

Van den Bergh reaction : negative direct; very strongly positive indirect reaction.

This blood picture is highly characteristic of acute hæmolytic anæmia.

The course of the case can be followed from the following blood examinations :—

9/9/33—Reticulocytes, 62 per cent.; normoblasts 20 per cent.

11/9/33—Reticulocytes 58 per cent.; normoblasts 6 per cent.; hæmoglobin, 38 per cent. Fragility of red cells very much increased. Patient shows almost complete hæmolysis in 0.5 per cent. saline; control blood showed hæmolysis in 0.38 per cent to 0.40 per cent.

13/9/33—Hb., 38 per cent.; red cells, 2,000,000 per cmm. No immature white cells seen. Reticulocytes, 36 per cent; normoblasts very scanty.

16/9/33—Hb., 44 per cent. Red cells, 2,300,000 per cmm.; white cells, 10,800 per cmm.; reticulocytes, 25 per cent. Film : Only one normoblast seen, but many red cells showed punctuate basophilia. Polymorphonuclears, 85 per cent.; lymphocytes, 13 per cent.; monocytes, 2 per cent. No immature white cells seen.

24/9/33—Hb., 60 per cent. Red cells, 3,320,000 per cmm.; reticulocytes, 10 per cent. Film : no normoblasts seen. The red cells show distinct megalocytosis.

2/10/33—Hb., 80 per cent. Red cells, 4,020,000 per cmm.; reticulocytes, 7 per cent. Film : no normoblasts seen.

5/10/33—Fragility of red cells : there was now no increased fragility. Patient showed hæmolysis in 0.43 per cent. saline; normal control hæmolyzed in 0.41 per cent. saline.

8/10/33—Hb., 84 per cent. Red cells, 4,230,000 per cmm.; white cells, 17,200 per cmm.; reticulocytes, 5 per cent. Film : no normoblasts seen. Red cells still show some megalocytosis. Polymorphonuclears, 67 per cent.; lymphocytes, 30 per cent.; monocytes, 2 per cent.; myelocytes, 1 per cent.

Van den Bergh reaction was now negative (direct and indirect); Wassermann reaction negative. A fractional test-meal was not carried out.

During her stay in hospital the patient received a simple iron mixture, containing 20 grs. ferri et ammon. cit., thrice daily, and one intramuscular injection of liver extract on 6/9/33. No other treatment was given. At the onset of the illness, blood transfusion was considered, but when it became obvious that spontaneous recovery

was likely it was decided to withhold treatment. If transfusion had been carried out, it would no doubt have received the credit of initiating the recovery.

The patient left hospital feeling and looking well.

She was not seen again until January, 1935. During the year she had remained well, and had been working as a waitress. Apart from slight headache she had no complaints, and did not appear anæmic.

Blood examination: Hb., 83 per cent. Red cells, 4,450,000 per cmm.; white cells, 13,000 per cmm.; colour index, 0.93; reticulocytes, 1 per cent. Film: red cells appear normal in size and shape; no normoblasts seen. Polymorphonuclears, 58 per cent.; lymphocytes, 22 per cent.; monocytes, 19 per cent.; eosinophils, 1 per cent. Fragility of red cells: normal. Van den Bergh reaction: very slight increase in indirect reaction.

I saw the patient again in September of this year. She has still remained quite well, and her blood examination showed:—Hb., 80 per cent. Red cells, 4,800,000 per cmm.; reticulocytes, 1.2 per cent. Film: no abnormality in red or white cells. Van den Bergh reaction: normal. Fragility: within normal limits.

It is quite evident from the blood picture that this was a case of hæmolytic anæmia; the Van den Bergh, the marked increase of urobilin in the urine, and the erythroblastic response are characteristic.

The differential diagnosis seems to lie between Lederer's acute hæmolytic anæmia and acholuric jaundice showing a "crisis." On consulting the literature at my disposal, I have been unable to obtain information which would decide this point. In both there is the same evidence of excessive bone-marrow activity, i.e., marked reticulocytosis, large numbers of normoblasts, and the presence of many immature white cells. It seems to be generally accepted, however, that the numbers of reticulocytes and normoblasts are higher in Lederer's anæmia than in acholuric jaundice, but Baty records a count of ninety-two per cent. reticulocyte in the latter disease.

As regards the red-cell fragility in Lederer's anæmia, it is stated to be usually normal (as in a case published recently by Joules and Masterman in the *B.M.J.*), but Parsons and Hawksley have shown that it may be increased. In acholuric jaundice a marked increase is, of course, characteristic.

