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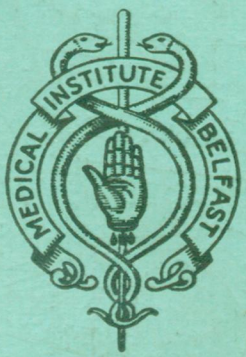

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THE
ULSTER MEDICAL JOURNAL

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VOL. IV 1st JANUARY, 1935 No. 1

Reminiscences of Janesh, 1916-1917

By S. R. HUNTER, B.A., M.D.

Presidential Address, Ulster Medical Society,

SESSION 1934-5

My first duty is to thank you for electing me as your president for the ensuing session. I need scarcely tell you how fully I appreciate this high honour; at the same time I must confess that not only do I thoroughly realize the high traditions and the great responsibilities that are attached to it, but even more do I realize the very capable and brilliant manner in which these duties have been maintained by my predecessors. I feel, therefore, that I must crave your kind indulgence for any apparent lack of efficiency on my part during my year of office, but I can promise you that I shall try to do my very best to maintain something of that high standard this Society is accustomed to expect from its president.

To decide on a subject which would be suitable for an address to-night was rather a difficult problem for me. Every medical student knows that a general practitioner, by his extremely varied daily work, of necessity becomes a "Jack of all trades and a master of none," so I decided to leave medical subjects almost alone and to give you a few impressions of my experience of service during the Great War.

I cannot give you an account of any very exciting or hair-raising incidents, but I hope I may be able to draw for you a sketch, certainly very imperfectly, of life behind the lines, which to me was always novel, interesting, and with an occasional thrill.

Twenty years ago, in the second year of the war, the demand for men, including doctors, was becoming more and more insistent. Men newly qualified had then no difficulty in making up their minds what to do, for even medical students were dropping their studies to join up as combatants. At Queen's the Corps of Veterans had been formed, in which professors, lecturers, and many of the older medical men of the city and district were being drilled for home defence. In Dunmurry, Dr. Gaussen and I were leading normal professional lives, with nothing more

exciting than the drilling of Ulster Volunteers and the teaching of Red Cross classes, in view of some civil trouble which was then threatening. Many of our friends, relations, and patients were joining the Ulster Division and other regiments; so we came to the conclusion that it would be possible for one of us to do all the work and allow the other to volunteer. Being senior and getting near the age limit, my colleague claimed it as his right to go first. He was accepted, and soon afterwards was appointed to the hospital ship "Britannic," where he found a Dunmurry friend and an old Queensman, Colonel Anderson, R.A.M.C., in charge, who made him his adjutant. After six months pleasant and useful experience he returned home, and a few days later I started my military career at the Victoria Barracks, Belfast. For the next month, in addition to the usual duties attending patients in the wards, I received the instructions necessary for running a military hospital, going through the routine work of the office.

This was very interesting work, but I never had an opportunity of putting my knowledge into practice, except for one day only, when I had the honour of being in charge of a hospital ship on the River Tigris, running between Amara and Baghdad. The usual medical officer in charge of this ship had been summoned to a court martial which he thought would put an end to his command. But he was sent back the following day, and I had to return to the stationary hospital in Baghdad, at which the previous night I had been given a farewell dinner. At the end of a month in Belfast I got orders for Egypt, and was told by my medical friends here that this was a nice "cushy" job, and from the experience to be gained there I should probably return a venereal expert.

On the 8th July, 1916, with about forty other medical officers, I sailed from Devonport in the Cunard liner "Franconia"—not the "Franconia" in which the B.M.A. members are sailing next year round the world to visit Melbourne, for our ship was shortly afterwards sent to the bottom of the Mediterranean by a torpedo. After calling at Gibraltar, we hugged the northern coast of Africa, passing sufficiently close to have a good view of Algiers. From this point till we arrived in Malta lifebelts had to be worn all the time and not simply carried, as had been previously done, because warning had been received that a submarine was in our close neighbourhood. On reaching Malta we were allowed the afternoon on shore, and some of the passengers found themselves wandering about the town still enveloped in their lifebelts.

Four days later we reached Alexandria, and were driven in ambulances to Mustapha Camp, where, as there was practically no work to do, nine very enjoyable days were spent bathing at Stanley Beach, playing golf at the Sports Club, and seeing the sights of Alexandria both by day and by night.

While in this camp many swallowed enough sand and also oily food polluted with flies, that they soon had sufficient reason to imagine that they were developing dysentery. As a matter of fact, on reaching Port Said, our next port of call, my cabin companion, the late Fred Davey of Belfast, had to be taken to hospital suffering from amœbic dysentery.

A stay of six days was made at Port Said for the purpose of having a stern gun fitted to our new ship, the "Ismailia." These days passed very pleasantly. Those

who wished were given leave to visit Cairo, and for those who remained there was good sea-bathing, with excellent meals in the Eastern and Casino Hotels. The temperature in the afternoons was generally a little over 80° F. in the shade.

Our ship, a small British India steamer, in addition to about one hundred officers, was carrying a cargo of ammunition and petrol in tins, unprotected except for our new stern gun. Fortunately we again managed to dodge the submarines which were frequenting these waters, and sailed into Salonica Harbour one month after leaving England, passing on our way up the wrecks of several large steamers which had not had our good luck.

Probably many members of this Society have had the pleasure of sailing up the Gulf of Salonica and seeing what I can only very feebly attempt to describe. On one side are the blue rugged hills of Calcidice, and on the other the mountains of Macedonia, with the great peak of High Olympus, sacred to Zeus, the Thunderer, almost ten thousand feet high, dazzling white and dominating the whole view. Straight ahead lay Salonica, the ancient Thessalonica of the Greeks, the scene of the early missionary efforts of St. Paul—a city with a troubled history of being ruined on many occasions in the past by fire, earthquakes, and plagues. In its time it had been held by Romans, Saracens, Normans, and Venetians. Captured in 1430 by the Turks, it had been held by them till the victorious Greeks recaptured it in 1913. Many of its buildings along the front and near the barracks shewed the bullet marks of this last fight.

Salonica approached thus from the sea is really a beautiful sight, resembling in shape an irregular quadrilateral composed of terra-cotta buildings with red-tiled roofs. Among these were visible many green spots formed of cypress and mulberry trees, as well as white, slender minarets and domed mosques scattered over the city as it rose tier upon tier to the feet of the bare, distant hills of Kalamaria. Along the water-front, which extends for a mile, ran the principal street; on its one side was the quay, and on the other in an unbroken row were many of the principal hotels, banks, cinemas, and the houses of the rich Turks and Jews. At one end was the famous "White Tower," formerly known as the Tower of Blood, owing to the numerous deeds of nameless cruelties perpetrated within its walls. I need not tell you what a disillusion awaits the traveller on landing. But still, there was much of interest to see in this ancient city, and this interest was greatly increased by the swarms of armed men which made Salonica at this time one of the most crowded and cosmopolitan spots in the universe. La Place de la Liberté was the centre of all its life, a large open square; on two of its sides were cafés, one of these being the famous "Flocca's." Small tables and chairs covered the sidewalks and roadway except for a narrow gangway for pedestrians, all other forms of traffic being barred. As a rule, every seat was occupied by the fighting men of over a dozen nationalities, enjoying an infinite variety of drinks, smoking and talking shop in half the languages of Europe. Among these frequently were seen English Army sisters and nurses having afternoon tea, and enjoying an hour or two off from their arduous work.

The varieties of uniform seen were endless. As well as those worn by the men of the British, French, Italian, and Russian regiments, were those of the sailors of

the same nations. In addition to the new uniforms of the revived Serbian Army and the newly recruited volunteer Greek regiments, were seen costumes ranging from those depicted in Biblical illustrations to city dressed men wearing fezes, as well as Greek gendarmes with their amply-seated baggy breeches.

Shortly after our arrival in Salonica an Irishman from Mayo and I received orders to join the 31st Casualty Clearing Station at Janesh, thirty or forty miles up country from Salonica.

Janesh was then the railhead for the 12th Army Corps and quite a busy spot. The C.C.S., which had been opened only a week before our arrival, was placed on a small hill a quarter of a mile from the railway. From it a plain extended northwards to the hills at Doiran, where the principal fighting was then taking place.

As is well known now, it was at Doiran that the first breach was made in the enemies' ring, which resulted in the capitulation of Bulgaria on 30th September, 1918, and brought Turkey, Austria, and finally Germany herself tumbling down in ruins.

Janesh was a station on the railway line which ran from Salonica up to Doiran Lake, and then on to Constantinople. Probably at one time there had been quite a fair-sized village, but it had been wiped out during the Balkan War of 1912. Macedonia had been dotted over with these derelict villages, but nothing was then left to mark where many of them had stood, because the stones were taken from their ruined walls to metal the roads used by our army. All that remained of Janesh was one large farmhouse still intact, and an ornate Greek church with a belfry in ruins; in this church was held each Sunday morning an English Church service. In addition to being a dump for the Divisions operating on the Doiran front, Janesh soon became the site of numerous corps camps, including an aerodrome.

In this C.C.S. the medical officers lived in double-ply bell-tents; inside the curtain of each tent was a wall of sandbags three feet high, which made them really very comfortable. During the summer months we risked sleeping without mosquito-nets, as the hospital was situated on a slight hill, which the constant breeze seemed to keep free from these pests. In the winter we slept in our valises after putting on more clothes than we were accustomed to wear during the day, for the nights were so terribly cold that even water was frozen in the tents by morning. A most irritating plague during the hot weather was the swarm of large flies that were everywhere; especially annoying were they during meals, when one had actually to knock them off each mouthful before swallowing.

Food occasionally was rather scarce, especially at those times when the submarines were having a bit of luck sinking our supply boats in the Mediterranean. Even tinned asparagus begins to lose its savour when one has it served more than once daily as the only vegetable. Bully beef and Maconochie make really good dishes, but much depends on the cook. Later on food became quite good and varied. The water supply was plentiful, and if found suspicious by our sanitary expert was chlorinated.

The scenery around was very wild and beautiful. To the north, and forming the boundary between Servia and Macedonia, was a range of mountains from four to

five thousand feet in height, the tops of which for the greater part of the year were covered with snow. In other directions were rugged and treeless hills.

A curious and interesting reason for this treeless state of Macedonia is supposed to be due to an old Turkish law which fixed the amount of taxes to be paid by landowners according to the number of trees they had growing on their land. To diminish the amount to be paid, the landowner simply cleared off all his trees, and thus brought the hillsides to their present state of barrenness.

We became in time quite accustomed to finding lizards, centipedes, tortoises, scorpions, snakes, streams of black and red ants, with many other forms of insect life, wandering among our tents and marquees. At night the croaking of innumerable frogs was continuous. No one who was on this front will soon forget the Vardar winds, which blew for at least seventy-two hours, very bitingly cold in winter and dust-laden in summer. They sprang up suddenly and as suddenly died down again. Loose articles or a badly put up tent with its contents were soon sent flying in a "dust devil."

From the hill on which our hospital was situated, a splendid view could be had of that stretch of the front line between Lake Doiran and the Vardar River, which was the Ypres salient of the Macedonian front, not because it was really a salient, but because of the bitter and heavy fighting that constantly raged along here, because of the heavy casualties, and because of the dominating enemy positions—the Grand Couronné, three thousand feet high, and the "Pip Ridge," which overlooked every movement that the British made from there right down to Salonica. During a 'strafe' at night the scene was marvellous, the thunder of the big guns, the explosions of both our shells and those of the enemy, the continuous rattle of the rifles and machine-guns, the flashes of powerful searchlights and rockets of various colours, the whole scene lit brilliantly up at intervals by Véry lights.

When reporting my arrival to the colonel in charge of the hospital, I was greatly astounded to hear another officer in the orderly room telling him in a very emphatic tone that what he wanted done must be done at once and that no one in that hospital had any right to interfere with his marquees. On turning round to leave, this dictatorial person bumped into me, and to our mutual surprise and pleasure we recognized each other as old fellow-students of Queen's. He was our good friend Captain Thomas Carnwath, sanitary expert for the Salonica Army and temporarily attached to the C.C.S. with his marquees, orderlies, motor-car, and a pile of baggage. Later on, in the hospital, Carnwath gave a series of very interesting and useful lectures on military sanitary science to the medical officers of the different battalions, who came down from the front in batches for a week at a time. Among these were several Ulstermen, including our good friend John Weir. The staff of the C.C.S. consisted of a lieutenant-colonel and six other medical officers, one of whom was a surgical expert. Later on an eye specialist arrived and also two dentists.

Attached to the hospital was a very clever bacteriologist, Cecil Clarke, from Bristol, with a well-fitted-out laboratory. Each medical officer had charge of five marquees, which held from fifty to a hundred stretcher-beds; in addition, four bell-tents for infectious cases were allotted to me. Very soon a wooden operating-theatre and a surgical ward had to be erected, as it was found impossible to operate

with success in a marquee whose walls were flapping about and sending up clouds of dust. Although the hospital had been opened only a few days before our arrival, cases of sickness were flowing in rapidly. The daily admissions varied from 150 to 350, and included all sorts of maladies common to a warm climate, as well as many cases of the different varieties of wounds. These were sent to us by the field ambulances, one of which was brilliantly commanded by Lieutenant-Colonel Gerald Stevenson, D.S.O., a brother of Howard Stevenson of Belfast.

After being admitted, each case was put to bed, fed, and medically treated. The next day all those fit to travel were driven in ambulances to the railway station and forwarded to the base hospitals at Salonica.

The two principal diseases at this time were malaria and dysentery. Malaria was a very deceptive disease, and so closely resembled many other diseases in its signs and symptoms that cases were constantly sent in labelled gastritis, jaundice, typhoid, paratyphoid, influenza, rheumatic fever, pneumonia, pleurisy, nephritis, sand-fly fever, cholera, and even tetanus; and from these it could be differentiated only by finding the parasite in the blood. Quite a number of sudden deaths for which no cause could be assigned, proved to be due to malaria (on post-mortem examination). Cerebral malaria, unless treated promptly and energetically, often proved quickly fatal, the patient passing from one convulsion to another almost like a case of status epilepticus. In these and other severe forms, quinine bihydrochloride in 10 gr. doses was given intravenously. At first it was thought necessary to give this dose in a large quantity of normal saline. This necessitated the opening of a vein through a skin incision and running the solution through a needle and tube, a troublesome and very slow operation under the conditions then prevailing. Later, when record syringes became available, the 10 gr. dose was simply and quickly given direct into a vein in 5 or 10 c.c. of saline.

In ordinary cases when there was much gastric disturbance, or where the drug appeared to be failing to act when given by the mouth, it was given intramuscularly into the buttock; but complaints soon started coming from the base hospitals that many of these cases were developing abscesses at the site of injection, and orders were issued that quinine was to be given this way only under special circumstances.

Personally I never saw an abscess from this cause, though some of my cases may later on have developed them. It was quite a common occurrence to get patients into hospital who had already been receiving, in their regiments or in the field ambulances, quinine in tabloid form by the mouth for several days without any effect on their temperatures; but after only one dose given in the hospital, either intramuscularly or intravenously, for their temperatures to drop and not to rise again. Of course these cases had to continue taking quinine by the mouth for some weeks afterwards.

The malaria was of the benign and the malignant tertian types. I saw only one case of the quartan, and that was in the following year in Baghdad: it was very mild. Malaria struck our men down like a scythe cutting grass. In the morning Tommy felt perhaps a bit seedy, and by the afternoon was lying on his back in a high fever.

The summer of 1916 was particularly fierce in its heat, and after months of blazing sunshine and the arduous conditions under which the men were living, their vitality became lowered, with the result that in every battalion men went down by the hundreds; one battalion was actually reduced to one officer and nineteen men. During 1916 admissions into the hospitals at the base for malaria alone were 29,594, and the most of these were men from the front line. The next year this had risen to 63,396, and in 1918 to 67,059. During 1916 it was possible to evacuate freely patients from Salonica to Malta and to England, but by April, 1917, the submarine menace had compelled us to retain practically all these cases in Macedonia. To get rid of this terribly large accumulation of chronically ill and useless men in the hospitals at the base, a scheme was introduced by Sir Donald Ross known as the "Y Scheme," under which thirty thousand chronic malarial patients were transferred to England during the ten months preceding the end of the war. Preventative measures against malaria were initiated in three directions :—

(1) To protect the healthy from being bitten by the mosquito by : (*a*) sleeping under nets, (*b*) by living in mosquito-proof huts and dug-outs, (*c*) by wearing special shorts, gloves, and head-nets, (*d*) by the use of ointments obnoxious to the mosquito, but even more obnoxious to the user.

(2) To abolish the mosquito as far as possible : (*a*) by getting rid of marshes and stagnant water in which the insect breeds, (*b*) by cutting down brushwood, scrub, long grass, etc., near camps, in which the mosquito rests by day.

(3) To cure or to get rid of the chronic malarial patient who is carrying the germs in his blood, and by whom only can the mosquito become infected. This was only possible towards the end of the war, as I have already related. Although these anti-mosquito measures were carried out on a vast scale and every known method of combating the breeding of the mosquitoes was adopted, it is now considered that the work was in a great part wasted because the area covered by the troops was far too large for them to be effective, the mosquito's range of flight being probably two or three miles instead of half a mile, as was then believed. These pests flew in from outside the cleared areas, and in some districts from within the enemies' lines, to the cleared areas full of troops and therefore centres of attraction.

Dysentery.

Dysentery was present all the time, but was most prevalent when the flies were most numerous : that was in the early summer and in the late summer and early autumn. There are three methods by which bacillary dysentery is believed to have been spread :

(1) by carriers—especially those who had mucus in their stools,

(2) by infected drinking water,

(3) by flies.

Many of the milder cases were treated by the battalion medical officer, and did not reach us, but the severer cases running temperatures up to 104° required hospital treatment. The majority of the cases were of the bacillary type, with very few amœbic ones. This epidemic bacillary dysentery is caused by one or more of

the bacilli constituting the dysentery group; the bacillus of Shiga and those of the Flexner type were the ones commonly met with.

Unfortunately at first the anti-dysenteric serum was not available, but as a rule many of these cases did very well on a mixture containing one drachm doses of mag. sulphate given every hour till the hæmorrhage and the griping ceased. Practically all the medical officers in the hospital had good opportunities to test in their own person their favourite method of treatment, and we all finally agreed that nothing was so effective and so soothing as the treatment with mag. sulphate. The polyvalent anti-dysenteric serum is a specific for the bacillary type, and was given in 20 c.c. doses subcutaneously, and repeated every other day for three or four doses. For the amœbic type caused by the *entamœba histolytica*, emetine hydrochloride in doses of two-thirds of a grain is the specific—in the bacillary type it is quite useless. As the amœbic type was rare in Macedonia, practically no cases of liver abscesses were seen; whereas the following year in Baghdad the opposite was the rule, many cases of liver abscesses being diagnosed and operated on. These two types of dysentery cannot be distinguished by clinical examination alone, although often in bacillary dysentery the onset is more acute and the pyrexia more marked. The stools were sent to the bacteriologist immediately after evacuation, and if no entamœbæ were found, the serum was given without waiting for the result of the cultural investigation.

In addition to cases of malaria and dysentery, there were many patients suffering from para-typhoids A and B, at that time new diseases, and diagnosed only by blood-cultures and the agglutination tests. Some of the para. B had such profuse rashes that they were sent to us as doubtful measles or scarlatina, causing endless trouble, but the majority came labelled as P.U.O. malaria, or even dysentery. The para. B cases were much the commoner, and as a rule did very well, the mortality being practically nil. The para. A occurred generally in men who had been in contact with units from India. The spread of these diseases was generally thought to be fly-borne. A useful help in making a diagnosis was the remarkably slow pulse compared with the rise of temperature; a pulse rate of 60 with temperature of 100° to 103° was quite the rule.

In this group, loss of appetite was generally present, in contrast to the malaria cases, where the patient frequently had a good one. Many cases were masked with jaundice. The impossibility of making a true diagnosis of the paratyphoids except by a bacteriological examination was well shown in a case which, after a positive blood culture, had been sent to the base labelled para. B. In a few days we were wired to have isolated all who had been in contact with it, as it had turned out to be typhus, although up to that time no case of that disease had to our knowledge passed through the hospital. Clarke, our bacteriologist, who had been medical officer with a Red Cross Detachment in the Balkan War of 1912, where typhus had been rampant, could not believe that his diagnosis was wrong, motored immediately to Salonica, where he was able to prove to those in charge and to his own great satisfaction that it really was para. B, and not typhus.