Whitby, in his recent book, remarks that the red-cell fragility in Lederer's anæmia may be increased in the acute stage. The fragility, therefore, does not seem to be a point on which one can base a differential diagnosis.

There is one fact, however, on which all observers appear to be agreed. The blood film in acholuric jaundice is definitely microcytic, i.e., the red cells appear to be much smaller and denser than normal on account of their characteristic globular shape.

In Lederer's anæmia, on the other hand, a generalized increase in the size of the red cells is common, though not invariable. In the case described there is no doubt that repeated examination of films showed this tendency to increase in size.

This fact, taken with the apparently isolated nature of the attack, the absence of enlargement of the spleen, the transient nature of the increased fragility, and the absence of any familial history of jaundice, splenomegaly, or anæmia, suggests that this is a case of Lederer's acute hæmolytic anæmia.

The Ganglionic Tissue of the Ileo-Cæcal Junction

By Richard H. Hunter, M.D., M.Ch., Ph.D., M.R.I.A.,
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The presence of nodal tissue at the ileo-cæcal junction, and at other sites in the gut, was postulated by Sir Arthur Keith[1] in an article published in 1915. In another paper[2] published in the same year, he described in the rat, tissue of this nature between the longitudinal and circular muscle coats of the gut wall. Keith stated that in his opinion this nodal tissue of the gut, which he described as forming a ring or collar around the termination of the ileum, was intermediate in kind between non-striped muscle and sympathetic nerve tissue, and that it was similar in nature to the Keith-Flack node of the heart. Alvarez refers to these observations in his book, "The Mechanics of the Digestive Tract," and states that so far as he is aware "no one has yet confirmed the anatomic findings of Keith." He also states that "he knows of several anatomists who have explored sections of the bowel without being able to satisfy themselves that anything like nodal tissue exists there." As the nodal tissue of the heart and its specialized extensions are intimately related to the initiation and co-ordination of the contraction of the heart, it would be certain that if nodal tissue is present in the gut, it would also be intimately concerned with contractile impulses and thus be of considerable importance in the physiology and pathology of the digestive tract. An investigation was therefore undertaken to search for the tissue described by Keith, and to make an examination of it; though, even before it was begun, it was felt that the mechanics of the two systems, heart and gut, were so different that it was unlikely that the same initiatory and controlling mechanism would exist. It was thought, also, that whatever mechanism did exist would be found in its fullest development at a transitional region of the gut, and especially at a part where not only was a co-ordination required between two segments of the gut, but where also between them there was an active sphincter. The ileo-cæcal junction was therefore selected.

The material studied consisted of serial sections of the whole cæcum and appendix with the terminal portion of the ileum and the beginning of the large intestine of the following animals: *Canis familiaris, Felis domesticus, Herpestes fasciatus, Hapale jacchus, Mus albicans, and Lepus cuniculus.* It was believed that this series of animals of differing diatetic habits would sufficiently demonstrate any differences of the tissue of the region of the gut.

Search was first made in the sections for the presence of tissue which would correspond to the description given by Keith and Flack[3] of the nodal tissue found by them in the heart, that is, of "fusiform striated cells with well-marked elongated nuclei, plexiform in arrangement and embedded in densely packed connective tissue." In the sections which were studied of the terminal ileum, there was no evidence of any trace of this tissue which could be compared, morphologically, to the nodal tissue of the heart, using as standards of comparison sections of the

sino-atrial node as were used for the illustrations in Quain's Anatomy (The Heart, vol. 4, pt. 3). There is, however, a considerable amount of specialized tissue between this circular and the longitudinal muscle layers, which forms a network collar around the terminal ileum and the ileo-cæcal, cæco-appendicular, and cæco-colic junctions, especially where the circular muscle is thickened to form the sphincters of these parts. This specialized tissue, constant in these positions in all the animals studied, and obviously belonging to the myenteric plexus, differs greatly in its gross arrangements through the series studied.

In the dog (*Canis familiaris*) (fig. 1), the tissue occurs in masses of considerable size between the outer longitudinal and inner circular muscle coats. These are present in all parts of the sections, but are largest and most abundant opposite the localized sphincteric thickenings of the circular muscle at the ileo-cæcal, cæco-colic, and cæco-appendicular junctions. In sections stained by Mallory's orange G. and wasser blau method, the ganglion cells of the masses are stained orange-red. They are remarkably few in number in each mass, relative to its size, are more numerous next the sphincter, and they are embedded in a large amount of fibrous-looking matrix which is stained a faint blue. The intermuscular and submucous connective tissue elements, on the other hand, are stained a deep blue; this differentiation of the stromal tissues suggests that the matrix of the masses is not a true connective tissue. The ganglion cells vary in size, and are pyramidal or pyriform in shape. Each cell possesses a large oval nucleus, situated at its basal end, and there is a well-defined nucleolus. The cytoplasm of the nucleus has scattered through it numerous coarse granules. The end of the cell away from the nucleus is drawn out into a protoplasmic process which could be followed through, but not beyond the matrix, and in it there is nothing of the nature of striation; it appears rather to be filled with fine acidophilic granules. The matrix, which is fibro-cellular in character—the cell bodies being small in size and the fibres very fine—is distinct from the surrounding tissue, but is not in any way encapsuled; it appears rather to be continuous with, and only with, the fibrous elements of the muscle coats.

In the cat (*Felis domesticus*) (fig. 2), similar masses of the tissue are found in the same muscle plane, and again they are most abundant at the same three sphincteric positions. The matrix of each mass gives the same staining reactions as in the dog, and as before, though there is no evidence of a capsule, it is distinct from the intermuscular fibrous tissue. It is more distinctly fibrous in character than in the dog, and is more freely continuous with the intramuscular fibrous tissue. At one part of the section, shown in fig. 2, the matrix appears to blend and be continuous with the muscle tissue, but after the most careful examination no continuity could be seen, and the matrix tissue presents no myogenic characters. The resemblances to the arrangements of nodal tissue, however, are extremely close.

Similar masses of the tissue are found in the mongoose (*Herpestes fasciatus*) (fig. 3). In their structure and arrangement they resemble the masses present in the dog.

In the common marmoset (*Hapale jacchus*) (fig. 4), the tissue occurs in smaller

masses, and around the ganglion cells there is a less amount of matrix. The masses are scattered in small groups along the whole length of the cæcum and proximal colon, and, as before, they are more abundant, and the individual masses are larger, where the circular muscle layer forms the several sphincteric thickenings. The matrix here is much more sharply defined at its periphery from the surrounding muscle and fibrous tissues, and though there is no proper capsule for it, it is isolated from the fibrous elements of the gut wall in the sense that no continuity is established between them. Further, it is less fibrous in its character, and over large parts of it the appearance is granular; the nuclei of the cell bodies, however, are distinct.

In the rat (*Mus albicans*) (fig. 5), the masses of the tissue are still smaller than in any of the types already described. The matrix is much less abundant and its fibrous character is almost totally lost; there is the definite suggestion of a capsule separating it from the surrounding elements of the bowel wall.

In the rabbit (*Lepus cuniculus*) (fig. 6), the masses are still smaller than those in the rat. The amount of the matrix is still further reduced, it is more cellular and granular, and there is a sharp capsule-like limiting membrane. The characters of the masses are those of the usual descriptions of Auerbach's plexus.

Summary.

In the animals studied there are present, therefore, at the end of the small intestine and at the beginning of the large gut, masses of ganglionic tissue between the longitudinal and circular muscle coats. They are most abundant and largest in size at the positions where the circular muscle is thickened to form sphincteric rings, that is, at the ileo-cæcal, cæco-appendicular, and cæco-colic junctions. The neural elements of these masses vary in shape and size, but most often they are pyriform or pyramidal, as has already been fully described by Spencer, Johnston, and others in their analyses of Auerbach's plexus. They are contained in a matrix which varies considerably in its amount, in its character, and in its relations to the surrounding tissues, but there are gradation forms between the extreme conditions of the dog and of the rabbit. The masses themselves must represent modifications of the same tissue, and be localized enlargements of Auerbach's plexus, and the matrix throughout its modifications must be the same element of the masses. The demonstration of its constituent cells, however, presents many technical difficulties, and has not, of course, been accomplished by the methods used in the preparation of the sections described in this paper. It is, however, probable that the faint blue staining cells form a protective, supporting, glial tissue; but its interpretation, and the interpretation of its differences, is difficult. The differences do occur in association with highly different forms of intestine, for in the large complex cæco-colon of the rodents the masses are small and isolated, i.e., rabbit, and in the simple large intestine of the carnivores, e.g., dog, the matrix is large in amount and its periphery is undefined. In this description of the tissue, therefore, it is only wished to draw attention to the constancy of its presence in the position described by

Keith, and in comparable positions in the cæco-colon, and to its possible influence on the initiation of movements in the large intestine.

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2. KEITH, SIR ARTHUR, 1915, *Br. Journal Surg.*, Vol. 2, p. 576.
3. KEITH AND FLACK, 1907, *Journ. Anat.*, Vol. 41, p. 183.