Late one night a man of the Royal Engineers was admitted to one of my marquees as a case of lumbago. The next morning numerous small papules were

found on his forehead and wrists, resembling those seen in smallpox. My friend Cecil Clarke agreed with the diagnosis, and this proved to be the first case of smallpox seen in the Salonica Force, of which disease I believe there were only five cases altogether. He and two nursing orderlies were immediately isolated some considerable distance from the hospital in two bell-tents. All the other contacts who had been in the marquee were isolated also. In a few days Corps Headquarters discovered that the Vardar breeze blew from the direction of this smallpox camp towards their quarters about one mile away, and orders were at once sent to have it shifted.

It finally settled down about a quarter of a mile away in the plain north of our hospital. Later on these two white tents standing by themselves must have proved a great cause of curiosity to the German airmen, because they seemed to reserve one or two bombs to drop on them when returning home from bombing over our lines. Fortunately they never in this case hit their target. The two orderlies, having little work to do, amused themselves by trapping hares and partridges and by digging deep holes in the ground into which they and their patients disappeared whenever enemy planes were seen.

No wonder the patient on recovering from his severe attack of smallpox developed great cardiac weakness and for a time was waterlogged. He had been vaccinated as an infant, but had not been re-vaccinated on joining up. The appointment of public vaccinator naturally fell to my lot, and everyone, including the whole staff of our hospital, had to be vaccinated, unless they had been done recently. These vaccinations took well as a rule; most of the lymph was obtained from the French, but I am sorry to say many developed sore arms, as the men when vaccinated had to carry on their jobs just as usual.

Post-mortems were done on all who died in the C.C.S., sometimes with rather surprising results. As I mentioned earlier, many of the cases of sudden death were proved thus to be due to malaria.

A well developed sergeant-major whose illness was thought to be cerebro-spinal meningitis, died suddenly, and his body was sent to us for a post-mortem. Death in his case was found to have been caused by the rupture of a small aneurism in one of the arteries forming the circle of Willis at the base of the brain. A dysentery case on post-mortem showed a most remarkable colon—from the ileo-cæcal valve to the anus it was so rigid, thickened, and dilated, that it resembled a large, thick, firm rubber tube. In it lay quite a number of tabloids, probably aspirins and quinines, exactly as swallowed, standing out white against the green-coloured bowel. This specimen Colonel Leonard S. Dudgeon, our consultant physician, sent home to the University College Museum, London.

There were several cases of relapsing fever, but these were all in natives of the country, several of them arriving at the hospital in wheelbarrows or on donkeys. They were treated with intravenous injections of kharsivan in 3 to 6 gr. doses; one dose as a rule was sufficient to terminate the disease within twelve hours. Also it was found that if the salvarsan were given in the apyrenial period, it usually prevented the occurrence of any relapse.

Like typhus, the infection is conveyed by lice. Until the parasite is discovered in the blood it is easily mistaken for typhoid, typhus, or cerebro-spinal fever.

In the air the Germans gave us a nasty and very unwelcome surprise. They had established in secrecy a squadron specially trained in formation bombing and equipped with fast and powerful modern machines. On Monday afternoon, 26th February, 1917, this squadron made its first appearance. Twenty machines in "V" formation flying swiftly and beautifully down the valley of the Vardar surprised a French aerodrome at Gosgop. Twelve French machines were damaged or destroyed, a very serious loss on a front where replacements were so difficult. They next tackled Janesh, where they bombed the aerodrome and the other camps in close proximity to our hospital and the railway station. It was a terrifying sight to see and hear the bombs exploding in these camps; the aerodrome especially seemed to be one mass of red flames and black smoke. Fortunately our own machines managed to get into the air just before the bombing commenced, so that little material damage was done on this occasion, but there were twenty-eight casualties to the personnel.

The following afternoon, just at tea-time, we saw all our planes suddenly rising from the aerodrome, and the men at the railhead running from it as quickly as they could go; then in absolute silence except for the hum of the planes we saw again in fear and trembling the German bombers flying overhead, but this time they made towards Salonica, where they bombed the dumps, doing great material damage, and also Summerhill Camp, just outside Salonica, where they caused nearly three hundred casualties, chiefly among men who were on their way home on leave.

Our planes this times were ready for them on their return, and we saw some good fighting, but they managed to bring down only one German plane. Our hospital received its share of the bombs. The Germans later informed the authorities that the hospitals were not marked in any way to distinguish them from the other camps and dumps among which they were usually placed. No time was therefore lost before a large red cross, in a circle of white stones a hundred feet in diameter, was made on the top of the hill beside our hospital. Bombproof shelters were made for all the patients able to run into them, while the bed cases, on the alarm being sounded, were placed on the ground by quickly knocking the trestles from below their stretchers.

These bombing attacks were a frequent occurrence till the following May, when it was discovered that the enemy hangars at Hirdova had been dismantled and the German bombers were gone; but before they left they managed to set fire to a large dump of our ammunition at Karasuli, where it was said £2,000,000 worth of shells went popping off for a week. Later some of the raiding planes brought down in England were identified as our friends from the Doiran front.

An R.A.F. officer, Bamford by name, from Kilrea, County Derry, had a very narrow escape from death. When flying he collided with another plane, which lost its propeller; however, its pilot by clever stalling managed to glide safely to earth. Bamford at twelve thousand feet found as a result of the collision that he had lost one wing off his plane, and that the tail along with the rudder had been broken off just a short distance behind his seat. The plane, completely out of control, with its

engine roaring, began to fall in a spin. Suddenly he realized that his machine-gun was at the back of his head, and knew it would give him a nasty knock when he hit the ground; he had the presence of mind therefore to loosen it and let it fall overboard. This caused his plane to roll over on its back, and he finally crashed on his remaining wing. He escaped with only slight concussion and two lovely black eyes.

The same evening in hospital he was able to sit up in bed and enjoy a light dinner. After two days he was evacuated to the base, and while on his way to Egypt for a rest, his ship was unfortunately torpedoed and he was swimming about for an hour before being picked up. A few months later, after a short but very gallant fight against six opponents, he was sent spinning to earth, and later was reported by the enemy to be killed.

I have left out all about the fighting as probably not just the thing for this audience to-night, but perhaps you would allow me to give very briefly just one example of what it was like.

In February, 1917, the 10th Devons, a well trained battalion of real fighters, had a go at Petite Couronné, the strongest point in the enemy's main line of defence. The lower slopes of this hill, which was about nine hundred feet in height, were very steep, while the upper ones were covered with broad belts of wire. After an artillery preparation lasting two days, which resulted in the wire being considerably damaged, the battalion crossed the Jumeaux Ravine in two columns and managed to reach the summit. Fighting was very hot with bomb and bayonet, but, after holding on for some hours, our men were overwhelmed by large numbers of the enemy and had to retire. The casualties were very heavy—about one-quarter of the attacking force and a still higher proportion of the officers. Twenty-seven Bulgar prisoners were brought in, but a large number of others were so severely wounded that they could not be brought across the Jumeaux Ravine. In view of the steepness of the hillside and the depth of this ravine, a number of our men had been specially trained to carry wounded on their backs, if necessary strapped on with puttees. These men carried nothing but a long walking-stick and one extra pair of puttees. This method of evacuation proved very successful, as we had very few missing in proportion to our casualties. The medical officer of the battalion, Hammond by name, was severely wounded, having both feet almost blown off. He was operated on in our hospital, but in a few days died of his wounds. He was awarded the D.S.O. for his gallantry and devotion to duty in evacuating a large number of wounded under the most difficult circumstances. Although severely wounded, he ordered his stretcher-bearers to carry away other wounded before removing him.

At the end of my year I returned home—with a feeling of regret, it is true, at having to leave a spot so full of interesting work and where certain important military operations were expected to commence at an early date. In a French liner, accompanied by an Italian one and escorted by three destroyers, we experienced a most peculiar voyage home. During the daylight this convoy lay in protected harbours in the Greek Islands, but as soon as it grew dark it left its anchorage and with all lights out scurried through the night to our next place of safety, till we finally reached Taranto, and then travelled home by rail via Rome and Paris.

Medicine and Surgery in Belfast Fifty Years Ago

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I HAVE noticed that it is customary when rising to address meetings of this kind, to formulate some suitable excuse for one's temerity. I am in the unfortunate position that I can think of no excuse of sufficient magnitude to condone the meagre fare that I have provided for my listeners this evening. If I were asked why I am on the platform instead of being one of the mute members of the audience, as I usually am, I should be compelled to admit that it is only because I have a sense of justice which makes me feel that those who receive should also give. I have learned much from the Society, and if I do not hope to be instructive or learned myself, at least I hope that I shall not be unduly dull.

For some time past I have been puzzling over the choice of a suitable subject. Statistics and lists of cases make little appeal to me, besides being somewhat ambitious. My instinct was to seek for something which would interest most of you a little. I turned to the past for inspiration. After scanning ten or fifteen years of the Transactions of this Society, I realized that they chose a far wider range of subject formerly than we are apt to do to-day, and often chose subjects of more general, rather than strictly medical, interest. Many of the speakers cultivated a literary style, others at times burst into poetry.

For years it was quite a small Society, and the average number of doctors in attendance was about fifteen. The speeches, however, were as carefully prepared and as well thought out as if they were to be delivered before a vast concourse. One is indeed as much impressed by their general excellence as by the wide range of subjects chosen.

Choosing them at random, we find Dr. Anderson lecturing on the "Morphology of the Omo-hyoid Muscle." In the same session an account was given of the Medical Charities in Belfast, their uses and abuses. The presidential address of the same year was delivered by Dr. Walton Browne on "Anæsthetics." He comments on the recent attacks made on chloroform in the journals, and quotes a writer who goes so far as to say that "a surgeon who used chloroform in preference to ether, should a death occur in his practice, deserved to be tried for manslaughter." He refers to the "peculiar ether craze which has seized the minds of some men." He also reminds his audience that when considering the dangers of chloroform, it is not the drug itself which is to blame, but the mode of its administration. At the date of his speech (1880) he calculated that chloroform had already been administered over seven thousand times in Belfast, and no death had as then occurred.

On one occasion there was a discussion on the British Pharmacopœia, and the changes recently introduced into it. A naval doctor gave the Society an interesting paper on the influence of what he called "ship malaria" in the production of pulmonary disease. On another evening a most erudite paper was read on "The Disposal of the Dead," dealing, amongst other things, with ancient methods of embalming in India, Persia, Greece, etc. At the close of this lecture a resolution

was passed to the effect that "as the practice of wearing shoulder scarves by medical men at funerals was objectionable, it should be discontinued."

A lengthy discussion took place one session on "Alcohol—Is Its Moderate Use Beneficial or Injurious?" This subject occupied four nights, and many were the speakers in both camps. The conclusion, however, was tame enough : a resolution was passed (by a very small majority) to the effect that "in health alcoholic stimulants are unnecessary, and that they are generally hurtful."

On another evening the question of the propriety of keeping the reading-room of the Society open on Sundays arose, and the members showed a very commendable toleration for one another's views, inasmuch as they agreed to the following resolution : "That, inasmuch as the Society consider it inexpedient and unnecessary to make any rule on the subject, each member is allowed the right and afforded the means of acting in the matter according to his own judgment." (Each member had a key.)

On another evening the speaker is again Dr. Walton Browne, his subject "Operation for Hernia." He remarks that his mortality for this type of operation was 36 per cent., which he considers fairly satisfactory. He compares it with the figures from the Belfast Royal Hospital, 1850-86, of 218 cases of strangulated hernia, of which 76 died, a mortality of 34.86 per cent., which he regards as extremely satisfactory. Billroth, he says, in his "Clinical Surgery" mentions seventy-three herniotomies and 52 per cent. of deaths. He also mentions that he recently had a conversation with Mr. Lawson Tait, who advanced the view that the operation of the future for strangulated hernia would be abdominal section and the drawing of the hernia from its sac by traction from within.

One evening during the same session Dr. Dempsey, in his quiet and convincing way read a highly instructive paper on "Abortion : Its Etiology and Treatment." Dr. Byers later in the session dealt with the same subject, but confined himself solely to the question of treatment.

In a very excellent paper on "Mammary Tumours," we find the president reminding the Society that the most effectual hæmostatic, which serves at the same time as a grateful soothing application, is the puff-ball, introduced into practice by Dr. Thomson, the distinguished surgeon of the Tyrone Infirmary. He discusses palliative treatment versus radical operation, and, speaking of doctors who favour the palliative, he says : "While respecting their honest conviction, I pity them for entertaining such, but I pity still more their confiding patients." He strongly advises removing the pectoral muscles, glands, etc. Quoting Mr. Jonathan Hutchinson, he says : "Too late, too late is the sentence written but too legibly on three-fourths of these cases of external cancer concerning which the operating surgeon is consulted. It is a most lamentable pity that it should be so, and the bitterest reflection of all is that usually a considerable part of the precious time which has been wasted has been passed under professional observation and illusory treatment." "Only when the doctrine of the pre-cancerous stage shall be widely recognized," he says, "shall we witness a considerable reduction in the mortality of cancer."

Another evening Dr. Burden relates his impressions of Parisian hospitals, which he visited recently. He extols the skill with which stethoscopes, plessors, and plexi-

meters are used, but speaks in somewhat scathing terms of surgery as he saw it. "How far, how very far," he laments, "French surgeons then were from having arrived at that exquisite cleanliness in every detail of treatment for which skilled surgeons now battle with all their might and with all their soul, would be too painful to relate in full."

So much then for the papers in general read before the Society, but now I wish to take you back with me fifty years and to formally introduce you to the session of the Ulster Medical Society in the year 1884. The scene is laid in a room of the "Old Royal." It is the last occasion on which the meeting of the Society will be held there, as the Council has decided to take a room in the Belfast Museum. The president, Mr. Fagan, is in the chair. Dr. Lindsay, the hon. secretary, is on his left. The clock has struck 8.30, the members are filing in through the door, after their "social cup of tea." Dr. Whitla is chatting with Dr. Dill. Dr. Mackenzie and Dr. Byers are already seated, obviously enjoying an amusing reminiscence. Young Dr. Sinclair, the pathological secretary, keeps in the background. Dr. Harkin, with his usual fiery zeal, is emphasizing a point to a small group, amongst whom we recognize Dr. Aicken, Dr. Wheeler, and Dr. Esler. Professor Cuming and Dr. Dempsey are deep in conversation. Dr. O'Malley, Dr. Graham, and Dr. O'Neill bring up the rear.

The president, Mr. Fagan, rises to thank the Society for the honour they have done in electing him. His address is of the masterly type that one would expect, though his subject matter is of the most simple. "I am sure," he says, "that every thoughtful and observant practitioner, when he looks back over his past labours, must be forcibly reminded of some weak points in the continuity of his practice, such as a wrong diagnosis, an erroneous treatment based on it, a case gone wrong owing to a timid, careless, procrastinating way of dealing with it. In casting about for a subject, it occurred to me that I might with advantage dwell for a little on some of these points, and by directing our attention more particularly to them we might be able to detect and strengthen those weak links in the chain of our professional labours. To the enthusiast surgeon such an everyday subject will appear dull and uninviting, lacking, as it does, the glamour of novelty or daring enterprise; but to the thoughtful mind it will meet with the reception that its importance and usefulness deserve. As I grow in years and experience the more strongly do I become impressed with this idea, that we allow ourselves to be carried away by speculative theories and novel practices, very often to the neglect of the first simple principles."

"The subject matter of my discourse to which I shall now direct your attention," he continues, "is the great importance of, first, accurate and early detection of disease and injury; second, the adoption of a timely, judicious, and decided mode of treatment. While there must always be differences in men's diagnostic powers, there is one important particular in which all should be equal, and that is, the desire to leave nothing undone to make our diagnosis as accurate as possible. I do not propose to consider the best methods to be employed in making a diagnosis. Ability as a diagnostician is one of the highest attributes of a physician or surgeon, for excellence in it demands that they be possessed not alone of many highly developed physical qualities and a large and varied experience, but presupposes as well an

accurate knowledge of a wide range of scientific subjects. With all these qualities the highly accomplished consultant makes his mistakes in diagnosis as well as the humblest practitioner, and *humanum est errare* may with peculiar appropriateness serve as a motto for all of us. I have somewhere heard the statement, and often seen it verified, that there is nothing more humiliating to the pride of our profession than the records of the post-mortem room. I will draw your attention to what I consider to be some of the main defects to which not a few are liable: First, a tendency to form a rapid conclusion on very slender data; second, putting leading questions to a patient; third, imperfect or ill-conducted physical examination, or no examination at all.

"I knew a very eminent surgeon who, forming his diagnosis on the presence of one or two prominent symptoms, pronounced a case to be one of hip-disease; accordingly he gave instructions to have the best room in the house given up to the patient, as her case would be tedious, and likely to confine her to bed for three, six, or perhaps twelve months. A week later the child passed a large quantity of pus per anum, and in three weeks was up and about. It was a pelvic abscess."

He then proceeds to tell the following story against himself. "After I had concluded my lecture on hip-disease at the Children's Hospital, the students of my class, during my absence, examined a case that was brought for me to see, and pronounced it to be one of hip-disease. They detailed as present most of the symptoms common to the affection—viz., lameness, flexion of the thigh, fattening of the buttock, pain and swelling in the groin. And seeing the child, who was now dressed, walking with the characteristic gait, I coincided with the opinion expressed by them that the case was one of hip-disease in the first stage. I told the mother of the child what my opinion was, and that a splint (which I then ordered) would be necessary. A few days afterwards while the child was waiting in bed for her splint, I happened to examine her, and finding some important symptoms absent, and others not so well marked, my suspicions began to be aroused concerning the correctness of the diagnosis. I asked her if she suffered pain in walking, and if so, where? She replied that she had very little pain now, as her heel was nearly well."

That public opinion was often as valueless in 1884 as it is to-day, may be gleaned from a story that he quotes of a child with early hip-disease treated with such marked success by himself and a distinguished colleague that the parents began to doubt the original diagnosis and took her to a metropolitan surgeon, who assured them that there was nothing wrong with the child. Over this rebuff he consoles himself with the thought that the child at least was saved from a cripple's life. A story which fortunately shows the reverse side of the picture he quotes from Sir James Paget. It is that of a distinguished London surgeon who, while operating on a gentleman for strangulated hernia, with great carelessness cut right into the intestine. Fæces flowed out, and all the miseries of a wounded intestine followed. After much anxious care, at last the patient recovered. His firm conviction was that by this very incision into his bowel, he had escaped some dreadful calamity, and that nothing but the most extreme skill could have either made the incision into the bowel or recovered him after it; and he presented the surgeon who had done this with a very handsome gold snuff-box.

The scene changes now to a room in the Belfast Museum. Here the members are meeting for the first time, and we are glad to welcome as new recruits Dr. Wm. Calwell, Dr. John McCaw, Dr. R. D. Purdon, and Dr. S. B. Coates. The speaker for the evening is Dr. Robert Esler, senior physician to the Ulster Hospital, his subject "Early History of Medicine in Belfast." He depicts the landing of Schomberg with his ten thousand men at Bangor in August, 1689. One Thomas Pottinger, the governor, furnished a "great" hospital at his own expense for the care of the sick of this army. A Dr. Lawrence was placed in charge. The mortality was well nigh incredible. In six months 3,762 men died.

For an explanation we may well look to the sanitary laws of the period. Here is one: "No one to make dunghills to continue longer than three days in the open street before the door, or throw carrion, dying stuff, or any loathsome thing into the river, under a penalty of five shillings." Another: "Complaints are made that great annoyance is caused by butchers suffering the blood and garbage of their slaughter-houses to lie in the street, and run in the kennels and ditches of the town, to the corruption of the river and annoyance of the neighbours, by reason of the evil and infectious smells; and it is ordered by the authorities that all blood and garbage be carried twenty yards beyond high-water mark, under a penalty of twenty shillings."