The Physiology of Labour: Some Old and New Views

By D. H. SMYTH, M.SC., M.D.,
Queen's University, Belfast

EARLY in the history of civilization, man must have found it necessary to anticipate and make provision for new arrivals, both to his own family and also to those of his domestic animals. The discovery would follow that in each animal pregnancy runs a certain fixed course peculiar to the species, and in the great majority of cases its termination can be predicted to within a few days. At the end of this fixed time some hidden change takes places in the organism, with the result that the fœtus gives up its tenancy of its mother's uterus and comes to exist as a separate entity. What mechanism has nature provided to initiate a step so vital to both mother and fœtus, and when such a process is begun, how is it controlled and regulated so that events follow in a definite and orderly way, leading to the birth of the child, then the expulsion of the placenta, and finally the resumption by the uterus of its original size and condition? The complete investigation of this problem raises a great many issues, but here only one aspect of the birth process will be discussed, namely, the question of the labour pains, how they are elicited and controlled, and what is their significance.

Of all the features associated with child-bearing, probably the labour pains have always attracted most attention. Is it not significant that the very word which we use to denote the termination of pregnancy should express not the arrival of a son and heir, nor the responsibility of a new dependant to be provided for, not even the relief from long weeks of anxiety, but simply the physical pain endured by the mother. It is also noteworthy that to impress the highest flights of mental and physical endurance and suffering, men have used words which refer to the pains of motherhood. Let us examine, therefore, some of the views which have been held concerning the nature and cause of these pains.

"In sorrow thou shalt bring forth children," was the curse of the Garden of Eden, and the spirit of this people for centuries regarded labour pains as an heritage of womankind to expiate for the sins of their early parents. It is less than a hundred

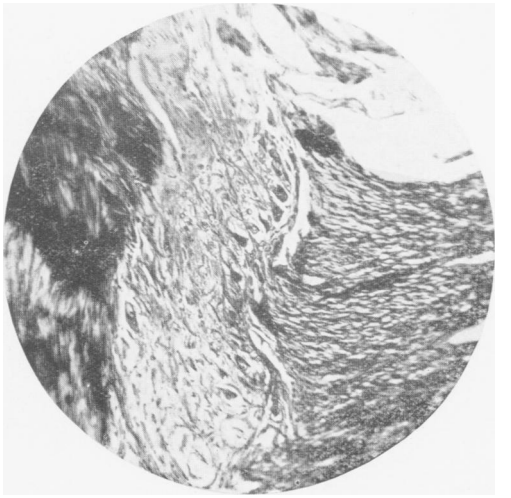

Fig. 1 — Canis familiaris

Fig. 2 — Felis domesticus

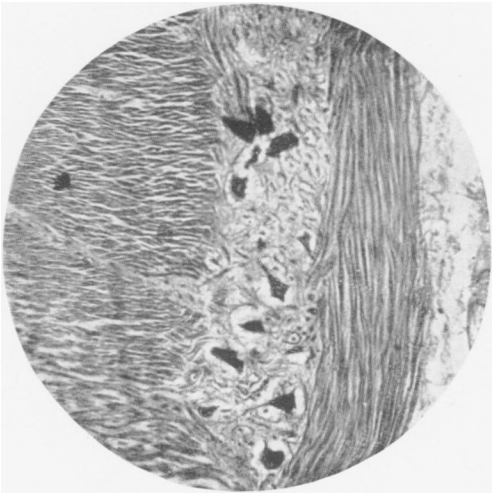

Fig. 3 – Herpestes fasciatus

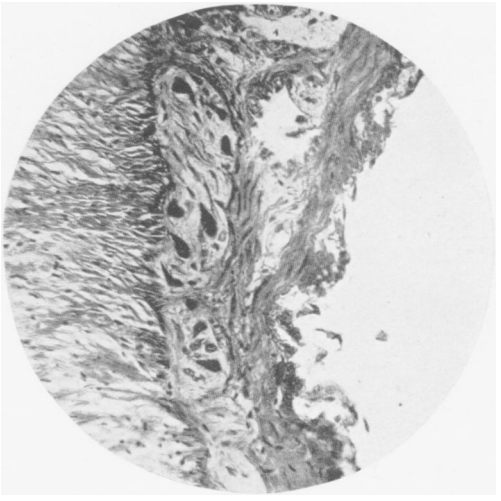

Fig. 4—Hapale jacchus

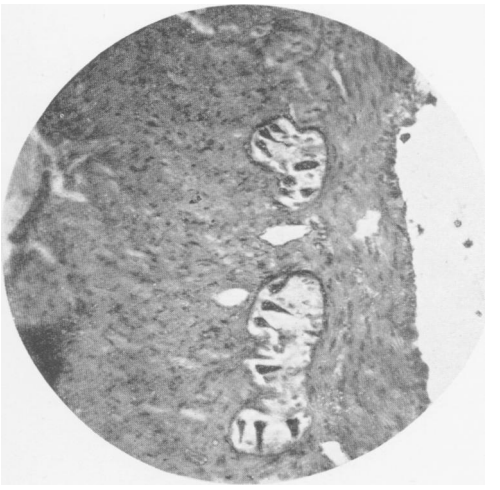

Fig. 5 — Mus albicans

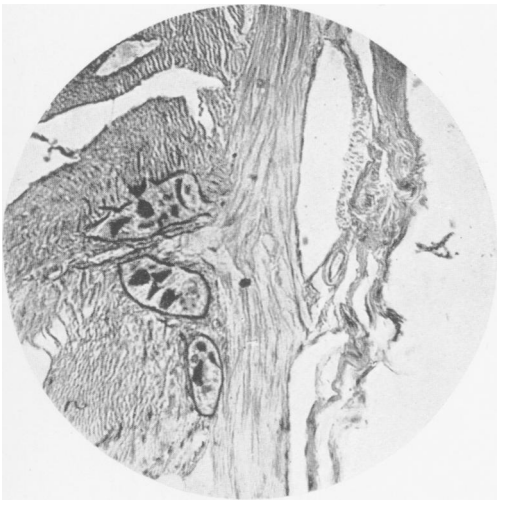

Fig. 6 — Lepus cuniculus

Keith, and in comparable positions in the cæco-colon, and to its possible influence on the initiation of movements in the large intestine.

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Of all the features associated with child-bearing, probably the labour pains have always attracted most attention. Is it not significant that the very word which we use to denote the termination of pregnancy should express not the arrival of a son and heir, nor the responsibility of a new dependant to be provided for, not even the relief from long weeks of anxiety, but simply the physical pain endured by the mother. It is also noteworthy that to impress the highest flights of mental and physical endurance and suffering, men have used words which refer to the pains of motherhood. Let us examine, therefore, some of the views which have been held concerning the nature and cause of these pains.

"In sorrow thou shalt bring forth children," was the curse of the Garden of Eden, and the spirit of this people for centuries regarded labour pains as an heritage of womankind to expiate for the sins of their early parents. It is less than a hundred

years ago since Dr. Meigs of Philadelphia said : "The pain of labour is a desirable, salutary, and conservative manifestation of life force." Such an attitude, which was probably most acceptable to those who could never receive the great benefit of sharing in this salutary form of suffering, prevented any research into a scientific explanation of the pain. Great credit is due to the early pioneers who sought to investigate the physical significance of all the features of the birth process, and were more concerned with alleviating the pains of motherhood—as any other human suffering—than with theological discussions about the desirability or otherwise of the pain involved.

Many primitive peoples have held the view that labour consisted in an active struggle by the fœtus to get free from its confined prison. This explained many of the early methods of treating midwifery cases, where the onlookers directed their energies to coaxing or threatening the child if it was not quick in making a successful exit. The pains of the mother were laid to the charge of the bad disposition of the fœtus, and a vicious baby would tend to cause a protracted and severe labour. Such a view is interesting in view of the belief we still hear sometimes that many of the world's criminals have come into the world as breech presentations !

We now know that the pains of labour are an accompaniment of the uterine contractions in their efforts to expel the fœtus, just as severe muscular contraction in any of the other organs can cause severe pain. But this only puts the problem one stage farther back, and we face the question as to why the uterine muscle, after stretching and accommodating itself for nine months, should suddenly abandon this passive rôle and begin to contract to empty the contents of the uterus. Many are the reasons which have been put forward to account for the phenomena taking place, but even yet there is much to be explained, and we have by no means a complete picture of all the influences at work. Recent physiological and biochemical advances have thrown much new light on the problem, although often conflicting evidence has been brought forward which has seemed to make the problem more difficult. This especially applies, as we shall see, to the work in the fields of endocrinology.

Of the older scientific views which have been held as the cause of the onset of the labour pains, Stoeckel (1920) gives the following, most of which could play a part, but few can be definitely proved to do so :—

1. Owing to fatty degeneration of the placenta, the connection between the mother and child becomes looser toward the end of pregnancy. Finally the fœtus becomes quite separate, and is then expelled by the uterus as a foreign body.