Medical men seem to have played a leading part in the civic life here in the seventeenth century, and were held in high repute. Indeed, at the funeral of one Dr. Alexander no less than nineteen cloaks were hired, testifying to the great respect in which the deceased was held. In 1726 one Dr. James Macartney was chosen "sovereign" of Belfast. A little later we encounter the name of Dr. Haliday, one of the best-known literary men as well as the most eminent physician of his time. One gleans also that he was a very gallant gentleman. A friend writes of him thus: "Three nights before he died Bruce and I played cards with him, and the very night that was his last he played out the rubber. 'Now,' said he, 'the game is finished, and the last act near a close.' He was helped to bed, spoke comforting words to his wife—and the rest you know." In his will one reads: "I leave my wife a legacy of £100 by way of atonement for the many unmerciful scolds I have thrown away upon her at the whist table, and I further bequeath to my dear wife the sum of £500 in gratitude for having never given me, on any occasion from her early youth till this hour, any just cause to rebuke or complain of her; and I further leave to my said dear wife a further sum of £100 as an acknowledgment of her goodness in devoting an hour or two every evening, which she could have so much better employed, to amuse me with a game of picket when we happened to be alone, after my decaying eyesight would no longer enable me to read or write much by candlelight."

A sturdy Glensman comes next on the scene—Dr. James McDonnell of Cushendall. He originated clinical teaching in the hospital in 1827. In those days he was a familiar and striking figure, clad in drab knee-breeches and white stockings, driving through the streets reading a book with the aid of a magnifying-glass, his servant "Mike" at his side. He visited his mother regularly at Cushendall once a fortnight;

leaving home at midnight, changing horses at Glenarm, he spent a few hours lying on a sofa talking to his mother, and rode back to Belfast within the twenty-four hours (a ride of about 120 miles in all).

In 1752, Dr. Esler tells us, the Belfast Charitable Society was founded for the "reception of infirm and diseased poor and the employment of idle beggars." (Apparently in the matter of hospital sweeps, history is merely repeating itself, as this institution owes its start in life to two lotteries which raised £1,736 and £1,462 respectively.)

In 1797 the first hospital for fever in Ireland opened in Factory Row, Belfast, with six beds. This turned out eventually to be the modest beginnings of the old Royal Hospital, although the actual removal to Frederick Street did not take place till 1817, twenty years later.

Dr. Esler also tells us that the first Medical Association of this city was formed in 1806, under the name of The Belfast Medical Society. Nearly half a century later The Belfast Clinical and Pathological Society came into being, and it is by the amalgamation of these two bodies that our present Ulster Medical Society was formed in 1862.

A few weeks later in the season the members are again assembled. The speaker of the evening is Dr. Harkin, M.D., F.R.C.S., physician to the Mater Infirmorum Hospital, and member of the French Society of Hygiene, Paris. Here is an optimist such as we rarely see nowadays. His eyes flash with zeal and enthusiasm. He carries away his audience almost in spite of their better judgment. Listen to his flowing style, at times verging on the poetic. Hear his stirring advocacy of the blistering treatment of cholera, and be converted in spite of your better judgment. "The subject for discussion this evening is one of paramount importance," he says. "Cholera, that dread disorder, while ravaging some of the fairest cities of Continental Europe during the past year, has been hovering ominously round our coasts, and we know not the day nor the hour that it may gain a footing in our midst. The medical faculty in Paris, I have reason to know, are already preparing for its reception. It is therefore, in my mind, both wise and expedient that we should also take counsel together, and with the experience of those who, like myself, have witnessed every outbreak of the disease in this town, and encountered it in all its forms, and with the information supplied by modern science and experiment, we may be enabled to devise competent measures of prophylaxis, and to formulate a plan of treatment on a satisfactory basis. I well remember the feelings of terror and dismay exhibited by my fellow-townsmen on the memorable occasion of its appearance in April, 1832; and in the epidemic of 1849 the inhabitants of Lagan village were nearly decimated. At that time, although close to the River Lagan, there was not even an attempt at sewerage. All the nuisances of the houses passed into puddles in front of the doors, making their way as best they could to the riverside; the more solid matters were collected and piled up in a heap at the end house of the village till sufficiently large to be carted away. The sights and scenes of that locality," he adds, "are amongst the most painful of my recollections."

One is reminded that when a severe epidemic occurred in Edinburgh, the inhabitants petitioned Lord Palmerston to proclaim a day of fasting that the plague might be stayed. His reply was characteristic of modern discovery: "Clean out your drains." Graves, in his "Clinical Lectures," pays a striking tribute to the Irish when referring to cholera: "Barbarous, cruel, and uneducated as we in Ireland are said to be, the visitation was in no sense met with greater intrepidity and resignation than in our native land. When a city or town was attacked in Ireland we never witnessed the flight of the better classes; there was neither emigration into the country nor desertion of their poorer citizens. No, I record the fact with pride; everyone remained; everyone was ready to do his duty and abide in his place until the plague was stayed. The sick were never abandoned by their friends in private houses, nor in the least neglected in hospital (although the disease was believed to be contagious)."

During one of the epidemics in Belfast some of the deaths were so sudden that the ignorant people imagined that their friends had been poisoned by the doctors, one esteemed physician having had to fly for his life and to clear a boundary wall to escape from the fury of the women.

"Concerning the treatment of cholera," continues Dr. Harkin, "as a prophylactic there is none equal in efficiency to dilute sulphuric acid, ten to fifteen drops of which should be taken in a goblet of water. The causal relations of organisms to cholera have been much discussed, and later scien ists, such as Koch and his followers, insist that it is owing to the influence of a microbe or bacillus, comma-shaped, always present in the intestines or excretions of cholera patients. In the report of the Special Commission sent out to make a scientific inquiry into cholera in India, it is set forth explicity that the comma-shaped bacillus of Koch is neither universally present in cholera excreta nor to be found in any quantity in the intestinal walls; they deny to the bacillus any distinctive or pathogenic property."

"Whatever the remote cause," continues Dr. Harkin, "be it microbe or bacillus, or some yet undiscovered factor, under its influence the nervous system becomes rapidly involved. Vomiting and purging are apparently due to an abnormal or excited condition of the nervous supply to the stomach and bowels; the spasms, cramps, etc., betray their neurotic origin.

"In Dr. MacCormac's 'Exposition of the Nature of Spasmodic Cholera,' published in 1832, he gives it as his opinion 'that the poisonous agency which produces cholera acts by destroying or diminishing the action of one of the three grand divisions of the nervous system by whose powers the human frame is maintained in life and vigour—the respiratory, the cerebral, and the sympathetic'; and it is by the lesion or injury of the latter that we suppose cholera to be produced. It being admitted that cholera is due to a lesion of the sympathetic system, it would naturally follow that we should seek out an agent that will control and influence the system at fault. Discarding all internal remedies when given *carte blanche*, I merely apply some epispastic fluid behind the ear with a camel's-hair brush, commencing behind the ear, and extending in the course of the pneumogastric nerve, as far as the

angle of the lower jaw. The result is that purging at once ceases; the patient often falls asleep and awakes cured.

"I append a few striking cases, selected from a large number. The first two appeared previously in the 'Lancet' of August, 1884.

"Case 1—Constable C. sent for me from Queen Street Barracks on 18th September, 1883, at 8.30 a.m. I found him in the act of vomiting, with small, quick pulse, violent cramps, forcible palpitation of the heart, great debility, fainting, and coldness of the extremities. He was purging at frequent intervals, and the dejecta were of the usual rice-water character. I painted him at once behind the ears down as far as the angle of the jaw with liquor epispasticus, assuring him at the same time that he would not have any recurrence of the symptoms. I visited him again at 10.30 a.m., and found him convalescent, not having had either sickness or purging, as I had predicted.

"Case 2—I was summoned to a child aged twenty months at 11.30 p.m. It was lying prone on the mother's knees, with its arms and legs hanging listlessly on either side; it was cold and feeble, almost pulseless, and was vomiting and purging at the same time. I applied the blistering fluid behind both ears and on the neck. Calling the next day I found the child in its mother's arms quite lively and well.

"Third Case—I was sent for on 14th October to see a child aged six months who had suffered from purging and vomiting for twenty-four hours. It was cold and wan, the pulse almost imperceptible. I painted the little one in the usual place, informing the mother that all sickness would immediately cease. Next day the mother informed me that sleep soon overtook the child and that neither vomiting nor purging had returned."

Now we shall bid good-bye to the Ulster Medical Society and pay a visit to the old Royal Hospital. We are met in the hall by the house-surgeon. His duties are varied in the extreme, and in addition to his routine medical work we find some curious tasks allotted to him, such as "The admission of visitors to patients and the responsibility for carrying out the rules regarding such visits"; also "The charge of the surgical instruments and seeing that they are kept in good order"; also, last but not least, "keeping the stock of stimulants under his own control." Next we encounter the resident pupil. This gentleman, in addition to his duties of a purely medical nature, has a strange one allotted to him—it is his duty to see that "no nurse leave her post of duty till relieved by her successor."

It is still rather early, so whilst awaiting the arrival of the visiting staff we shall have a look at the hospital financial report, which is on the superintendent's desk. We find that the income of the hospital is derived from a variety of sources differing a good deal from those of to-day. Hospital Saturday has made its appearance for the first time in Belfast in the summer of this year (1884). Students' Day is as yet unknown, although in an earlier report we find the entry, "Funds from the students of Queen's College, surplus from torchlight procession, £6. 17s." The church collections, which included all creeds, were not very large; only twelve provided over ten pounds each. The workmen's collection is just beginning to assume considerable proportions. In 1881 it was a paltry £300, but three years later

it has almost reached the not inconsiderable figure of £1,700. Paying patients are contributing about £800 per annum. Ordinary contributions amount to about £2,000, and donations to £750. Proceeds of the sale of liquor seized at a shebeen brought in 8s. 7d. A Sabbath bet enriched the hospital to the extent of two shillings. The total expenses were over £6,000. The average cost of the patient per day was 2s. 7d. The bill for wines and spirits amounted to more than half the bill for medicines. The consumption was approximately—brandy 30½ gallons, whisky 55 gallons, port 28 dozen, porter 59 dozen, ale 166 dozen.

There were 1,818 in-patients this year, of whom 1,447 were free and 371 were paying. The scales for the payment of patients had been fixed at 5s., 14s. 7d., and two guineas weekly, also two guineas for fever cases and three guineas for cases of delirium tremens.

The superintendent is keenly alive to the difficulties of the drink question in its bearing on routine hospital life. He reminds us that the Ulster Medical Society seven years ago debated the question of alcohol for four evenings, and that the statement was then made by the president that "drink is the largest factor in the medical man's practice." In 1880 it was decided that cases of alcoholism should no longer be admitted. Apparently, however, that pious resolution went the way of many another, for amongst the in-patients for the current year were delirium tremens 24 cases, dipsomaniacs 3 cases, and poisoning by alcohol 17 cases.

The question of an almoner had already been discussed at a meeting of the Ulster Medical Society, and approved of, but so far no steps had been taken to secure one for the hospital.

The visiting staff are now arriving. Let us follow Dr. Whitla into the male medical ward. It is a Tuesday morning, so there is a goodly concourse of students, of whom there are now over 180 on the books. Lectures take place in hospital twice weekly, on Tuesdays and Fridays, the fee being ten guineas. Dr. Whitla has chosen for the subject of his clinique a case of typhlitis. The disease sounds a little unfamiliar to our ears, especially as we find ourselves in a medical ward. Whilst we are puzzling over this we observe in the next bed a case of acute peritonitis *in extremis*. A student at the back whispers that this case was lectured on last week as typhlitis, but that clearly the original diagnosis was incorrect, as the case had not yielded to the usual treatment (poultices, hot stupes, sedatives, etc.). A great truth suddenly dawns on us : appendicitis, as yet unknown, is masquerading under the name of typhlitis, and is still a medical disease. Little wonder that the mortality of the medical side of the hospital is over eight per cent., whilst the surgical is only about four per cent.

Fever is the next subject to be dealt with, and Dr. Whitla is advocating the views of Stokes. "Purgatives," he says, "have been greatly misused in the treatment of fever. It has been a great blot on the history of British practice. Calomel, black bottle, and even jalap, aloes, and scammony have been prescribed for patients labouring under severe and extensive enteritis. Morbid stools are discharged, and the more morbid they are the more calomel and purgatives does the physician give to change their character. I want words to express the horrible consequences," he

says. "Practitioners will not open their eyes. They give purgatives day after day; a very easy practice and one for which there are plenty of precedents; but it is fraught with the most violent consequences. You will gain nothing by purging in fever; mild laxatives alone can be employed, and when there is the slightest sign of intestinal irritation present even these should be used with caution. There is one way of opening the bowels which you may always have recourse to in fever, that is, the use of enemata. For the tympanites you may prescribe lead acetate and oil of turpentine. If you are fortunate enough to see the patient within the first few hours of the onset of this fever, let me indicate to you the line of treatment in use here. The patient is bled straight away and an emetic administered. Later on give him James's powder and grey powder. If he shows signs of engorgment of the liver or of pneumonia do not hesitate to apply leeches followed by cupping glasses or hot dry flannel cloths, so that you may have less trouble in stopping bleeding. If you wish to blister, and indeed it is often advisable, only leave them on for a few hours; they act as stimulants. If cerebral irritation is present, shave and blister the whole scalp, then rub in irritant ointment so that violent inflammation may be produced. Later on in the illness you may again find use for the blister, i.e., in stages of weakness—then apply a series of them to the thighs and epigastrium. In private practice, when treating a case of fever, it is always well to have two beds in the room. After the eleventh or twelfth day the patient is removed from one bed to the other every twenty-four hours. Nothing can be more grateful than this removal from a tossed foul and wet bed to one that is smooth, clean, and in every respect comfortable. How often is the change followed by a sound and refreshing sleep! To be successful practitioners, gentlemen, you must not be merely scientific physicians, but you must understand the more minute duties of the nurse."

Now we pass on to a severe case of chorea. The patient, a little boy of ten, has been on all the usual remedies, such as carbonate of iron, zinc sulphate, stramonium, morphia, and arsenic, but so far without improvement, and indeed the case is so severe that it is feared that the child will not survive much longer, so as a last resource it is proposed to try the shower-bath treatment as recommended by Graves and others. The bath is to be used first warm, then tepid. The child is placed on a large mattress and is covered with a blanket. The child is held down by an assistant, inevitably destined to share the bath. Various helpers standing on chairs pour the water from several large watering-pots held high, on the patient underneath. When this has been done the child is dried and covered. This shower-bath must be perseveringly repeated three times daily. Astoundingly good results have already been reported from this treatment.

A diabetic patient occupies the next bed, and during the little dissertation to the students that ensues we gather that the chemistry of the blood is a subject for the most profound contempt. In the words of one of the great clinical teachers of the day: "Lately the investigation of chemists respecting the composition of the blood in fever and other diseases has exacted hopes that we are on the eve of discovering some more secure basis for our practices founded on the analyses of that fluid. I must confess that however I applaud these efforts of science, I entertain no hope that

they will be followed by the expected beneficial consequences. In truth it is vain to look for remedies founded on chemical principles when these principles cannot even approximate to affording us an explanation of the mode of action of our best established medicines; when chemistry reveals why tartar emetic vomits, jalap purges, or opium causes sleep, then we may begin to hope that this science can conduct us still further."

Let us leave these scornful physicians and turn for solace to surgery. We will do a round with Mr. Fagan. He is discoursing to the students on the wonders of surgery, and speaks of "the great champions of our profession who, by their labours, are daily gaining fresh laurels, by their skill and daring penetrating the most sacred chambers of the organism, and each succeeding year astonishing the world by some novel and bold surgical enterprise. Such victories," he says, "are of frequent occurrence, and our journals duly chronicle those achievements under such headings as hysterectomy, oophorectomy, splenectomy, ovariotomy, nephrotomy, cholecystotomy, and gastrotomy." He reminds them that already two years have elapsed since the first nephrectomy was performed in Ireland by Mr. F. J. O'Reilly, surgeon to the Trim Union Infirmary (the patient, however, unfortunately died later of shock), "and to-day comes the news from London of the first removal of a cerebral tumour by Mr. Godlee." (25th November, 1884.)

As we enter the male ward we first come upon two cases of enlarged prostate. The "bold surgical enterprise" to which they are being subjected is regular catheterization. Next comes a case of surgical erysipelas following on amputation of the foot. An accident case labelled "compound dislocation of the great toe" lies alongside. Farther along is a case of anthrax. In the bed beside him is a case of submersion. A fractured femur lies in the next bed. Just opposite is a case of cancer of the lip awaiting operation. Beside him is a case of Potts' caries. A case of strangulated hernia operated on a few days previously is dying in the next bed. Passing on we see an accident case labelled "concussion of the brain." Alongside is a bad case of burns swathed in carron oil dressings. Beside this case is one which made a great stir in the surgical world only the previous week when Dr. Fagan performed the new and daring operation of gastrotomy.

We are lucky in having arrived on an operation morning. The chink of instruments and the smell of chloroform draw us to the operating-theatre, where there is a scene of tense excitement. A surgeon has just finished the successful performance of the recently introduced spectacular operation of ovariotomy. We are naturally disappointed at having missed this piece of daring surgery by one of our local men, but our disappointment quickly changes to eager anticipation as rumour has it that young Dr. Sinclair in the absence of his chief is about to undertake the procedure recently introduced by Hutchison known as abdominal taxis. Whilst awaiting the arrival of Dr. Sinclair we listen with amazement to the heated discussion that is now in progress in the theatre on Mr. Lawson Tait's recently expressed views on ovariotomy, and the scathing comments to which he has given vent on the rashness amounting almost to unscrupulousness on the part of general surgeons, who have not hesitated to open into the peritoneal cavity and attack operations of such

delicacy and difficulty as ovariotomy. The surgeons, however, maintain that their training essentially fits them to deal suddenly with grave and unexpected situations; that they do not approve of this parcelling out of the body into watertight compartments, and they feel themselves capable of dealing with an ovarian tumour even should it be complicated by adhesions.

A lull in the stormy discussion reveals the arrival of four stalwart policemen. They are directed to remain outside the operating-theatre door till their services are required. Dr. Sinclair's patient, a young man of about twenty-five years of age, is being deeply anæsthetized. The operator, already scrubbed up and gowned, is superintending the preparation of a large basin of soapsuds. To the little crowd of onlookers he comments that the method which he is now about to employ makes little appeal to him, as it is not sufficiently precise, and that he would prefer a surgical procedure of greater nicety, as even Mr. Hutchison admits that his method is both undignified and inexact. The case is fortunately a fairly early one of intestinal obstruction, though Dr. Sinclair assures us with thinly veiled sarcasm that "up to the present the rule of practice still is to wait till the patient is moribund, and to charge the inevitable death to the account of the operation, a proceeding that is scarcely generous to surgery."

The patient is by now deeply anæsthetized, and the stalwart policemen are called in. They are directed to take hold of him by the four limbs, and to shake him very forcibly and thoroughly; Dr. Sinclair meanwhile powerfully manipulates the victim's abdomen. The policemen are now directed to invert the patient and to shake him more thoroughly upside down. Dr. Sinclair meanwhile makes use of the large basin of soapsuds to administer copious enemata. We heave a sigh of relief when it is over—so does the operator and so do the policemen. These were apparently days of heroism for surgeon and patient alike, and it must often have been a case of the survival of the fittest. Whilst on the subject of heroism of this kind, what could equal the following story recounted by a doctor in our hearing. He referred to it as a case of auto-abdominal section. The "surgeon" was a woman of 69, the mother of eleven children, and lived in one of the back streets of Belfast. She used to have severe attacks of colic, for which she always blamed a small fatty tumour in her abdomen. The doctor who told the story had received an urgent message to say that Mrs. G. had disembowelled herself, which was apparently what had actually happened, as she had, on his arrival, about two feet of bowel protruding from the wound and was pulseless. She had performed the operation with a scissors, standing over a basin to catch the blood. Needless to say, she made a perfect recovery. One story led to another. An obstetrician amongst the group told the celebrated story of the Countess Margaret, daughter of the Earl of Holland. She was stated to have, on Good Friday, A.D. 1276, at the age of 42, brought forth at one birth 365 infants, whereof 182 are said to have been males and 182 females, the odd one being a hermaphrodite, all being baptized, those by the name of John, these by the name of Elisabeth, in two brazen dishes.

After this somewhat frivolous interlude we turn our attention to the operation book. From it we learn that chloroform was administered 211 times during the

year. In all there were 207 operations performed. That is, an average of four per week, probably only one of these being a major operation. Thirty-one were amputations, thirty-three were excisions, and almost all the rest were quite trivial—the usage of the stomach pump (which appears to have been a fairly frequent procedure) even ranks as an operation. Gastrotomy was performed once during the year. Many of the excisions were of cancerous or sarcomatous growths, and it is all too obvious that malignancy was only diagnosed when it was seen externally—the sites being mainly the breast, lip, tongue, skin, etc. The enlarged prostates were apparently recognized as surgical conditions, although catheterization was the treatment in vogue. Chloroform was still the anæsthetic of choice, but methylene was creating a place for itself.

The record of cases treated in the wards was also instructive. Submersion cases, of which there were about fifteen that year, were apparently always kept in surgical beds. Cases of peritonitis, typhlitis, and intestinal obstruction were, however, relegated to their medical wards. The medical wards had a much greater proportion of cases of Bright's disease, bronchitis, and cardiac disease than any other type of case—the cases of bronchitis indeed outnumbering any other disease. Infectious diseases were well represented, mainly scarlet fever, typhoid, and typhus. Rheumatic fever appears to have been fairly prevalent, also pneumonia. Cases of alcoholism exceeded in number any single type of case, except bronchitis.

Before we leave the hospital we must pass through that most unsavoury of all spots within the precincts of the building, the extern. Here we see Dr. Wheeler cauterizing bites, stitching 'drunks,' dressing burns, etc. The problem was a much worse one than to-day (even on our worst Saturday nights). The record book shows that anthrax was not rare, and that bites were extremely common, the human variety coming second only to the dogs in point of numbers, and far outstripping the combined bites of horses, asses, cats, and monkeys.

Through the open door we see one or two carriages arriving; Mr. Fagan's white hunter "Solomon" paws the ground with impatience. The work of the morning is over.

If this glimpse into the past has brought home to you in ever so slight a degree the wonderful strides made by both medicine and surgery during the last half-century, my paper will have fulfilled its object. Most of us feel from time to time how very little we know of disease, its cause or cure, and at times feel disheartened, forgetting that "it is a better thing to travel hopefully than to arrive"; or, as another poet has it:

"Say not the struggle naught availeth,
The labour and the wounds are vain,
The enemy faints not nor faileth,
And as things have been they remain.

"For while the tired waves, vainly breaking,
Seem here no painful inch to gain,
Far back, through creeks and inlets making,
Comes silent, flooding in, the main."

Notes on Two Cases of Sub-Dural Hæmorrhage

By Robert Marshall, M.D., F.R.C.P.I., D.P.H.,
Physician, Royal Victoria Hospital, Belfast

It will be remembered that in January, 1934, Dr. James Purdon Martin gave the Society an interesting account of the syndrome of sub-dural hæmorrhage, and described certain illustrative cases. In the course of his paper Dr. Martin said that the condition and its treatment had been first clearly described by Trotter in 1914. While the source of the hæmorrhage is not clear, it probably occurs from tearing one of the small veins passing from the surface of the brain to the dura, as the result of sudden dislocation of the brain within the cranium by trauma. The hæmatoma so formed gradually extends until it covers one cerebral hemisphere, and in some cases is bilateral. One curious feature is that the blood may be partly clotted, but a large part of it remains fluid. It has been suggested that it becomes defibrinated as a result of the movement transmitted to it by the pulsation of the brain. The blood is enclosed by two membranes, the firmer of which is attached to the dura, the inner membrane of which is much more delicate, lying on the arachnoid but very tenuously attached to it. Virchow regarded these membranes as being derived from the organization of inflammatory exudate.

Age is an important factor, as in older subjects relatively slight trauma is required to cause this hæmorrhage.

The clinical course was, you will remember, very graphically described by Dr. Martin as a drama in three acts. Act one, the accident; act two, symptoms of headache, mental disturbance, and variable drowsiness; act three, coma. The interval between act one and act two is likely to vary inversely with the severity of the trauma. The syndrome of act two is frequently characteristic. The patient complains of headache, which becomes more frequent and severe. He becomes rather apathetic, his memory is impaired, and he develops a tendency to drowsiness which, however, is usually variable in degree. The focal signs of cerebral disease are rare; papillœdema may be present, and other ocular signs, notably inequality of the pupils, occur in about fifty per cent. of cases. The C.S.F. is nearly always normal, and its pressure is not raised.

The first case which I now report is that of Mrs. K. I saw her for the first time on 13th February, at the request of Dr. Robert Cocks of Banbridge. She had been brought to him a few days before because of general weakness, loss of memory, and mental confusion, all of recent onset. Before seeing the patient I interviewed her son, who said that her age was about sixty-two years, and that her medical history had been uneventful except for an operation for carcinoma of the left breast performed by Sir William Wheeler eighteen years ago.

She had slipped on a polished floor, striking her head on the handle of a door, "soon after Christmas" (1933). As she had been alone in the house at the time, the immediate effects of this injury were somewhat difficult to assess, but it is clear

that there ensued a period of freedom from symptoms lasting for two or three weeks. She then began to complain of headaches, and this phase lasted for a further period of two or three weeks before her friends noticed slight, but definite, mental changes.

On examination I found her quite able to answer questions and reasonably alert. Her memory seemed to be a little vague, making her remind one of a woman of much greater age. Her pupils were unequal, the right being definitely larger than the left. There was no other physical sign of injury or disease of a cranial nerve. Her knee-jerks and ankle-jerks were absent; the left plantar reflex was definitely, and the right indefinitely, downwards; the abdominal reflexes could not be elicited. There was no alteration of objective sensation, and no definite motor paresis. Her heart-sounds were feeble; her blood pressure 120/80, and her electrocardiogram showed flat T waves in lead 1, and an extra-systole of auricular origin.

I moved her to a nursing home in Belfast the following day. Stereoscopic radiograms of her skull showed nothing definite, but the left parieto-frontal suture seemed to be a little wider than the right. The pupils had become equal again, and a few hours later the left had become definitely larger than the right. I did a lumbar puncture: the fluid was under increased pressure, and Dr. J. C. Davison reported as follows:—

Fluid is definitely yellow-tinged.

Cell count: lymphocytes 32 per c.m.

A very occasional red cell present.

Nonne-Apelt Gloublin test: strongly positive.

Total protein: 234 mgms. per 100 c.c. (large increase).

Chloride content: 740 mgms. per 100 c.c.

Sugar content: .094 per cent.

Benzidine test for blood pigment: positive.

No organism found.

Wasserman: negative.

On 15th February, Mr. G. R. B. Purce opened her skull by an osteoplastic flap on the left side. No clot was seen, but the brain was congested and under increased pressure. As her general condition was wonderfully good, we decided to explore the right parietal region by a moderately large trephine opening. On opening the dura a definite cyst-wall, presumably composed of organized fibrin, was found. As its boundaries could not be reached, it was opened, and about four ounces of yellow-stained fluid escaped, showing the subjacent brain concave in outline because of its pressure. This sanious cyst had extended forward to the frontal lobe, and backwards, we thought, almost to the occipital lobe. A rubber drain was inserted and the scalp wound closed. The anæsthetic used was intra-tracheal ether administered by Dr. S. Geddis.

Her condition was wonderfully good for thirty-six hours afterwards, and then her pulse-rate increased and the pulse-volume became very poor. There was no bulging of either scalp wound. The left pupil became much larger than the right. She died at midnight on Saturday. I regret that we did not get an opportunity to examine the brain after death.

The pathological report on the specimen of cyst-wall sent for examination was as follows: "Microscopically, the specimen consists of blood-clot which is undergoing organization, and contains a large number of macrophages filled with iron pigment; the specimen is enclosed within a fibrous layer from which organization is proceeding; thus the appearances are more consistent with those of a sub-dural haemorrhage than with those of a sub-arachnoid. There is no evidence of tumour formation in the section examined."

The second case had a happier ending.

The relatives of one Samuel C., a farmer, aged 49, sent to Dr. Carlisle of Dromore, to request him to visit Mr. C., because "he wouldn't talk to them." When the doctor called the patient would "talk all right," but seemed indefinitely altered in his manner. When the doctor called a few days later the patient's dullness and apathy were more definite, and, as his friends put it, "he did not seem to care what happened on the farm." He was disinclined to get out of bed, and at times had incontinence of urine. Dr. Carlisle asked Mr. T. J. Gibson of Banbridge District Hospital to see him in consultation. Mr. Gibson was at once reminded of the case of Mrs. K., in whom he had been interested. He elicited a history that the patient had fallen from a horse on 1st January without obvious serious injury. Mr. C. had noted, however, that he felt dizzy on attempting to ride a bicycle the day after his fall, and it was some weeks afterwards that he began to complain of headaches. Mr. Gibson suggested that I would be interested to see him.

On examination the man was mentally dull and apathetic, his speech was slow and rather thick, his memory uncertain, and he showed a tendency to repeat his story in a way that showed that he had forgotten how recently he had told it. His pupils were unequal, the right being larger than the left. No other physical sign was detected, except that his right hand was somewhat tremulous. I admitted him to my ward the following day. Lumbar puncture showed normal fluid with ten cells. X-ray showed a marked area of rarefaction at vertex, with thinning of surrounding skull.

On 23rd March, Mr. G. R. B. Purce elevated a flap of bone in the right side of the skull. A red, bulging mass was seen under the dura, which was incised and a mass of blood-clot which measured about three inches by three and a half inches was removed.

The patient made an uninterrupted recovery. I kept him at rest in hospital for some weeks. He is now completely well.

A Case of Ewing's Tumour Treated by X-Ray Treatment

By F. P. MONTGOMERY, M.B., D.M.R.E.CANTAB.,
Royal Victoria Hospital, Belfast

HISTORICAL.—The classification of bone tumours had been very unsatisfactory up to the beginning of the last decade. In 1920 Dr. Ewing, in conjunction with Doctors Codman and Bloodgood, formed a registry of bone sarcoma in America. In 1921 this registry was adopted by the American College of Surgeons. The following is the classification of bone tumours adopted by the registry :—

(1) Metastic tumours of bone.
(2) Periosteal fibro-sarcoma.
(3) Osteogenic tumours—benign and malignant.
(4) Inflammatory conditions.
(5) Benign giant-cell tumours.
(6) Angioma—benign and malignant.
(7) Ewing's tumour.
(8) Myeloma.

Ewing originally described his tumour as an endothelial myeloma of bone. The histogenesis is, however, by no means settled. Geschickter and Copeland, in their recent book, state that it is non-osseous in origin and possibly arises from the bone lymphatics. Connor of Harvard has recently stated : "Ewing's tumour has brought forth a diversity of opinion and nomenclature that shows the confusion concerning it. It has been classified heretofore as 'a round-cell sarcoma, but of a different nature to the usual osteogenic sarcoma or myeloma.' "

MICROSCOPIC.—The cells are usually round with little light staining cytoplasm. They are closely packed in sections or rows without definite structure. They are hyperchromatic and may show numerous mitotic figures. The nuclei are oval or round, and generally there is only one nucleus to a cell.

ETIOLOGY.—This is unknown. The disease occurs in early life. In ninety per cent. of the cases the age is between 4½ and 25. There is frequently a history of injury, and seventy-five per cent. of all cases are males. The lapse of time between trauma and the appearance of the tumour is usually six to twelve months.

CLINICAL CHARACTERISTICS.—Pain is frequent, occurring in eighty per cent. of cases. Generally the tumour can be palpated. Some cases show regression of the tumour for a time, with disappearance of symptoms. There may be a rise in temperature (98.6 to 101° F.); the blood picture is indefinite. There may be spontaneous fracture, while the general nutrition is usually not disturbed until late in the disease. The common sites of the tumour in order of frequency are : tibia, femur, humerus, fibula, radius, ribs, ileum, scapula, and clavicle.

X-RAY DIAGNOSIS.—A good deal depends on the stage of the disease at the time of examination. In the early stages, an X-ray diagnosis is frequently impossible.

There is roughening of the periosteum and a widening of the cortex, with areas of increased density. These appearances could equally well be caused by an early osteomyelitis. Later the periosteal involvement may assume the "onion skin" appearance or parallel layers of new bone, which is generally accepted as the typical radiological appearance. The epiphyses are never involved, and the tumour can be seen invading the soft tissues.

The best diagnostic test is the response to X-ray therapy, which gives just as reliable information as a biopsy and microscopic study, and without the attendant dangers of biopsy. The differential diagnosis is from osteomyelitis, benign giant-cell tumour, and osteogenic sarcoma, none of which responds to X-ray therapy.

Prognosis.—The outlook is bad, whatever method of treatment is adopted. Geschickter and Pollard report ten per cent. good results following amputation and X-ray therapy.

Secondaries.—True to its nature as a malignant disease, dissemination occurs in all cases which terminate fatally. The most frequent sites are the lungs, the lymph-nodes, and the skull. The most striking feature is the dissemination of the secondary deposits to other bones. The involvement of a single bone early in the disease with later dissemination to other bones constitutes a striking and important feature of Ewing's tumour, and distinguishes it from all other tumours of bone.

Case Report.

H. C., aged 11 years, schoolboy.—Personal and family history unimportant. In April, 1933, patient hurt his right arm at the swimming-baths. There was some swelling and pain as a result in the upper third of the arm, and this has continued off and on since then. Patient was admitted to Mr. Irwin's ward in the Royal Victoria Hospital on 27th September, 1933. On admission he was well nourished, but pale, and had a hard swelling in the region of the upper end of the humerus. There were no glands present and nothing in the chest. There was a little venous dilatation over the skin of the shoulder.

On 3rd October, 1933, Mr. Irwin operated. He found the periosteum greatly thickened, the bone expanded and soft and gritty. A section was taken, and the wound closed without anything further being done. On 7th October, 1933, the laboratory reported that the specimen presented the characteristics of a round-cell sarcoma, tumour-cells showing clear large vesicular nuclei. The diagnosis of Ewing's tumour of bone was made.

On 17th October, 1933, X-ray therapy began; twelve treatments each consisting of 216 R units were given to three areas in five weeks. On 5th January, 1934, a second series was begun, lasting six weeks (216 R units is equivalent to a one-third B or skin erythema dose). A third course was commenced on 2nd May, 1934. There was marked improvement in the condition of the tumour and of the patient following these treatments. On 20th November, 1933, there was definite evidence of repair, and by the 6th January, 1934, when the second series was commenced, considerable sclerosis and consolidation had taken place. By 2nd March, 1934, the repair was practically complete and the activity gone. On 13th April, 1934, a little

retrogression on the inner aspect was present. Between the middle of June, 1934, and 7th September, 1934, the boy kept well and was not seen. When he did return there was a swelling over the lower end of the radius on the same side, which shows definite evidence of secondaries. The primary growth meanwhile had lost much of its sclerosis and was evidently active again. Treatment to both areas was re-instituted at once, but in three weeks the patient was obviously going downhill rapidly and was unable to continue further treatment. He complained of much pain over the spine, but no other evidence of secondaries was found in the chest, spine, or glands. When last seen he was obviously dying.

A Case of Acute Infectious Mononucleosis (Glandular Fever)

By J. T. Lewis, M.D., M.R.C.P.LOND.

Patient (D. C.), male, aged 19. History :—Good health until about ten days before onset; during this time he complained of slight sore throat and some enlargement of the cervical glands.

On 23rd September, 1934, the patient's throat became much worse, and his temperature was found to be 102° F. I saw him on that day with Dr. Lyttle. The tonsils were swollen and red, with moderate exudate; all the superficial lymph-glands (neck, axillæ, and groins) were enlarged, discrete, and tender. The spleen was easily palpable, but the liver could not be felt. There was no rash and nothing else noteworthy on general examination. A provisional diagnosis of glandular fever was made, and a throat-swab and leucocyte-count taken.

Throat Swab.—Negative for B diphtheriæ, mainly mixed streptococci on culture. This swab was not examined for Vincent's organisms.

Leucocytes 15,000 per c.m.; polymorphonuclears 31 per cent., lymphocytes 15 per cent., monocytes 53 per cent.

This picture was quite typical of glandular fever.

During the next week the temperature remained high, with marked daily variations (see fig. 1). On 25th September he developed some dullness at the base of the right lung, which cleared up without effusion. At this time a few spirochætes and fusiform bacilli were present in the throat. The throat became steadily worse during the first week. On 30th September the glands were much smaller, but the left tonsil was covered by a dense slough, which on examination showed very large numbers of spirochætes and fusiform bacilli (Vincent's angina). The temperature

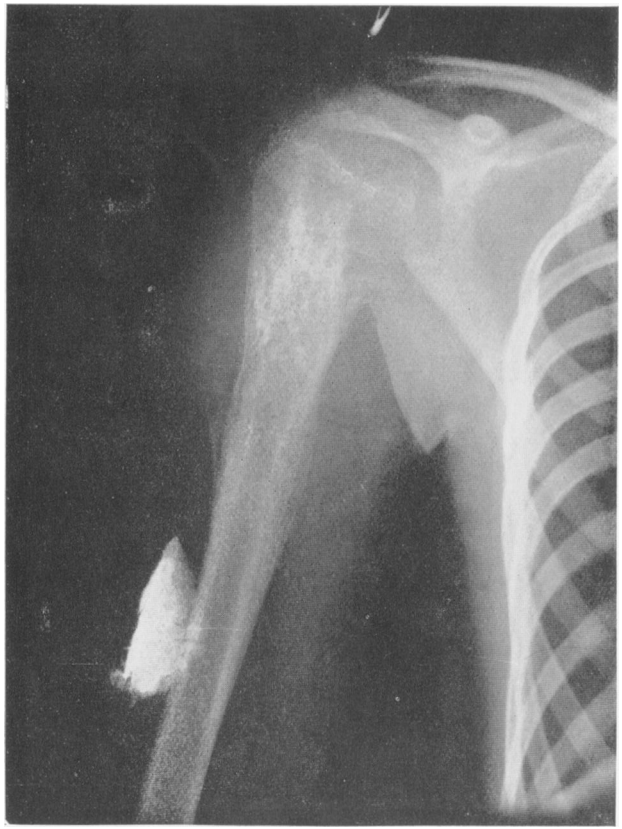

Fig. 1.

11 10 1933.—Ewing's Tumour : Breaking down of cortex of upper half humerus. Typical "onion-skin" appearance inner and lower aspect of shaft.

Fig. 2.

6 1 1934.– Ewing's Tumour : Showing evidence of sclerosis following treatment.

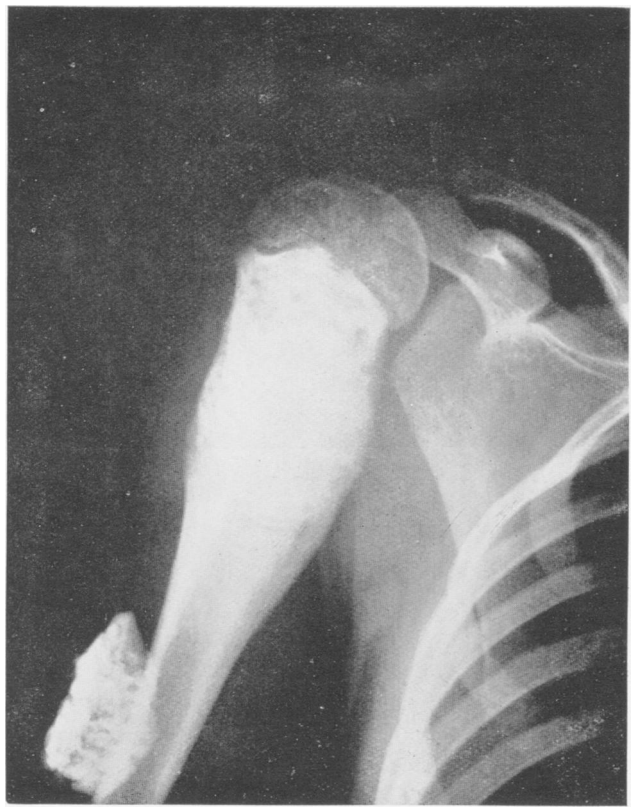

FIG. 3.