2. Thrombosis in the placental sinuses leads to excess carbon dioxide, and the accumulation of this substance finally stimulates the uterus.

3. The quantity of amniotic fluid becomes relatively and absolutely smaller as full term approaches. Hence the child's movements come into closer and more intimate contact with the uterine wall, and thus stimulate uterine activity.

4. Pressure of the contents of the uterus in the region of the internal leads to stimulation of the uterine cervical ganglion, which is regarded as a local centre

for uterine contractions. The uterine cervical ganglion is also held responsible for miscarriages and abortions following nervous factors such as fright, shock, etc.

5. As the fœtus grows, the smooth muscle of the uterus ultimately comes to a limit by which it can stretch no farther. Such a condition tends to cause the onset of muscular contractions.

6. A uterine inhibitory centre has been postulated, and the onset of labour is due to an inhibition of the activity of this centre.

7. Placental growth does not keep pace with the growth of the child, and therefore the placenta becomes relatively smaller. From the thirty-sixth week the difference becomes so marked that the vital stimulation of the fœtus, which normally prevents the onset of labour, is weakened, and finally lost, and thus labour begins.

8. The blood in pregnancy is gradually enriched with adrenaline, which sensitizes the uterus to contractile stimuli.

9. Fœtal excretory products lead to an intoxication of the mother's blood, and cause hæmolysis. This helps to supply the calcium need of the fœtus. Also there is formed from a combination of placental proteins, with side-chains of erythrocytes, a substance which inhibits the onset of labour. Toward the end of pregnancy the breakdown of erythrocytes increases, there are insufficient numbers left for the formation of the side-chain combinations, and hence labour begins.

10. Experiments have been made in which the circulatory systems of two rats were joined. In these cases, if one rat was pregnant and the other not, the non-pregnant one showed symptoms of severe illness when the first came into labour. If both were pregnant, the one in early pregnancy aborted when the other came into labour. Such experiments were said to show the presence of some substances in the blood during labour which were not normally present.

In addition to these, other reasons which have been suggested for the onset of labour are infarction of the placenta, accumulation of toxic products which stimulate uterine contractions, and the menstrual periodicity. It is well known that abortion when it occurs is more likely to do so at a time corresponding to the menstrual periods.

Some of these causes may, and probably do, play a part in the onset of labour pains, but it must be admitted that the experimental evidence in support of them is very slender, and some of them are speculation, which it would be very difficult either to confirm definitely or to disprove. We turn now to the more modern theories which are based on experimental findings, and of these will be considered, first, the endocrine theories, and later the possibility of a local chemical mechanism.

The great advances in endocrinology which have been made recently have ascribed to the ductless glands a controlling and regulating part in many of the body activities, but more in the reproductive system than in any other has it been recognized that hormones play a very important rôle. The sexual growth, development, and activities of the animal depend largely on these secretions, and it is also thought now that they exert an influence on the maintenance of pregnancy and the

onset of labour. The amount of experimental evidence on the question which has been accumulated within the last few years is very extensive, but it has lately been well reviewed by Robson (1935). The brief account given here is based on this work. It it probable that an endocrine mechanism of the onset of labour will consist of one or more of the following phenomena :—

1. An increase in concentration in the blood of some substance which can act on the uterus and cause it to contract.

2. An increase in the sensitivity of the uterus to some substance which will not normally cause contraction.

3. A removal of some inhibitory substance which can prevent contraction of the uterus.

The possible sources of such substances are the fœtus, the placenta, the ovaries, and the pituitary. Of these, there is no definite hormone known to be produced from the fœtus, but such a possibility is suggested by the fact that removal of the fœtus leaving the placenta *in situ* is said to result in a cessation of certain secretory activities characteristic of pregnancy, resulting in regressive changes in the breasts and ovaries. The placenta may act as an additional source, or possibly only a storing place of œstrin, but otherwise does not appear to produce any hormones influencing the course of gestation. More important are the secretions of the ovary (œstrin and progestin) and pituitary (oxytocsin and prolan B). Oestrin is the secretion of the interstitial tissue of the ovary. In addition to its controlling action in menstruation, it also during pregnancy sensitizes the uterus to the action of oxytocsin. Progestin is the secretion of the corpus luteum. It has an inhibitory action on oxytocsin, and prevents it causing contraction of the uterus. Parks (1928) claims to have shown that removal of the corpus luteum during pregnancy always results in abortion. Prolan B is contained in the extract of the anterior lobe of the pituitary. It has an effect on the formation and maintenance of the corpus luteum. Injections of prolan B prevent degeneration of the corpus luteum and can cause postponement of labour. Oxytocsin is contained in the posterior pituitary extract. It has a stimulant action on uterine muscle both *in vivo* and *in vitro*. The sequence of events leading up to the onset of labour may be of the following nature. During pregnancy there is a gradually increasing sensitization by œstrin of the uterus to oxytocsin. In the early months the stimulating action of oxytocsin is inhibited by progestin. The degeneration of the corpus luteum, which may be associated with some change in the prolan B secretion, removes the inhibitory effect of progestin. This, together with the increased sensitivity of the uterus, and also probably increased secretion of oxytocsin, causes a setting in of the labour pains. Such a scheme has been suggested, but many objections can be found. It has been shown that labour can still follow after removal of pituitary. Allan and Wiles (1932) showed that normal pregnancy and labour has continued even after removal of the ovary. Nevertheless, it seems certain that the hormones must play an important rôle in the maintenance of pregnancy and the onset of labour, even although the exact part played by each hormone is still obscure.

The newest theory of the physiology of the labour pains postulates a local

chemical mechanism which causes the uterine contractions. It is of the greatest significance that the chemical agents which are said to be involved are the base choline and its very active acetyl ester, as these substances are now known from the work of Dale (1929) and others to play an important rôle in the humoral transmission of nerve impulses. The principle of this theory, briefly, is that at some stage in labour choline is liberated from a chemical substance in the placenta. From this choline, acetylcholine is formed, and this substance causes contractions of the uterus. Let us look in some detail at the facts which support this theory, and their interpretation.

Bischoff *et al.* (1931) drew attention to the large amounts of acetylcholine in the human placenta. Chang and Wong (1933) showed that this acetylcholine is contained mostly in the placenta villi. Strack and Loeschke (1931) showed that the pregnant uterus is choline-free and its sensitivity to acetylcholine is increased. The important question which arises is the possible source of choline or acetylcholine in the placenta. Strack *et al.* (1935) found that the placenta contains free choline, and that the amount of free choline increases if the placenta is not removed from the uterus immediately after cutting the umbilical cord. This is on account of the autolysis which takes place, the uterus, of course, providing an ideal incubator for the activity of autolytic enzymes. These German workers believe that during this autolysis, choline is set free from a precursor in the placenta. They had evidence that this was a compound containing choline, sphingosine, and phosphoric acid. Booth and Milroy (1935) succeeded in isolating a substance of this nature in a highly purified form from the liver. Smyth (1935), by a similar process, showed that this body also occurred in the human placenta in very small quantities. On hydrolysis it yielded choline, and also from this placental precursor could be formed an acetylated derivative which, like acetylcholine, inhibited the action of the heart, caused a fall in blood-pressure, caused increased tone of the intestine, and caused contractions of the guinea-pig uterus.

Such are the actual findings. What is the significance of these? First, there is a substance present in the human placenta which can yield choline, and possibly acetylcholine, under the action of autolytic ferments. Strack *et al.* has suggested that it may yield choline early in labour, and actually be the cause of the labour pains. Whether or not this happens early in labour is doubtful, but certainly it produces free choline once the umbilical cord is cut, for with this disturbance of the circulation autolysis begins. There is no definite evidence yet that any of this free choline is acetylated, but the possibility of such an occurrence cannot be doubted. Also the altered pressure relations in the uterus following on rupture of the membranes would be exceedingly favourable for the expression from the placenta of active principles contained in it.

The findings of Chang and Wong that the acetylcholine occurs in the placental villi indicates that this substance comes into close relationship with the uterine wall. Also the final expulsion of the placenta by removing the source of the choline would automatically put an end to the severe painful contractions of the uterus. It seems likely, therefore, that this chemical mechanism may play at least in the

third stage of labour. Another possible participation of such a mechanism would be in the emptying of the uterus after death of the fœtus early in pregnancy. In this case few of the other local mechanisms described could play a part, and the endocrine mechanism would not be mature. The autolysis of the fœtal products which would take place after the death of the fœtus could, by liberation of choline and formation of acetylcholine, lead to an emptying of the uterus. The old theory of infarction of the placenta also takes a new interest when it is remembered that in these infarcts might be a breaking down of the choline mother-substance, with the formation of acetylcholine.

Much more work requires to be done in regard to the amounts of choline and its precursors and derivatives in the placenta at various stages of pregnancy and labour. The conditions necessary for the building up and breaking down of these substances also call for investigation. It is assumed that these processes are due to enzyme action, but the details of the action are unknown. Even with a fuller knowledge of the chemical changes involved, it is not to be expected that we shall arrive at a complete insight into the production of labour pains. Like all the other theories advanced, the chemical one is open to much criticism, and fails to explain all the observed facts of pregnancy and labour. The chemical findings, however, on which the theory rests, are in most cases fairly definitely established, although increased knowledge may lead us to a different interpretation of them.