2 3 1934.—EWING'S TUMOUR: Advanced state of repair; good sclerosis.

FIG. 4.

13 4 1934.—EWING'S TUMOUR: Stage of maximum repair following two courses of deep X-ray therapy.

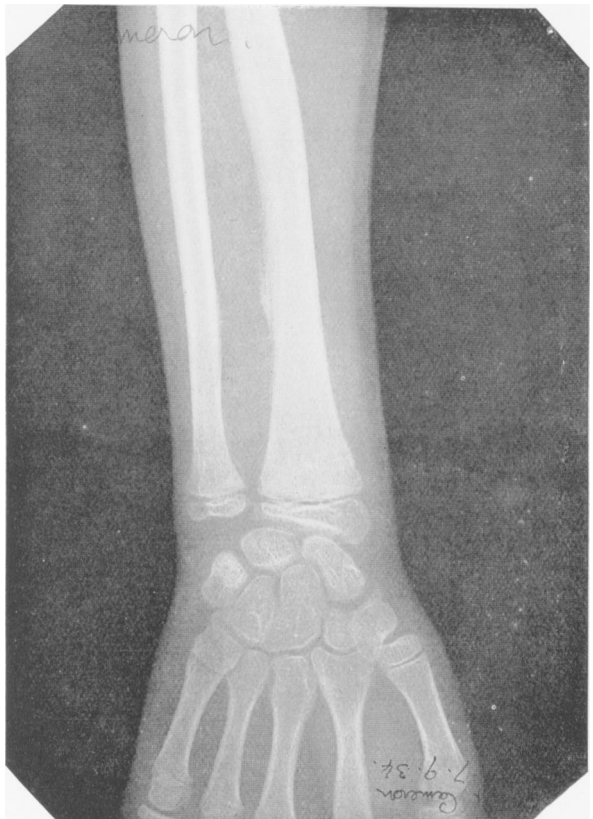

Fig. 5.

7 9 1934.—Ewing's Tumour : Secondary deposit, lower end of radius of same side.

Fig. 6.

3 10 1934. Ewing's Tumour : Commencing activity upper and lower aspects, inner margin of shaft of humerus.

retrogression on the inner aspect was present. Between the middle of June, 1934, and 7th September, 1934, the boy kept well and was not seen. When he did return there was a swelling over the lower end of the radius on the same side, which shows definite evidence of secondaries. The primary growth meanwhile had lost much of its sclerosis and was evidently active again. Treatment to both areas was re-instituted at once, but in three weeks the patient was obviously going downhill rapidly and was unable to continue further treatment. He complained of much pain over the spine, but no other evidence of secondaries was found in the chest, spine, or glands. When last seen he was obviously dying.

A Case of Acute Infectious Mononucleosis (Glandular Fever)

By J. T. Lewis, M.D., M.R.C.P.LOND.

Patient (D. C.), male, aged 19. History :—Good health until about ten days before onset; during this time he complained of slight sore throat and some enlargement of the cervical glands.

On 23rd September, 1934, the patient's throat became much worse, and his temperature was found to be 102° F. I saw him on that day with Dr. Lyttle. The tonsils were swollen and red, with moderate exudate; all the superficial lymph-glands (neck, axillæ, and groins) were enlarged, discrete, and tender. The spleen was easily palpable, but the liver could not be felt. There was no rash and nothing else noteworthy on general examination. A provisional diagnosis of glandular fever was made, and a throat-swab and leucocyte-count taken.

Throat Swab.—Negative for B diphtheriæ, mainly mixed streptococci on culture. This swab was not examined for Vincent's organisms.

Leucocytes 15,000 per c.m.; polymorphonuclears 31 per cent., lymphocytes 15 per cent., monocytes 53 per cent.

This picture was quite typical of glandular fever.

During the next week the temperature remained high, with marked daily variations (see fig. 1). On 25th September he developed some dullness at the base of the right lung, which cleared up without effusion. At this time a few spirochætes and fusiform bacilli were present in the throat. The throat became steadily worse during the first week. On 30th September the glands were much smaller, but the left tonsil was covered by a dense slough, which on examination showed very large numbers of spirochætes and fusiform bacilli (Vincent's angina). The temperature

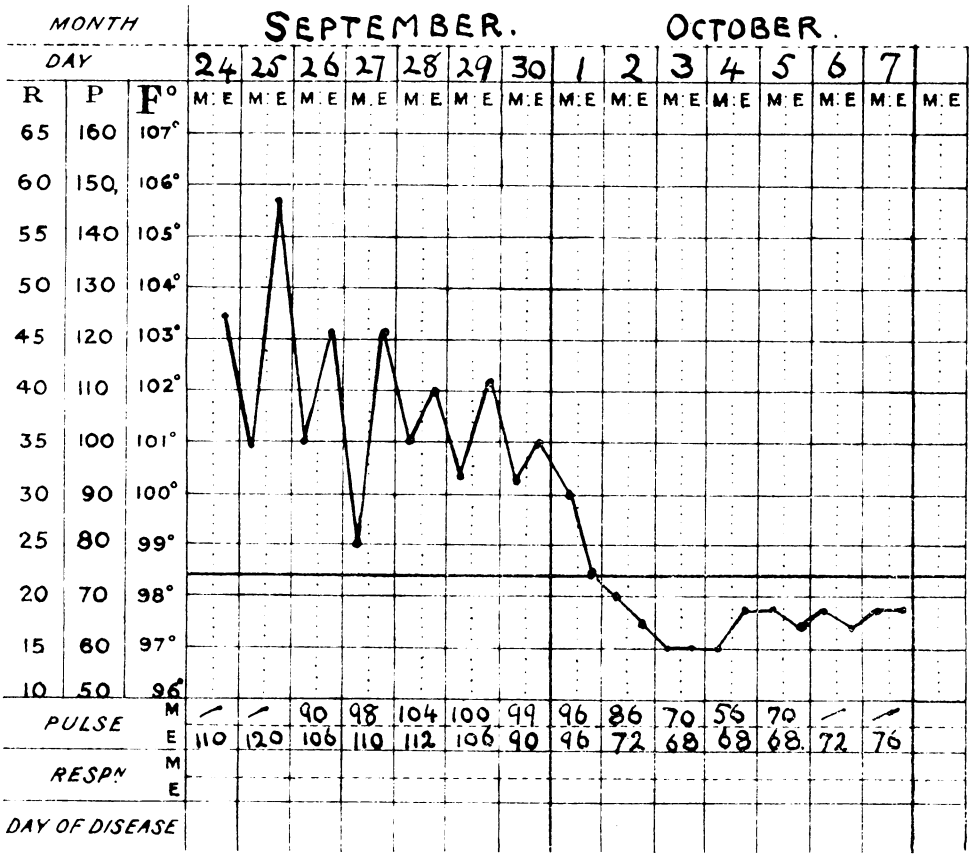

Fig. 1.

became normal on 2nd October, and two days later the glands had practically all subsided, with the exception of the cervical glands, which were still enlarged and tender. The spleen was no longer palpable. The throat was clearing slowly, and it could be seen that a large part of the left tonsil had sloughed. On 4th October the general condition of the patient was unsatisfactory: he was drowsy with a slow low-tension pulse. Daily leucocyte counts (see table 1), showed a steady fall in the polymorphonuclear cells, and it was thought advisable to administer pentose nucleotide. He was given 10 c.c. by intramuscular injection. This was immediately followed by dyspnœa and a sense of oppression in the chest, which passed off in a few minutes. There was marked general improvement in the clinical condition during the next few days, and on 8th October the tonsils were practically clear. On the next day the patient was allowed to sit up, but as the polymorphonuclear cells had again fallen, 6 c.c. of pentose nucleotide were given, and this was repeated on the following day (for response to nucleotide therapy see fig. 2).

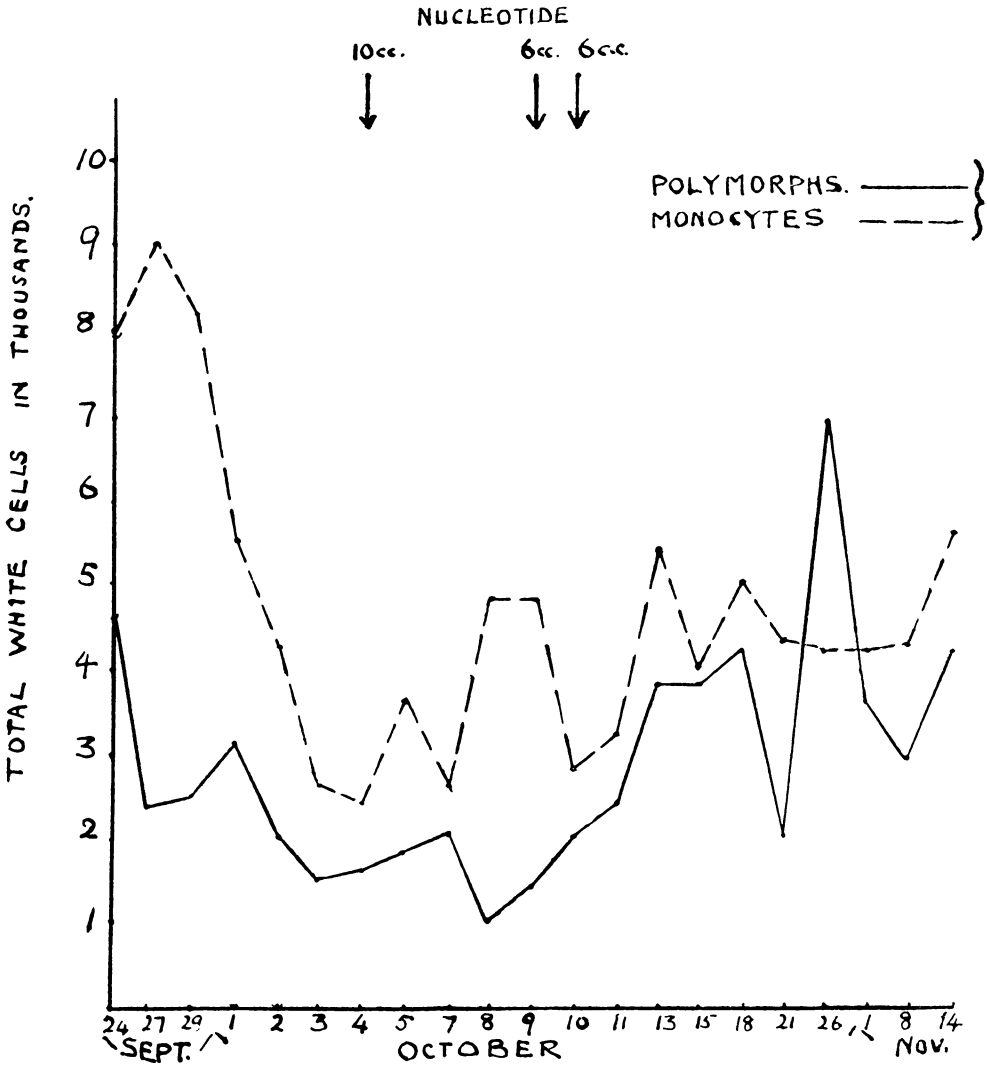

FIG. 2.

There was a slight recurrence of sore throat on 21st October, but otherwise the patient has made an uninterrupted recovery.

As will be seen from table 1, the monocytosis has persisted.

The following points in this case are worthy of comment :—

1. The intense tonsillar sepsis and high temperature, which are unusual in this disease.

2. The association of the disease with a Vincent's infection of the throat. The occurrence of these organisms in the throat in glandular fever has been reported by

many observers, and attempts have been made to establish an etiological relationship between the Vincent's infection and the blood changes. However, it has not been shown that monocytosis is a constant finding in Vincent's angina, and many cases of glandular fever do not show the Vincent's infection. It is probable that these organisms are secondary invaders.

3. The presence of heterophil antibodies in the patient's serum. It has been pointed out by Paul and Bunnell (*Amer. Jour. Med. Sc.*, 1932) that the serum of cases of glandular fever will agglutinate sheep's corpuscles in high dilution. The only other clinical condition in which a comparable agglutination occurs is serum sickness. In the case described, agglutination occurred in a dilution of 1 in 256, whereas two normal controls only agglutinated in dilutions of 1 in 4 and 1 in 8 respectively.

In a case seen some time ago a similar high titre was found. It would seem that this might prove a useful test in differential diagnosis.

In conclusion, I should like to express my thanks to Dr. H. L. Tidy, who examined a film and expressed himself satisfied with the diagnosis.

TABLE 1.

	Total Leucocytes	Percentage Polymorphonuclears	Percentage Lymphocytes	Percentage Monocytes	
Normal ...	8,000	65-70	25-30	5	
24/9/34 ...	15,000	31	15	53	
27/9/34 ...	13,600	18	13	67	
29/9/34 ...	12,300	20	13	67	
1/10/34 ...	10,600	30	17	52	
2/10/34 ...	8,000	25	21	54	
3/10/34 ...	4,800	31	12	55	
4/10/34 ...	4,600	36	9	53	—10 c.c. nucleotide
5/10/34 ...	7,200	26	24	50	
7/10/34 ...	7,400	30	35	35	
8/10/34 ...	6,700	16	12	72	
9/10/34 ...	8,700	17	27	56	— 6 c.c. nucleotide
10/10/34 ...	6,800	26	29	42	— 6 c.c. nucleotide
11/10/34 ...	8,000	31	28	41	
13/10/34 ...	10,700	36	11	51	
15/10/34 ...	9,600	40	19	41	
18/10/34 ...	10,600	40	7	48	
21/10/34 ...	7,800	26	18	56	—sore throat
26/10/34 ...	13,600	51	15	31	
1/11/34 ...	10,600	35	20	40	
8/11/34 ...	8,100	36	11	51	
14/11/34 ...	12,600	34	18	45	

CASE OF HÆMOLYTIC STREPTOCOCCAL MENINGITIS WITH RECOVERY

By

J. C. DAVISON, M.D., B.Sc., *Clinical Assistant, Royal Victoria Hospital, Belfast;*

and

D. C. PORTER, M.B., *House Physician, Royal Victoria Hospital, Belfast.*

STREPTOCOCCAL meningitis is almost invariably a rapidly fatal disease. This case, in which the patient made a satisfactory recovery, is therefore of interest.

The patient, a male, aged eighteen years, was admitted to the medical wards of the Royal Victoria Hospital on 18th November, 1933. His main symptoms were :—

(1) Almost constant severe frontal headache of three weeks' duration.
(2) Simultaneous onset of frequent vomiting unrelated to food and of projectile type.
(3) Attacks of vertigo with diplopia during this period.
(4) Drowsiness.

Previous History.—At four years of age he had operations on both mastoid regions. Since then he had been a victim of marked bilateral deafness with constantly discharging ears and recurring abscesses in the mastoid regions.

Examination of his central nervous system showed the following positive signs :—

(1) Bilateral optic neuritis to a degree of two dioptres, with congestion of veins and minute retinal exudates.
(2) Contracted pupils reacting normally.
(3) Bilateral middle ear deafness.
(4) Absent abdominal reflexes.
(5) Bilateral Kernig's sign.
(6) Neck rigidity.
(7) Slow cerebration, mental irritability, and photophobia.
(8) Sensory aphasia.

The diagnosis of meningitis was confirmed by lumbar puncture. The fluid was under a greater pressure than 300 mm. water.

Examination.—Opalescent. Cell count : 2,500 cmm., mainly polymorphonuclear cells. Total protein : 0.12 gms. per cent. Nonne-Apelt positive. Chloride content : 0.705 gms. per cent. (later in the illness this fell to 0.587 gms. per cent.). Sugar content : 0.07 gms. per cent. (this fell very markedly in succeeding specimens).

A profuse growth of hæmolytic streptococcus was obtained on culture (blood agar, aerobic).

His blood leucocytes were 10,700 per cmm.

Polymorphonuclear cells, 72 per cent.; lymphocytes, 15 per cent.; monocytes, 5 per cent.; transitional cells, 2 per cent.; eosinophilic cells, 4 per cent.; basophilic cells, 2 per cent.

The treatment adopted was frequent lumbar puncture, the amount withdrawn each time being increased gradually from 10 to 40 c.c. On the seventh day his

condition became worse. Headache and vomiting became more severe, with accompanying rise of temperature and pulse-rate. On the tenth day, 10 c.c. of anti-scarlatinal serum was introduced intrathecally, and after an almost immediate attack of generalized urticaria his condition began to improve. The anaphylactic phenomenon was treated with adrenaline and collosal calcium. Daily lumbar puncture was continued for nine days longer. The fluid was then under normal pressure and clear. Vomiting, headache, and vertigo had ceased. His optic discs were still slightly swollen.

He was discharged in good general health three months after admission to hospital. His mastoid condition, however, remains to be dealt with as a potential focus of fresh infection.

We are indebted to Professor Thomson for permission to publish this case.

LUMBAR SYMPATHECTOMY FOR CHRONIC ULCERATION OF THE TOES

By J. S. Loughridge, B.Sc., M.D., F.R.C.S.Eng.,
from the Royal Victoria Hospital, Belfast.

The operation of sympathectomy, while still in the experimental stage, has the advantage over many other new surgical procedures in that it is possible to forecast what end-results are going to be obtained in the individual case. This holds at least for the more immediate end-results. The effect of operation is judged beforehand by the temperature response of the skin after producing local anæsthesia of the sympathetic nerves to the part. A rise of ten degrees Fahrenheit under suitable room-temperature conditions indicates a degree of arterio-spasm which will respond satisfactorily to sympathetic denervation. The temperature of the skin is measured by thermocouples and a sensitive galvanometer.

D. L., aged 21, telegraphist, complained of pain and burning in the great toes of both feet for two years. The left foot improved, but the right foot became progressively worse and finally ulcerated. He was then seen and treated by Dr. J. B. Young, who found that spt. ætheris nitrosi produced temporary subjective improvement. When admitted to hospital the patient had an ulcer covering most of the medial and plantar surfaces of the distal phalanx of the right great toe. There was also a similar smaller ulcer on the second toe. The foot was cold to the touch, the skin was thin and anæmic, and the veins were thin and small. The blood-pressure was 98/66. The Wassermann reaction was negative. The radiogram showed some necrosis of the terminal phalanx. A part of the margin of the ulcer was excised and examined microscopically by Professor Young. He reported that the section showed a disorganized artery which was the seat of a thrombo-angiitis, but that disorganization was too advanced to say whether this change was primary or secondary to the ulceration. The patient was kept in bed for six weeks. Adequate local heat and

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a variety of antiseptic dressings were applied without appreciable change. It was then decided to consider the question of a sympathectomy. The skin of the foot showed four degrees of a rise during spinal anæsthesia. As the temperature of the theatre was seventy degrees Fahrenheit, this rise was taken to indicate a degree of vasospasm justifying operative interference. Accordingly on the 11th November, 1933, with the help of Mr. H. P. Malcolm, the right lumbar sympathetic chain was exposed by displacing the cæcum and ascending colon towards the left. The second, third, and fourth sympathetic ganglia and their connecting strands were excised. The post-operative response was rapid and striking. Pain disappeared almost immediately, and within a few days the sloughs were thrown off and healing commenced. The ulcer was healed before the patient was allowed out of bed, three weeks after operation. Twelve months later the ulcer is represented by a small scar under the nail. The temperature of the legs has been noted periodically since. Typical figures are :—

14th January, 1934 - Room temperature 60°F., right leg 91°F., left leg 65°F.
5th April, 1934 - - Room temperature 68°F., right leg 92°F., left leg 82°F.
17th September, 1934 - Room temperature 68°F., right leg 92°F., left leg 90°F.

Pathological Report.

Dr. P. A. Clearkin kindly examined the ganglia removed at operation. His report reads : "Many of the ganglion cells were degenerate, their outline distorted, cytoplasm badly stained, nucleus eccentric or missing. There was an increase in the amount of fibrous tissue, much of which appeared to be of recent formation. Though there was no evidence of acute inflammatory process in the sections examined, the number of polymorphonuclear leucocytes present in the lumen of the capillaries was larger than that usually seen in sections."

My best thanks are due to Professor P. T. Crymble for permission to publish the report of this case.

A Primary Tumour (Mixed-Cell Sarcoma) of the Pleura

By S. B. Boyd Campbell, M.D., F.R.C.P.Ed.,
and J. S. Young, M.A., M.D., B.Sc.,
from the Royal Victoria Hospital, Belfast

A school teacher, aged 44, was first examined on 11th October, 1933. Apart from an operation for appendicitis eight years previously, she had had no serious illnesses. She gave a history of sudden onset of pain in right side of chest one year ago, which lasted a week and was worse on breathing or on movement. Since then she has complained of slight soreness radiating towards the right shoulder, and of progressive weakness. Two weeks prior to examination she began to suffer from dyspnœa, which was worse on exertion. There was no œdema of her ankles, and her bowels and kidneys were functioning normally.

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By S. B. Boyd Campbell, M.D., F.R.C.P.Ed.,
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On examination her general condition was good, apart from some cyanosis. There was marked dullness of the whole of the right side of the chest up to the level of the third rib, with complete loss of breath sounds. X-ray showed that this dullness was due to a large effusion. On aspiration, two pints of bloodstained fluid were removed, and a similar quantity on 6th November, 1933. The radiogram taken immediately after the removal of the fluid showed a thickening of the basal pleura (fig. 1). As the effusion rapidly reappeared she was admitted to the Royal Victoria Hospital at the end of December, and an artificial pneumothorax after the removal of the fluid showed, on X-ray examination, multiple round shadows in the area of the collapsed lung and protruding from the peripheral pleura (fig. 2). A clinical diagnosis of pleural endothelioma was made. The rapid recurrence of the fluid necessitated frequent aspiration of one to two or more pints of bloodstained fluid, the patient only obtaining relief from her dyspnœa and discomfort after each aspiration.

The patient lived for five months after the last radiological examination (22nd January, 1934). During this period, the tumour involving the right pleural sac had grown rapidly. At the post-mortem examination on 6th June, 1934, the right lung was collapsed and was ensheathed by a mass of cellular tumour tissue which measured three inches in thickness over the costal surface of the lung and filled the pleural sac. The tumour was necrotic and extremely friable, but its natural relations were preserved as far as possible by stripping the parietal pleura from the chest wall. No growths, either primary or secondary, were observed in any part of the body outside the chest, and the breasts were normal. Both bronchi were congested, but neither the right nor the left showed any evidence of ulceration. In view of these findings a provisional diagnosis of "endothelioma of the pleura" was made at the post-mortem examination. The appearances of a coronal section through the fixed specimen are illustrated (fig. 3). Two small nodules of growth are present in the substance of the lung: they occupy a superficial situation in direct continuity with the pleural mass. The bronchial lymph-glands are anthracotic, but they are not notably enlarged and they show no evidence of invasion by the growth. Microscopically, the growth is extremely cellular and shows very extensive necrosis. In general, the tumour cells are small and spheroidal or ovoidal, but perhaps the most conspicuous feature is the large number of multinucleated giant cells (fig. 4). No papillary proliferation is apparent, and it is only occasionally that an alveolar structure is suggested. There is an abundant formation of reticulum. In short, the tumour is best described as a mixed-cell sarcoma.

Diffuse pleural growths which form a thick investment of one lung are uncommon, nevertheless the present case was the third of a series of three (Ser. Nos. A1014, A1026, A1143) observed within five months. In all three cases the growth was confined to one pleural sac, with or without gross involvement of the bronchial lymph-glands on the same side. In one case (A1014) a simple tumour, namely, a cortical adenoma, was found in the left adrenal, but no malignant growth, either primary or secondary, was disclosed by a thorough post-mortem examination in any other part of the body, either in this case or in the other (A1026). The bronchi were free from

ulceration in both cases. Microscopically, these two pleural tumours possess a papillary or an alveolar structure, and are composed of spheroidal cells with vesicular nuclei; they contain no reticulum. They have many features in common, but they differ in the respect that giant multinucleated cells are numerous in A1026 and absent in A1014.

The classification of pleural tumours of this type is uncertain. It has not even been established that they are primary growths of the pleura. Indeed, their primary nature has been vigorously contested by Robertson and by Willis and others. These authors are of the opinion that, with the exception of rare primary sarcomata of the pleural tissues, all such growths are "secondary, representing extensions, implantations, or metastases from an unrecognized or latent primary source, usually the lungs." They base their opinion principally on the diversity of the histological picture of "endotheliomata of the serous membranes," and assume too readily perhaps that the structure or the cytology of the serosal endothelium lining the pleural sac is quite inflexible. I agree with these authors that the term "endothelioma of the serous membranes" is a misnomer. Ten years ago I had an opportunity to study two more tumours of this pattern, and one of them proved to be a squamous epithelioma on microscopical examination. At that time I was inclined to think that Robertson's explanation was correct, and that the squamous epithelioma of the pleura had been secondary to a latent primary source, which had been overlooked at the post-mortem examination. A few years later, however, I was able to show that the serosal endothelium covering the visceral pleura of the rabbit can undergo metaplasia to an epithelium of cubical, columnar, transitional, or stratified squamous type. Since such a wide range of metaplasia can be induced experimentally, it can scarcely be denied that it may occur under natural conditions even in the human subject. If a malignant growth were to supervene upon any such metaplasia—and this is a common enough sequence of events in other situations—the histology of the growth must be as diverse as the metaplasia. Every pathologist is aware that a primary growth may be small or even insignificant compared with the bulk of its secondary growths, but it is hard to believe that pleural tumours, which are characterized above all things by their bulk and by their habit of ensheathing the lung, are generally secondary to a latent primary source in the lung, whereas gross primary sources in the same organ are seldom attended by any considerable infiltration of the pleura. In view of these considerations I cannot accept the generalization that all diffuse tumours of the pleura are secondary to a latent primary source in the lung, and, as a matter of fact, I hold that the four tumours mentioned in this short report are *primary* tumours of the pleural serous membrane, in spite of the diversity of their microscopical appearances.

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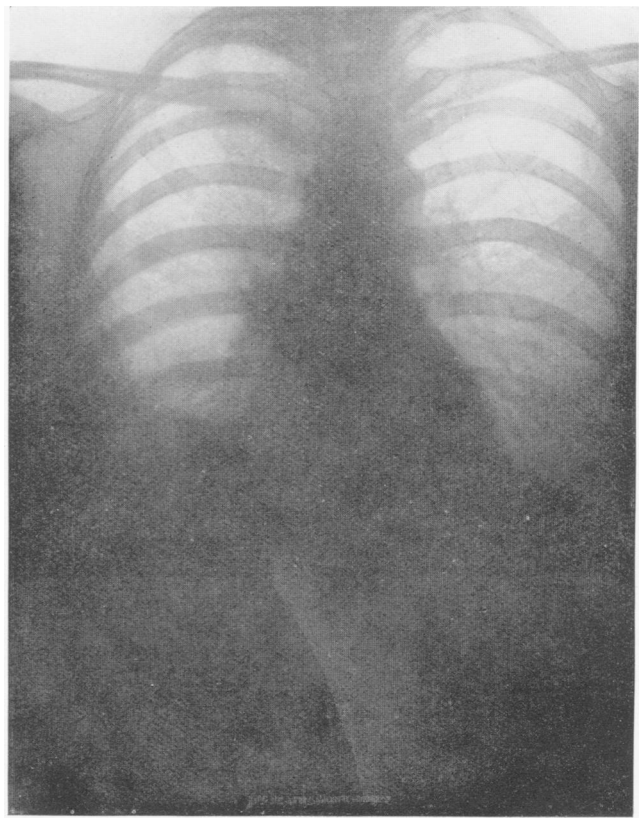

FIG. 1.

6 11 1933.—Radiogram immediately following removal of two pints of fluid from right side of chest, showing thickening of basal pleura.

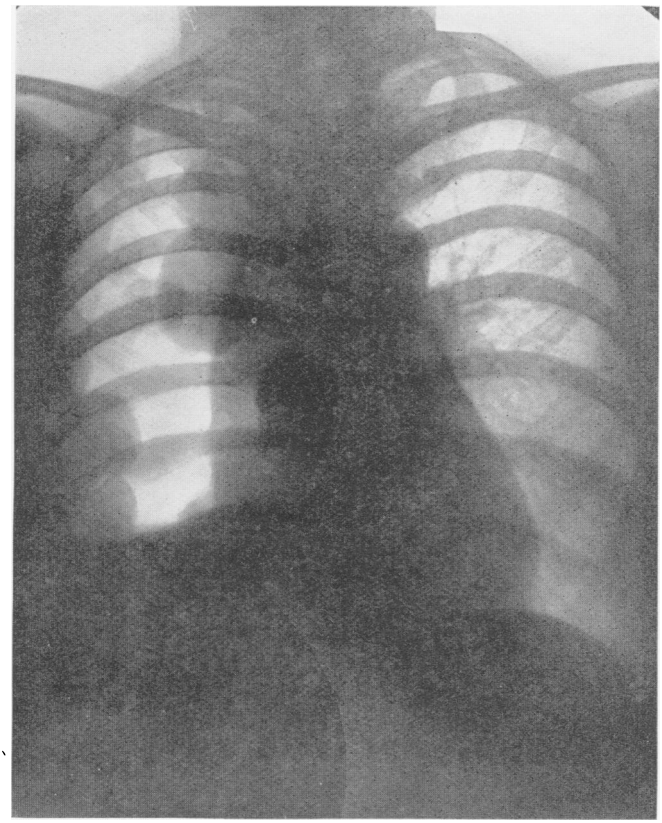

FIG. 2.

3 1 1934.—Radiogram following removal of fluid and replacement by air, showing large nodular growths in pleura.

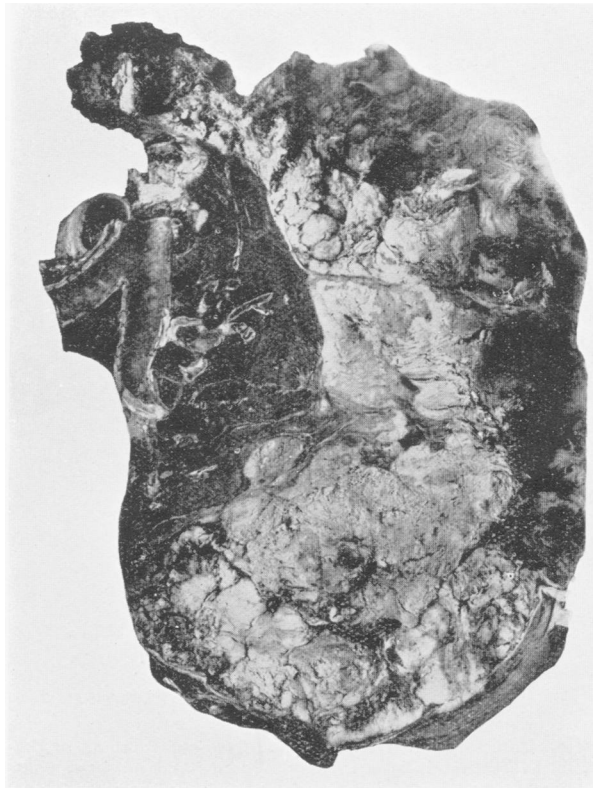

FIG. 3.

Coronal section through fixed specimen of primary mixed-cell sarcoma of the pleura.

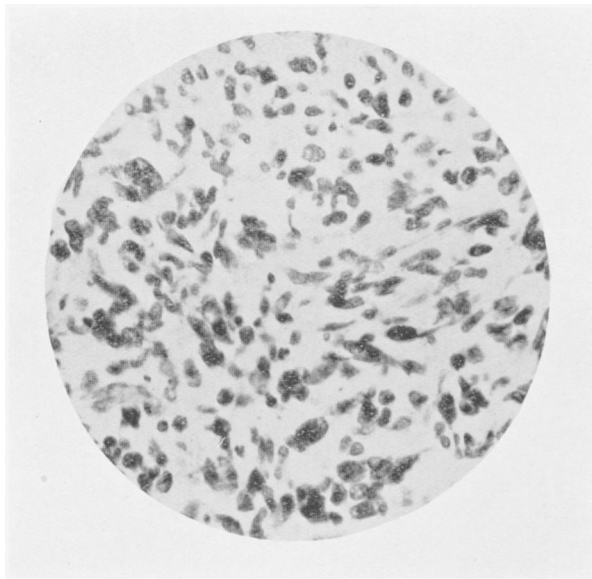

FIG. 4.

Microscopic section from primary mixed-cell sarcoma of the pleura. Note that it is extremely cellular, and note the conspicuous feature is the large number of multinucleated giant cells.

Biochemistry

By JOHN A. SMYTH, M.D., B.SC., D.P.H.

The Opening Address to the Students of the Royal Victoria Hospital, Belfast

SESSION 1934-5

It cannot be claimed, as by Mayow when writing of rickets in 1668, "There has been only one so far as I know who has written anything on the subject, and that may seem strange, because as a rule disease as it stalks through the land cannot keep pace with the incurable vice of scribbling about it." Biochemistry has a good press.

Medicine and chemistry have been closely linked from the earliest times, and in their long histories each has owed much to the other. In recent years, although chemistry has not derived much from medicine, medicine has gained enormously from chemical research, and its modern advances are mainly due to the application of accurate scientific principles.

Medicine at the present time may be described as an applied science. Many of its problems have been too difficult for solution in the past, and theories and speculations still occupy a prominent position. Thanks to researches, however, new facts are being constantly added, so that as time advances theories and speculations are being replaced by deductions based on exact scientific observations.

It is doubtful if medicine can ever possibly become a science characterized by an exactitude such as obtains in chemistry. Too many complicated factors play a part in the processes of physiology and disease to render this attainable. Yet it is quite certain that the application of exact chemical methods in the solution of problems pertaining to medicine has done a great deal to clear away error and lead to the proper understanding of the difficulties with which it is confronted.

Organic chemistry is concerned with the chemistry of the substances which occur in animals and plants; physiological chemistry has to do with the changes which these substances undergo in the living body, dealing mainly with the finished end-products, whilst biochemistry investigates these changes in connection with the living cell, working especially on the internal medium of exchange, the blood. An example may make the differences clear. Urea, an organic substance, was first prepared synthetically in 1828 by Wohler, who thus, by doing away with this distinction between organic and inorganic compounds, did much to undermine the common belief in vitalism. Organic chemists are interested in the chemical structure of urea and its chemical similarity to other compounds; physiological chemists study the formation of urea in the liver by the deamination of amino acids, but a modern biochemist like Van Slyke is concerned with what he calls "urea clearance," a test of the kidney's power to excrete the urea in the blood and an index of renal efficiency.

Biochemistry as we know it is a modern subject. Physiological chemistry is its parent, but it owes much of its technique to its grandparent—pure chemistry, which was only interested in discovering facts and not concerned with their practical

application. So it is that the love of knowledge and its altruistic pursuit has often conferred on man gifts of the greatest practical value. Spurred on by the sufferings of the sick, physicians have ransacked the researches of chemists, physicists, and physiologists alike for discoveries which may ease or cure them. Thus medicine has been an important factor in the prosecution of further scientific research.

Paracelsus, who practised as a physician about A.D. 1500, may be regarded as the first physiological chemist. He taught chemical therapeutics, and in his teachings are, possibly, the earliest conceptions of asepsis and catalysis.

Van Helmot, who followed about a hundred years later, discovered carbon dioxide and made important observations with regard to gastric juice and bile. He was the founder of the Iatrochemical school, which became powerful under Sylvius about 1650. This school attempted to explain life entirely in terms of chemical operations and mechanical principles. As Michael Foster states, "It thought that it was unnecessary to take refuge in subtle influences and occult agencies, but that all the changes in the body were larger or more complex examples of the changes that could be produced in the laboratory." Their views were rather extreme, especially for those times.

The swing of the pendulum came with Stahl in 1660, who held that "the events of the body may be rough hewn by chemical and physical forces, but that the 'sensitive soul' will shape them to its own ends." Stahl thus comes at the close of the seventeenth century to be the founder of animism. The "sensitive soul" fell back later to the lower stage of "a vital principle," but it has thus maintained itself in the minds of many clinicians to the present day.

In 1669 John Mayow of Oxford had shown that there was a part of the atmosphere which was responsible for combustion, for respiration, and for all the chemical changes so essential to life. This part we now know as oxygen. Unfortunately, this work was neglected for more than a century owing to the effects of Stahl's animistic doctrine, which caused more attention to be paid to theorizing than to experimenting. It was only when in 1775 Lavoisier repeated this work, many other unexplained and apparently contradictory observations were fitted together as by the hand of a magician. From 1775 onwards we have had the "quantitative" period, and this period marks the development and growth of modern chemistry. Biochemical methods still remained rather vague, as there was as yet no firm foundation of known facts on which to work, but even so, the seeds of much modern research were sown about that time.

Digestion.

The discovery of gastric secretion resulted from Muller noticing, when he visited the fish market at Naples, that the marble slabs foamed when the stomach contents of the fish ran out on them. Muller and Brucke from this went on to the knowledge of digestive ferments, which were characterized by the infinitely greater activity which they showed when compared with previously known chemical substances.

About 1770 Spallanzani, Professor of Natural History in the University of Pavia, and afterwards at Padua, acted upon food by gastric juice drawn by means of a

sponge from the stomachs of various sorts of animals, and passed spheres containing food into the stomachs of different animals which he opened after the lapse of a given time. He also made animals swallow bits of meat attached to threads or wires, which he would after a time withdraw. On himself he experimented by swallowing linen bags containing food, and examined the contents after they had been passed per anum. In these ways he proved that the gastric juice dissolved various constituents of food, and that the juice of any particular animal is specially active on the natural food of that animal.

In 1777 Stevens experimented with a stone swallower, who swallowed and regurgitated little perforated silver balls containing foodstuffs, and studied digestion further in this way.

In 1822 Prout proved the presence of hydrochloric acid in gastric juice. The production of a mineral acid by living cells was surprising and unexpected, and no explanation was forthcoming for fifty years.

Over a hundred years ago Von Leube first employed a sound in investigation of gastric conditions, and a few years later a great advance was made by Ewald when he introduced his test-meal. On the results which he and others obtained by this method, in which one single sample is examined, our ideas of gastric secretion have been largely built until recent years. The variations in gastric acidity, the frequent absence of free hydrochloric acid in carcinoma and its excess in ulcers, both gastric and duodenal, were early discoveries.

In 1914 Rhefuss in Chicago originated the fractional method of carrying out the test-meal with which we are now so familiar, and by an extensive series of examinations was enabled to reach certain definite conclusions. It was introduced into this country by Bennett and Ryle, and has given us many entirely new conceptions of gastric digestion. Interesting discoveries by this method were the finding of achlorhydria in about five per cent. of normal healthy individuals, and the importance of the bactericidal function of hydrochloric acid in contra-distinction to its digestive action. Hurst has correlated these two discoveries in a most interesting way, and established an "achlorhydric" diathesis which Langdon Brown has described as a "predestination to disease."

Trypsin was discovered by Danilewski in 1862. Kuhne soon demonstrated that the protein molecule was broken up much further by this ferment than by pepsin, and that a substance was produced which gave a colour reaction with bromine water. The name 'tryptophan' was applied to the substance giving this reaction, meaning simply that it was an indication of tryptic digestion. It was isolated in 1901, and shown to be a constituent of many proteins. This fact, interesting chemically, was at first of only academic importance, but from it originated investigations which, later, had the greatest practical application, for in 1907 Hopkins found that if tryptophan was excluded from the diet of young rats they failed to grow. The importance was then discovered of what he called "accessory food factors," and of vitamins, that group of substances now known to be absolutely essential to life. Thus, beginning with an, in itself, unimportant colour reaction, we have ended in a discovery which has explained the causation and provided the treat-

ment of a universal group of diseases—a far cry, but it has all taken place in less than thirty years.