A survey of these theories of the onset of labour pains cannot fail to impress one with the very scanty knowledge which we possess of this all-important phenomena. Of all the hypotheses put forward, few can be proved with any degree of certainty, and none are sufficiently comprehensive to cover all the aspects of the problem. It is only, however, by an exhaustive exploration of every line of approach, and a complete scientific investigation of all the physical, chemical, and biological processes involved that we can hope to obtain a complete picture of all the agencies involved in the production of labour pains, and thereby learn to understand and to mitigate the sufferings of motherhood.

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REVIEWS

A PRACTICAL HANDBOOK OF MIDWIFERY AND GYNÆCOLOGY. By W. F. T. Haultain and C. Kennedy. Second Edition. Edinburgh: E. & S. Livingstone, 1935. Pp. 356; figs. 44; plate 1. Price 15s. net.

This very excellent handbook has now reached its second edition. It has been brought thoroughly up to date by the revision of the subject matter and the addition of several new chapters.

The book is written in a very concise and practical manner, and the text, if not illustrated as profusely as some books, is easily read and understood. In these days when most authorities regard ante-natal care as essential, not only for the well-being of the mother, but also the good health of the child, it is pleasing to see this chapter so admirably treated. It is also refreshing to see prognosis and treatment given such a prominent place, the latter in such a manner as to be practical for the general practitioner and yet including the most modern methods. The section on Gynæcology deals with the commoner diseases, and is treated in the same practical and concise manner.

The book should prove invaluable not only to the medical student, but also to the general practitioner, and once on the bookshelf will be often used as a book of reference.

AN INTRODUCTION TO GENERAL THERAPEUTICS. By H. K. Fry, M.B., B.S., D.P.H. First Edition. London: Cassell & Co., 1935. Pp. 223. Price 6s. net.

The novel approach to the subject and the attractive way in which it is set forth are one important features of this little book.

In approximately two hundred pages, the author has dealt not only with the chemotherapy found in the many handbooks of therapeutics, but with several more specialized and more recent branches of modern methods of treatment: thus about one-half of the book is divided equally between chemotherapy and physiotherapy, while the remainder includes chapters on subjects, important but often neglected, such as climatology, psychotherapy, organotherapy, and dietetics. The chapters on medical electricity, massage, medical gymnastics, and muscle re-education are especially valuable, as too often these subjects are omitted from otherwise good textbooks. The section on chemotherapy is disappointing and somewhat inaccurate, as, for example, the statement that salicylates are specific therapy in rheumatism.

In so far as the book is a concise summary of modern methods of treatment, it has fulfilled the author's purpose. It is not intended to take the place of the larger textbooks of therapeutics, but rather to outline the principles underlying modern treatment.

The book is written in an easy, straightforward style, and makes enjoyable reading. It may confidently be recommended to both students and practitioners as an interesting and helpful introduction to the study of general therapeutics.

Wide margin of safety; no psychic shock; pleasant to take, no feeling of suffocation; ideal for chest cases, where inhalation anæsthesia is contra-indicated; does not aggravate any pathological condition present (liver excepted); accidental leak outside the vein does not cause damage to surrounding tissues; no sickness or headache; amnesia is the most striking feature of the drug.

J. M. HUNTER, Hon. Secretary.

36 Eglinton Terrace, Portrush.

REVIEWS

A PRACTICAL HANDBOOK OF MIDWIFERY AND GYNÆCOLOGY. By W. F. T. Haultain and C. Kennedy. Second Edition. Edinburgh: E. & S. Livingstone, 1935. Pp. 356; figs. 44; plate 1. Price 15s. net.

This very excellent handbook has now reached its second edition. It has been brought thoroughly up to date by the revision of the subject matter and the addition of several new chapters.

The book is written in a very concise and practical manner, and the text, if not illustrated as profusely as some books, is easily read and understood. In these days when most authorities regard ante-natal care as essential, not only for the well-being of the mother, but also the good health of the child, it is pleasing to see this chapter so admirably treated. It is also refreshing to see prognosis and treatment given such a prominent place, the latter in such a manner as to be practical for the general practitioner and yet including the most modern methods. The section on Gynæcology deals with the commoner diseases, and is treated in the same practical and concise manner.

The book should prove invaluable not only to the medical student, but also to the general practitioner, and once on the bookshelf will be often used as a book of reference.

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