The study of tryptic digestion led to two other by-products. Trypsin was found to break protein into amino acids, and it was soon realized that a complicated operation like the reforming of tissue protein from these could not be performed by the intestinal mucous membrane. The part played by the liver in this rebuilding was discovered, and this knowledge has altered our conception of Bright's disease in several ways. The belief that albuminuria could be directly caused by the ingestion of an excess of protein is no longer tenable, i.e., the idea of alimentary albuminuria must be discarded.

The second by-product of this research came when it was noticed that in some people certain of these amino acids were excreted in the urine instead of the normal breakdown products. Excretion of such substances is usually congenital and familial, and from this discovery Sir Archibald Garrod has developed his work on inborn errors of metabolism. Alkaptonuria, pentosuria, cystinuria, and porphyrinuria are not often found, but through the study of them diathesis has been placed on a scientific foundation, and it has been seen that the laws of inheritance formulated by Mendel are applicable to it.

Diabetes.

Turning from the external to the internal secretion of the pancreas, we trace the biochemical investigation of diabetes. In 1674 an English physician, Thomas Wallis, found the urine of a diabetic to be "wonderfully sweet, as if containng honey or sugar." Fifty years later Dobson, another English physician, determined the true nature of the sweetening substance. By alcoholic fermentation and by investigation of a "white cake about four ounces in weight obtained by evaporating down diabetic urine," he came to the conclusion that this substance was glucose. Although Brunner had described the successful extirpation of the pancreas of dogs in 1682, it was left to Mehring and Minkowski two hundred years later to note that such dogs became diabetic. Minkowski observed how the flies clustered round the urine of pancreatectomized dogs, and on testing found it to contain sugar. Lepine in 1909 suggested that the appearance of sugar must be due to the failure of a glycolytic ferment which formed an internal secretion. The work of Langerhans, Bensley and Homans, Arnozant and Vaillard, Opie and Scobolew, finally brought the source of this secretion home to the Beta cells of the islets of Langerhans, and even before it had ever been separated in anything like purity Schafer had named it "insulin"—evidence of the faith that was in him.

Up to 1922, when insulin came into use, the treatment of diabetic patients was a discouraging task. At first it was thought to make up for the sugar lost in the urine by giving large quantities of it in the diet, but this was soon found to make the condition worse. The pendulum swung in the opposite direction when it was found that limitation of carbohydrate intake relieved the symptoms, and an attempt was made to exclude this substance completely. This proved even more disastrous, ketosis developing with coma and death. The next step was a search for a carbohydrate which diabetics could metabolize, and at this time Von Noorden's oatmeal

diet became popular. In 1914, Allen in America and Graham in England came to the conclusion that the type of carbohydrate was of little importance, but that the important factor in the diminution of glycosuria was the low caloric value of the food ingested. From this beginning was evolved the principle of alimentary rest, which was the mainspring of treatment from 1914 till 1922.

So far back as 1907 the internal secretion of the pancreas had been prepared, though in very impure form, by Zuelzer, who undoubtedly saved the life of at least one patient by means of it. The method of production was even patented by the Schering Company of Berlin, who prepared it on a commercial scale, and all that was required for a huge success was some method of purification. Many other workers prepared extracts of greater or lesser potency and purity, but a great factor in the prevention of their development was the absence of any easy method of estimating the sugar-content of the blood. Von Noorden, writing as recently as 1907, says: "The quantitative estimation of sugar in the blood is one of the most difficult processes of clinical chemistry." It seems a long step from this to the present day, when there are half a dozen accurate methods, any of which can be carried out in half an hour. They have all originated within the last twenty years.

This, then, was the state of affairs when Banting and Best took up the work in 1921. They first prepared insulin from the pancreas of dogs in which the pancreatic duct had been ligatured ten weeks previously. This is sufficient length of time for the acinar tissue which produces the digestive secretion to degenerate, but not for the islets. They then prepared it from the pancreas of fœtal calves of less than five months' development, at which age the pancreas still contains no proteolytic ferment. By experiments with these extracts a great deal was discovered about the properties of insulin, and by its use depancreatized dogs were kept alive for considerable periods. An important part was that the extract was fairly pure, so that it gave rise to no general reaction even when injected intravenously. It now only remained to evolve some method of preparation on a large scale, and this was done by extracting the adult beef pancreas with ninety-five per cent. alcohol, which destroys the digestive ferment. Collip came in to help by a method of purification by fractional precipitation of the extract with alcohol. Largely owing to the amount of this substance required, insulin produced at this time was twenty-five shillings per capsule of a hundred units. Other methods of extraction and purification have since been developed, with the result that insulin can now be manufactured in a very high degree of purity and sold at the moderate cost of just over one shilling per hundred units.

The investigation of the chemistry of diabetes, beginning with Wallis in 1674 and going on through the earlier extracts by Zuelzer in 1906 to the final purification of insulin by Collip, Banting, and Best in 1922, is, as Lusk says, "typical of that scientific medicine which affrights the spirits devoted to a passing empiricism."

Thyroid Gland.

The rise of anti- and even more so of a-sepsis led to surgeons undertaking larger and larger operations. Goitres soon attracted their attention. At first they contented themselves with removing the definite tumour tissue, and then, becoming

bolder, larger and larger portions of the thyroid gland fell to their hands. This gave results much admired by both surgeon and patient, but not for long, however, for after some time it became evident that almost all those who had had the thyroid completely extirpated were attacked by myxœdema. In Switzerland, Kocher, who had operated on many of these cases, turned to the German chemist Baumann with the suggestion that he should try to discover the substance whose removal was accompanied by results of such importance to life. In 1895 Baumann noticed the very high iodine content of the thyroid in contrast with other organs, and came to the conclusion that it had the power of secreting iodine and supplying it as required to the tissues in general. From this a new conception arose that organs of the human body might elaborate substances which had nothing to do with their nutrition, but were concerned with the activity of other organs. From the Greek word 'hormon'—to rouse or set in motion—these substances were called "hormones." In quick succession many of the most important hormones were discovered, and the glands which produced them, and which in many cases had previously been considered to have no secretion, came to be known as endocrine glands.

The first internal secretion to be proved was that of the thyroid. Although thyroid feeding to humans was employed in the previous year, an actual extract was first prepared by Murray in 1891. This was a glycerine extract of fresh sheep's thyroid, and was administered hypodermically. Following this a long investigation was carried out on the nature of the potent factor in this extract and what part iodine played. By hydrolysis of thyroid tissue with ten per cent. sulphuric acid and extraction of the residue with alcohol, Baumann obtained a substance containing about ten per cent. iodine, which he called iodothyrine. Iodothyrine was found to produce the same changes, when administered, as dried thyroid gland, but, when the two are compared on the basis of their iodine content, much less in degree.

Oswald in 1899, by saline extraction of the gland, obtained iodothyroglobulin, which probably exists as such in the live gland. When it is treated with ten per cent. sulphuric acid the iodothyrine of Baumann is one of the products. Oswald and others showed that iodothyroglobulin has the same action as dried thyroid gland, both qualitatively and quantitatively, in proportion to content of iodine, and Harrington is satisfied that thyroxine, which was later discovered by Kendall, is a primary constituent of iodothyroglobulin. Thyroxine was first isolated by Kendall on Christmas Day in 1914, and Harrington, by a brilliant piece of work, synthesized it in 1927 from tyrosine, at the same time determining its structural formula. The name 'thyroxine' is the result of a single error in a very brilliant research. Kendall in his examination of the substance which he had isolated made a slight analytical error, and came to the conclusion that it was an oxidation derivative of tryptophane containing an indole nucleus, and coined the name 'thyroxine' from thyroid-oxy-indole. At first he considered it was the real and only active principle of the gland, but has recently modified this opinion, and thinks that thyroxine may be an intermediate form in the elaboration of a final substance which the gland secretes into the blood-stream. It has been found impossible to obtain thyroxine from certain samples of iodothyrine and of active dried thyroid gland,

thus proving that thyroxine is not essential to the normal action of the gland. Also, thyroxine does not increase the activity of the vago-sympathetic system, and it has no effect on an isolated strip of intestinal muscle, in contrast to what happens when whole gland is used. Schulhof finds that, whereas iodothyroglobulin can be found in the lymph and blood leaving the thyroid, free thyroxine cannot be detected in either. It is possible that thyroxine does not exist as such in the living gland, and Kendall has assumed an intermediate substance which, though not obtainable as thyroxine by extraction, has similar biological properties. It will be obvious that some doubt exists as to the true position of thyroxine, but on the whole, it would seem that a combination of it with a peptide, and the iodine containing substances from which it is elaborated, are probably the only active substances present in the thyroid gland. This compound of thyroxine with a peptide is probably the only substance passing into the blood. It increases oxidative processes tremendously, though whether by catalytic action or as a hormone is not certain. The injection of one mg. of thyroxine produces a rise in the basal metabolic rate of approximately three per cent., and there is a corresponding rise in pulse-pressure, volume flow of blood, consumption of oxygen, and production of carbon dioxide. This rise does not reach its maximum for ten or twelve days, remains thus for about another ten or twelve days, and only disappears after a period of weeks. The thyroxine normally in the body, exclusive of the thyroid gland, is only about ten to twelve mg., but it is responsible for forty per cent. of the total energy of the body while at rest; the average daily destruction of thyroxine in the tissues is from 0.5 to 1 mg.

Basal Metabolism.

The diagnosis and treatment of thyroid dysfunctions has given a great stimulus to investigation of metabolic rates and respiration.

Lavoisier realized the importance of oxygen, and declared that life processes were those of oxidation with the resulting elimination of heat. He made respiration experiments on man, and about one hundred and fifty years ago reported that :—

(1) The quantity of oxygen absorbed by a resting man at a temperature of 26° C. is 15 to $23\frac{3}{4}$ litres hourly.

(2) The quantity of oxygen required at a temperature of 12° rises to $27\frac{3}{4}$ litres.

(3) During the digestion of food the quantity amounts to $35\frac{1}{2}$ to $37\frac{1}{2}$ litres.

(4) During exercise 80 litres or over may be required.

These remarkable results are in strict accord with the knowledge of our own day.

In 1866 Voit and his pupil Pettenkofer constructed a chamber to contain a human subject, through which a steady current of air was passed. The air was analysed just before entry and just after leaving, and in this way the amount of carbon dioxide and water given off determined. Check tests revealed their error in these determinations to be under one per cent., and since the days of these researches repeated experiments have established the verity of the conclusions drawn.

The work was carried out in Munich, and King Maximilian II of Bavaria defrayed the cost of the apparatus, which was considerable.

Another pupil of Voit's, Rubner, discovered that the heat value of the metabolism of the resting individual is proportionate to the area of the surface of the body. For example, a man in starvation or on medium diet, an infant at the breast, a dwarf, a dog, a pig, and a mouse, all give off the same quantity of heat per square metre of surface. It is this law which makes the comparison of basal metabolic rates possible, otherwise there would be no basis on which one could compare that of one individual with another, and the determination would be without value so far as practical medicine is concerned.

A third pupil of Voit's, Atwater, with the aid of Rosa the physicist, constructed in 1892 a large calorimeter capable of measuring accurately the amount of heat given off by a man living in it. It was the product of many years of labour, and the cost was borne by the United States Government. The average determination in it requires three observers and involves about forty weighings, five hundred temperature readings, and the writing of more than four thousand figures. This apparatus formed the first means of carrying out direct calorimetry, and it has confirmed a great deal of work done by Voit, Pettenkofer, and Rubner.

Indirect calorimetry is the method of calculating heat-production by the measurement of the carbon dioxide and oxygen exchanged in respiration. It, of course, only involves the use of very simple apparatus. Its validity has been established beyond a doubt by the simultaneous measurement of heat by physical means and of the gas exchange in a respiration calorimeter. With the Douglas-Haldane method, most commonly used in England and carried out in the Royal Victoria Hospital, very accurate results can be obtained in the hands of well-trained and careful operators.

The practical application of calorimetry in clinical medicine is in the determination of the basal metabolic rate—the heat-production of an individual at complete muscular rest in the post absorptive period. An obstacle in the way of obtaining comparable figures for different individuals was the difficulty in determining the surface area of the body. It was surmounted by D. and E. F. Du Bois, who, having first made careful casts of the body, divided the surface into geometrical figures, cut paper patterns of these, and by weighing them determined their area. By doing this for many individuals ranging from obesity to emaciation they, in 1916, devised their formula, giving the surface area in square cms. as—the weight in kilos $^{0.425}$ × height in cms. $^{0.725}$ × 71.84.

Efforts to isolate the secretion of internal organs other than the pancreas and thyroid have not all been so fruitful, although a great deal of progress has been made. While theories concerning the internal secretion have been in existence for years, they have been without any basis in experiment, and, for the most part, purely speculative. It was not until the nineteenth century that these problems were attacked in a logical way. Then, through the work of Addison, the attention of physiologists and chemists was attracted to the suprarenal glands; following the writings of Marie, research on the pituitary body went on rapidly : Von Mering and Minkowski had begun to investigate the pancreas : Kocher's extirpations of the thyroid had brought about a search for its internal secretion : the endocrine function

of the reproductive organs was demonstrated by Brown-Sequard and others. Schafer and his co-workers went a long way towards clinching the results of some of these inquiries by the experimental subcutaneous or intravenous injection of extracts of these glands. The beginning of the present century saw the acceptance of the physiological action of practically all the organs of internal secretion, and it only remained to prepare the active principle of some of them, to evolve methods of purifying others which had already been separated, to determine their chemical composition, and ultimately to synthesize them.

Adrenal Glands.

The first achievement was the discovery of the secretion of the adrenal glands. In 1849 Addison published an account of the clinical condition supervening on the destruction of these glands. In 1856 Vulpian, working in Paris, noticed that when oxidizing agents were applied to the cut surface of the medulla of the gland it turned pink, and that this staining also took place in the suprarenal vein. He came to the conclusion that the pink staining was caused by the internal secretion, and that this secretion passed directly into the blood-stream. Eleven years later Holm succeeded in isolating the secretion in a fairly pure form. No further progress was made for another twenty-five years, and then in 1894 Oliver and Schafer began their injection experiments. These established many of the properties of the active principle obtained, and found that it was confined to the medulla. From this on efforts were directed towards improving the methods of extraction of the substance, and its purification, until in 1901 Takamine prepared it in crystalline form and patented it as "adrenalin." In 1904 its formula was worked out by Jowett, and a method of preparation by synthesis was discovered by Stolz in Germany.

Adrenalin does not form the only internal secretion of the suprarenal glands. So far back as 1856 Brown-Sequard had discovered that it would not keep alive animals whose suprarenals had been removed, and the majority of physiologists are now coming to the conclusion that it is not even an important factor in the maintenance of normal blood-pressure.

Attempts have been made by numerous investigators for many years to isolate a hormone from the cortex. Until it was demonstrated that it was the secretion of the cortex and not of the medulla which was essential to life, no criterion of the efficacy of the various preparations had been established, but when this was recognized it became possible to judge potency by the increase in time of survival brought about in animals which had had bilateral adrenalectomy. In 1927 Rogoff and Stewart, and Hartman and his co-workers were able by the administration of extracts to keep adrenalectomized cats alive for thirty-two and one hundred and seventy days respectively. Without aid they will live only seven or eight days after the operation. Later Swingle and Piffner with a more potent extract were able not only to keep such animals alive indefinitely, but also to revive them from a moribund condition. All of these extracts were found to be of value in Addison's disease, but their impurity was a barrier to their use. Since then work has gone on and increasing purity attained, but a difficulty has been the small amount of material which the

glands provide and the expense of the method of extraction; so much is this the case that in the opinion of Kendall and others working at the Mayo Clinic, "no method of extraction from the gland will solve the financial aspect of the problem." These workers therefore set out to prepare the hormone in pure form, to determine its formula and structure and to produce it synthetically. In three years they have been able to carry out the first two parts of their programme, and synthesis is now the only remaining objective.

Pituitary Gland.

When Marie first called attention to the relation between acromegaly and disease of the pituitary in 1886, interest in that gland was greatly stimulated. Horsley in the same year endeavoured to remove the gland, hoping thus to reproduce the disease. His technique was faulty, and it was not until Paulesco developed a new route of access in 1907 that it was definitely proved that death invariably followed removal of the whole gland and that the part absolutely essential to life was the anterior lobe. In 1909 Harvey Cushing published the results of his investigations, and added much to our knowledge of the various functions of the gland and its lobes. In his work on the pituitary, Cushing exemplifies that combination of savant and surgeon whose rarity he has himself deplored.

Various feeding experiments with whole pituitary gland and with anterior and posterior lobes have been carried out by Schafer and others, with very irregular and contradictory results. Evans and Long in California have prepared an extract from the anterior lobe which, injected into rats intraperitoneally, produced enormous animals, some of them twice as big as the normal controls.

It has been held for a considerable period that ovarian activity is regulated by some extrinsic controlling mechanism. Brilliant researches led to this mechanism being brought home to the anterior lobe of the pituitary and hormones produced by it.

Evans, in his experiments in 1924, found that in addition to the increase in growth, the œstrous cycle ceased in the animals into which anterior lobe extract was injected. Much to his surprise, he found that when these animals were killed their ovaries were simply full of corpora lutea. Smith and Engle and Zondek and Ascheim in 1924 were able by implantation of anterior pituitary tissue into immature female mice to produce all the changes of the œstrous cycle. Thus it was evident that as well as a growth factor there were two separate sex hormones secreted by the anterior pituitary—a luteinizing hormone and an œstrous-producing hormone. Attempts have been made to separate these two hormones from the pituitary gland and prepare them in purity, as yet without complete success.

The centre of interest was shifted from the gland itself by Zondek and Ascheim in 1928, when they discovered that the urine of pregnant women contains substances with closely similar action on the ovary. They have named these prolan A and B, and have carried out a huge amount of work in connection with them. While they have not as yet been prepared in pure form, this goal is being rapidly approached, and it is already possible to make a guess at their chemical composition.

Recently some doubt has been cast on there being two separate substances A and

B, and it is possibly true that results obtained are really only different manifestations of one substance.

Another question engaging attention is whether prolan is really elaborated in the pituitary or whether it is not a substance closely similar to the pituitary secretion but produced in the placenta.

A side-result of this work has been the well-known Zondek-Ascheim test for pregnancy, the urine of the woman in question being injected into mice, or, in the Friedman modification, rabbits, and examination being later made for the typical changes in the ovaries.

To sum up, the anterior pituitary secretes at least two hormones—(1) a growth-promoting, and (2) a gonad-stimulating, which controls the cycle and function of the ovary and stimulates it to produce œstrin, the œstrin in turn producing the secondary sexual characters and œstrus. Van Dyke has produced concentrated extracts of these. The first he has named "Phyone" (from the Greek 'phyo'—I cause to grow) and the second "Hebin" (from the Greek 'hebe'—puberty).

The posterior lobe did not excite curiosity until a good deal of work had already been done on the anterior, but in 1895 Oliver and Schafer published an account of injecting extracts. They demonstrated the pressor effect which has since been so amply confirmed, but it was left to Dale in 1906 to discover the action on the uterus. This must be ranked amongst the most important observations in the investigation of the secretion of endocrine glands, since, in addition to introducing pituitrin into clinical medicine and surgery, it provided a basis for a method of assay. Since then a good deal of investigation has been done in trying to determine what the exact nature of this pituitrin is. It is pretty certainly not a single chemical entity. The most recent work has been done in America by Kamm and his associates. They consider that there are two active principles—pressor and oxytocic. From two hundred beef pituitaries they isolated 0.5 grms. of the purified pressor principle and 0.15 grms. of purified oxytocic principle. Both of these they considered to be substantially pure. The pressor principle has been named beta-hypophamine, vasopressin or pitressin, and the oxytocic principle alpha-hypophamine, oxytocin or pitocin.

The pressor principle is responsible for the anti-diuretic action of pituitary extract, while oxytocin has no such effect. It acts only on the uterus. These two bodies, while they are very closely related and almost indistinguishable chemically, have very different pharmacological actions.

Raab has found that the administration of large subcutaneous or small intraventricular doses of posterior pituitary extract (pituitirin) decreases the amount of neutral fat present in the blood, and as a result of experiment he has come to the concluson that this is by promoting the absorption and destruction of circulating fat in the liver. The stimulus which brings this about seems to originate by the action of pituitirin on the tuber cinereum, and to travel to the liver by a nervous path via the cervical cord and abdominal splanchnics. If these conclusions be correct, we have a ready explanation of Frohlich's syndrome and similar conditions where obesity is a prominent feature, and of the fact that cerebral lesions in the

region of the pituitary, though not affecting the gland itself, may produce the syndrome.

Parathyroid Glands.

It is only recently that attempts to isolate the secretion of the parathyroid glands have met with any success. They were at first thought to be accessory thyroids, and the difficulty of separating them from the larger gland has given rise to much confusion.

Koch in 1913 and Noel Paton in 1916 showed that parthyroidectomy gave rise to a great increase of guanadine in the urine and blood, and it is still thought by some that the secretion of these glands has an important action in the rendering harmless of certain toxic substances as well as controlling calcium metabolism.

Vassale, an Italian, in 1905 obtained an extract which he named 'parathyroidon,' but little is known of its properties. For a considerable time a commercial extract of the gland has been sold and used therapeutically in many ways—to control tetany, to cure chilblains, to increase the action of insulin in diabetes, and some years ago it had a great vogue in the cure of varicose ulcers. This extract is now known to be valueless, and the beneficial results claimed merely exemplify the danger of uncontrolled clinical optimism.

What seems to be the real hormone of the gland was discovered by Collip in 1924, and named by him "Parathormone." It can be used subcutaneously or intravenously, and is effective in keeping parathyroidectomized animals alive. As it is destroyed by incubating with pepsin or trypsin, it is inactive when administered orally. The blood calcium in the normal animal can be raised by more than one hundred per cent. by its frequent parenteral administration, and death from hypercalcæmia may result. Collip concludes that it affords a complete replacement therapy, and there can be very little doubt that he has succeeded in obtaining a very potent extract which contains the active principle of the parathyroid glands. It has not, however, been possible to prepare it in the pure state.

In clinical medicine it has application in the treatment of infantile tetany, in which it was first used successfully by Hoag and Rivkin in 1925, and in cases where some of the parathyroid tissue has been removed accidentally in the operation of partial thyroidectomy.

The Ovaries.

The connection of the ovary with sexual characters had long been recognized, and the results of spaying animals was well known, but treatment by ovarian tissue and extracts has only been tried in the last quarter of a century. That it played a part in the carrying on of the œstrus cycle was proved by Knauer in 1900, when he discovered that ovarian grafts could produce this phenomenon in spayed animals. At that same time Landau began to administer dried ovarian tissue by mouth in the treatment of the syndrome characteristic of the climacteric, whether natural or artificial. Mainzer in 1903 reported a number of cases in which symptoms following on ovariectomy had been to a large extent relieved by the administration of tablets

prepared by drying minced pig and cow ovaries at a temperature of 60° C. for twelve hours. In one case the benefits were so extraordinary that Mainzer was sceptical, and substituted, without the patient's knowledge, scraped meat. The symptoms immediately reappeared, but were again dispelled by a return to the dried ovarian tissue.

It was only in 1912 that any controls by the use of these substances on spayed animals were carried out. Adler at that time published results of a series of experiments, in which he had been able to produce typical œstrus by the injections of a watery extract of whole ovary. In 1915 Hermann and Frankel took out a patent for a method of preparing a hormone from ovaries or from placenta, with which they were able to produce premature sexual maturity and œstrus out of the rutting season. This work, carried out between 1912 and 1915, seems to have been forgotten, although the substance prepared appears to be identical with that produced more recently, for example, by Doisy and Allen in 1923.

As absence of any easy method of determination of blood-sugar values impeded for long the extraction and purification of insulin, so the absence of any simple and accurate test for the potency of ovarian extracts did much to hold up the separation of the hormone. In 1923 Doisy and Allen evolved a reliable method based on the observation made by Stockard and Papanicolaou on the changes which take place in the cells seen in the vaginal smears of small mammals during œstrus. By injecting extracts into ovariectomized rats and examing vaginal smears from them at regular intervals, it was possible to assess the potency of the preparations by their power of producing changes similar to those found in normal œstrus. The amount which could produce œstrus in a spayed rat was termed a rat unit.

The hormone was given the name "Œstrin," and it was soon prepared in highly potent form.

A very important step was the discovery in 1927 by Ascheim and Zondek, and by Margaret Smith, that œstrin was excreted in large quantities in the urine during pregnancy. As full term is approached, as much as one hundred thousand mouse units per day may be present. This provided a convenient and cheap source for the preparation of large amounts for use in investigation.

Recent work by Butenandt and others has shown that œstrin is composed of several substances very closely related and having similar properties. The formulæ of some of them have been determined, and one of them has a potency of forty million mouse units per grm. They are chemically closely related to cholesterol, as is also vitamin D, and it is interesting to note that the injection of vitamin D in fairly large quantities is capable of producing œstrus.

A recent paper by Schoeller has shown that by hydrogenation of œstrin a substance is produced which, when injected, promotes the growth of combs in capons—in other words, its action becomes that of the male sex hormone, which may thus be a hydrogenated derivative of the female sex hormone.

Up to the moment the actual compounds which form œstrin have not been synthesized, but Cook and Dodds have prepared a substance similar to œstrin in constitution and having a powerful œstrus-producing action.

Œstrin does not account for many of the processes connected with pregnancy and the period during which the corpus luteum is active—for example, the full development of the endometrium. In 1929 Corner and Allen prepared a lipoid extract of the corpus luteum which they named "Progestin," and which produced a proliferation of endometrium similar to that obtained in pregnancy. They showed, too, that it is a vital factor in the maintenance of this state. The removal of the ovaries of rabbits, if carried out early in pregnancy, invariably ends gestation, but if subsequent to the operation this extract of corpus luteum be injected daily, pregnancy continues normally.

It is probable that progestin is really composed of two separate hormones, one producing the progestional proliferation and the other inhibiting the pituitirin reaction. It also inhibits ovulation and œstrus changes, and there is some evidence to show that there is a third hormone, "Relaxin," which brings about relaxation of the pelvic ligaments.

Not much is known about the male sex hormone. Koch and his associates have elaborated from the testes a hormone which can bring about the growth of the comb in capons and enlargement of the seminal vesicles and sexual organs in male castrate animals. It has been obtained in crystalline form by Butenandt, and its presence has been demonstrated in the urine of adult men, though the amount is very small. As has been stated, Schoeller and his collaborators have shown that it can also be prepared by the hydrogenation of œstrin, but again the amount has been minute, and it has been impossible to investigate it fully, largely on that account.

Renal Function.

Biochemistry has revealed the errors of trying to classify nephritis on the basis of morbid anatomy, but it has not itself up to the present replaced the old by any very satisfactory new scheme. Until recently, attention was focussed on what the kidney allows unduly to escape, but biochemistry has gradually brought us to recognize that what it fails to excrete is of much greater importance. Ludwig in 1853 introduced a method for the quantitative estimation of urea in urine, and, subsequently, one more applicable clinically was evolved by Doremus, but for some time the results were misinterpreted. This was largely because it was not realized that the amount of urea in the urine was partly dependent on the protein intake. The discovery that food proteins were disintegrated into amino acids, which were largely converted to urea by the liver, drew attention to this point, and it was soon realized that to form an opinion of the efficiency of the kidneys it was important to know the amount of urea in blood as well as in urine. This determination was first made by Widal and Javal in 1905. The method most generally used nowadays was evolved by Marshall in 1913, and modified by Van Slyke and Cullen in 1914 and by Maclean in 1917.

In 1914 Ambard, after considerable experiment, formulated his laws of renal secretion and based a mathematical co-efficient on them. Unfortunately, experience has not borne out his claims of its utility. Such an eminent authority as Folin considers the co-efficient to be unreliable, and Addis and Watanable, as a result of their

experiments, found that urea excretion depends on factors other than its concentration in the blood and urine—a contradiction of one of the postulated laws on which Ambard's formula is based.

Recently, Van Slyke has evolved a much more reasonable formula for kidney efficiency which depends on the volume of urine excreted in addition to the concentration of urea in the blood and urine. It really amounts to a determination of the volume of blood cleared of urea in a unit of time, and although care is requisite in its performance, it seems to give good results and to be worth carrying out.

The non-protein nitrogen in the blood was extensively investigated by Folin, and his adaptation of the Kjeldahl method, published in 1912, is now generally used for the determination. He came to the conclusion that the test is of great value, and the correctness of his opinion has constantly been proved ever since. The technique of the method is a little tedious when large numbers of examinations have to be carried through, and where assistance is limited it has been largely displaced by determinations of the blood-urea. The values obtained generally run closely parallel, and there is little to choose between them in practice.

In 1915 Myers and Lough drew attention to the great prognostic value of the creatinin in the blood. Creatinin is the easiest of the end-products of protein metabolism for the kidneys to excrete, and no retention of it takes place until a very severe degree of kidney inefficiency is present. Myers and Lough showed that when the creatinin in the blood, which normally has a maximum value of about 2 m.g. per cent., rises to 5 mg. per cent. or over, a fatal termination is certain to result. Many observers have confirmed their finding, and the only exception seems to be when the rise has been caused by some acute condition which will ameliorate or be capable of relief, e.g., as in acute suppression or retention of urine, in acute nephritis, and in prostatic obstruction.

The urea concentration test introduced by Maclean and de Wesselow just after the war, and Calvert's range modification of it, were distinct steps of advance. They aim at estimation of the reserve power of the kidneys, and are especially valuable in giving some idea of what the kindeys will be able to face in the way of a temporary emergency, such as an anæsthetic and operation. Used intelligently, Calvert's method is often of the greatest assistance, and may pick out a really bad risk which would be accepted by other tests.

Surgeons especially have placed reliance on dye excretion tests. The use of indigocarmine was first suggested by Heidenhein, but the actual working modification was produced by Volcker and Joseph in 1903. In it the ureters are catheterized and the dye injected, the time of appearance of the dye being noted for each kidney. The interval should not be more than about eight minutes. This method is of more value for comparing the relative efficiency of the two kidneys than for arriving at any opinion as to absolute renal efficiency. In 1910 Rowntree and Geraghty described the use of phenolsulphophthalein as the dye. This test had a considerable vogue, but there are several grave objections to it, and it is now rarely used.

Another method of determining the renal efficiency which has fallen into disuse is that of cryoscopy, which was first utilized by Koranyi. The freezing-point of a

liquid depends on the number of molecules present, it being lowered when the number is increased. Therefore in kidney disease the freezing-point of the blood falls. Of more practical importance is the cryoscopy of the urine, especially in comparison of specimens taken from the two kidneys at the same time. If the urine from one kidney has a lower freezing-point it means that more molecules are present, and therefore that that kidney is more efficient.

Efforts have been made at estimating renal function by examination of urine excreted at short intervals after a standard meal. As a rule the urine is passed at two-hourly intervals, and variations in the volume, specific gravity, urea- and salt-content, and their absolute values, are the bases on which an opinion is formed. This method was introduced by Mosenthal in 1915, and has been used in America with much success, but has not become popular in this country.

Recently, owing to the writings of Epstein, a great deal of attention has been paid to cholesterol in the blood of nephritics. In 1905 Muller in Germany first differentiated a group of cases, which one might have classed as parenchymatous or hydræmic nephritics, and named it 'lipoid nephrosis,' laying stress on the idea of degeneration in contra-distinction to inflammation. Epstein diagnoses these cases and evaluates the treatment of them by determination of the blood cholesterol. Cholesterol has, of course, been investigated by various observers from about 1914 onwards, and admittedly it is raised in many other conditions—for example, diabetes and gall-stones. These can, however, generally be excluded on clinical examination, and there is no doubt of the value of the determination in this particular type of the disease.

Another blood-test sometimes carried out in nephrosis is the estimation of the albumen globulin ratio. In normal subjects the albumen is about three times the globulin, while in this condition it may fall to one and a half : at the same time the total protein may also fall by about fifty per cent. Unfortunately, these determinations are rather tedious, and cannot be undertaken in a very large number of cases.

Epstein holds that the œdema which is such a prominent feature is caused by the excretion of protein in the urine, thus robbing the blood of its normal indiffusible colloids, with a consequent reduction in its osmotic pressure. Experiment actually demonstrates that this reduction in osmotic pressure takes place and is very characteristic. This allows fluid to pass from the blood into the tissues, being thus a factor in the production of œdema. A high protein diet restores the blood proteins, thus increasing the osmotic pressure and drawing fluid from the tissues. The increased excretion of urea may also act as a diuretic and increase the urinary output.

The fall in osmotic pressure is not, however, the whole explanation, even supposing it may be part. There is no constant relation between the reduction of osmotic pressure in the blood and the degree of œdema. Epstein then called in another factor—the hypercholesterolæmia. Hypercholesterolæmia occurs, however, in other diseases of which œdema is not a feature. The most usually accepted view of renal dropsy now is that there is an alteration of the affinity of the cells for water

as a result of an altered metabolism. This again is simply trying to cover up our ignorance with words.

Widal believed that the œdema was consequent on the salt retention, and that it was a case of physical cause and effect. Izod Bennet put forward evidence in 1928, however, which makes it appear likely that salt retention is the result instead of the cause of the œdema.

In this type of case, although chloride is generally retained among other salts and the total body chloride is increased, its percentage in the blood does not alter much owing to the parallel retention of water. It is in the urinary output that the chloride retention may be detected, and the estimation of the twenty-four-hour excretion is often of considerable value.

Gradually, biochemistry has thrown light on the different types of failure of renal function, and a separation of certain groups has taken place. While it does not appear likely that the disease may be divisible into clear-cut varieties, it is possible that a satisfactory general classification may yet be arrived at.

The pigments of the body and their relationships have had a considerable influence on medicine. Hæmoglobin, the most important, has been fully investigated by Hoppe-Seyler. He was able to prepare it in crystalline form in 1860, thereby driving another nail in the coffin of vitalism. His work has led to the methods for its estimation, in this way initiating part of the investigation of anæmias.

Hoppe-Seyler believed bilirubin was one and the same thing as the hæmotoidin of old blood-clots, which Virchow had described twenty years previously. From this originated a long controversy about hepatogenous and hæmatogenous jaundice. At one stage it was fairly generally accepted that "all cases of jaundice are due to the re-absorption of bile already formed in, and by, the liver."

Just at this time came the clinical recognition of acholuric jaundice, and threw the whole question back into the melting-pot. It was ultimately answered in 1921, when van den Bergh, who had applied Ehrlich's diazo test to the examination of the bile pigments which are present in the blood, produced proof of the reality of a purely hæmolytic jaundice, and this work forms an integral part of our modern conception. By the help of van den Bergh's test we can now distinguish clearly between hæmatogenous and hepatogenous jaundice, and separate hepatogenous into the early obstructive type and that caused by hepatitis. A side-result of the greatest importance has been the differentiation of any active primary anæmia in which there is blood destruction, from any secondary type in which there is only failure of blood production. The van den Bergh reaction, for this reason, forms one of the most valuable tests in the examination of any case of anæmia.

Pernicious anæmia has provided a further field for the chemist and biochemist. About A.D. 150 Galen propounded the hypothesis that the liver was the organ of "sanguification," converting chyle into blood, and so it has turned out to be. In 1925 Whipple and Robscheit-Robbins, by experiments on dogs, found that fresh liver contains some principle which exerts a profound influence on promoting blood regeneration. Also, pernicious anæmia in many of its symptoms resembles beri beri, sprue, and pellagra, which are associated with faulty diet, and treatment with liver

soup had been found to be very beneficial in sprue. These observations led Minot and Murphy to treat cases of pernicious anæmia with a generous diet rich in liver, and out of this has grown the present specific liver treatment. In 1927 Cohn, Minot, and their associates separated from liver a fraction "G," which was effective in the treatment of the disease. Sufficient of the impurities have been got rid of to allow of its use intramuscularly or intravenously, but no one has yet isolated it in completely pure form or been able to determine its exact nature. Doubtless we shall sooner or later see both these facts accomplished and the substance synthesized. The factor is also present in the gastric mucosa, and it is probably elaborated there and stored in the liver.

This discovery of the use of liver in the treatment of pernicious anæmia may be classed with insulin in diabetes as one of the two greatest recent medical discoveries. Both diseases have frequent incidence and bad prognosis, and in neither were older methods of treatment of much avail. Although we are still unable to cure either in the sense that the disease is done away with, yet the sufferers can be kept fit and well, free from symptoms, and useful members of the community.

Vitamins.

There are elements in our food which, though small in bulk, are large in importance. This lack of proportion between size and function and the very small amounts consequently necessary are features characteristic of the vitamins. Despite the small amounts in which they occur, they are without any doubt definite entities, and much is now known of their actual chemical nature. At least one has been artificially prepared. Continued investigation has also revealed new ones from time to time. Eight years ago three only were known, while now eight are recognized. Except for one, they are only formed by green plants either on land or sea, and the animal is dependent on the vegetable kingdom for their supply.

In 1881 Lunin, as the result of feeding experiments on mice, stated that "a natural food such as milk contains, besides the known principal ingredients, small quantities of unknown substances essential to life." This finding remained for years unnoticed.

In 1897, Christian Eijkman, a military doctor in the Dutch Indies, came to the conclusion that the disease beri beri arose from the continued consumption of polished rice, and found that birds fed on this food developed a polyneuritis very similar to human beri beri. Ten years later Hopkins found that young animals fed on purified protein, fat, and carbohydrate diets failed to grow, and in the same year two Norwegians, Holst and Frolich, showed that typical scurvy could be produced in guinea-pigs by deficient diets, and cured when the deficiencies were made good.

Stepp, in the years 1909-12, investigated the question of the necessity for fats and lipoids in the dietary, and concluded: "It is not impossible that unknown substances indispensable for life go into solution with the lipoids, and that the latter thereby become what may be termed carriers for these substances."

Funk, in 1912, first used the term "vitamine." He spelt it ending with an 'e.' The importance of the substances to life is indicated by the prefix 'vita': the ending 'amine' suggests that they are of the nature of organic bases. There is no proof

that any of them has this composition, and it is now known that some of them do not even contain nitrogen. By dropping the 'e' the unjustifiable implication is avoided, and the name "vitamin" is now accepted.

It was originally thought that A was the only fat soluble vitamin, but evidence gradually accumulated that there was a second or anti-rachitic fat soluble factor—vitamin D.

Many attempts have been made to prepare vitamin A in pure form, but although very potent preparations have been produced, the actual substance has not yet been isolated. The strength of these preparations is determined colorimetrically. With arsenic trichloride and antimony trichloride a deep prussian blue colour is developed in proportion to the amount of the vitamin A present.

In the last fifteen years a great deal of attention has been paid to carotene, the orange pigment in carrots, tomatoes, and other vegetables and fruits. There seems to be little doubt that it is converted directly into vitamin A *in vivo*, possibly in the liver, by an enzyme which has been provisionally called carotenase.

Fairly definite evidence of the existence of the anti-rachitic factor was produced by Mellanby in the results of feeding experiments lasting from 1918 till 1921. He recognized rickets as a deficiency disease, and demonstrated that it could be produced in puppies by diets deficient in this substance. Many clinicians held, however, that rickets was caused by bad environment—unhygienic surroundings, lack of exercise and fresh air. Among these were some of the Glasgow school, in which city rickets was exceedingly common. A long and interesting controversy raged between the upholders of these opposite views, and eventually both were proved to be more or less right. It was first noticed that patients could be cured of rickets by light rays, and then, that if food which would bring about rickets in puppies fed on it was first exposed to the light of a mercury vapour-lamp, rickets did not develop. By patient investigation the preventative action was first brought down to the changes produced by the rays on the fats present, and then to the cholesterol of the fats, this last being discovered by three groups of observers simultaneously and independently. Certain of the results were rather unexplainable on the basis that the irradiated cholesterol was the anti-rachitic factor, but for a long time no further discovery was made. At length it was found that a special and complicated method of purification of the cholesterol did away with its anti-rachitic properties and a further irradiation did not renew them. Spectroscopic investigation was then made, and it was discovered that this purification had removed two faint absorption bands present in the original cholesterol. It was also found that by fractional crystallization of the original cholesterol the bands could be deepened. It was then realized that the original cholesterol had contained a minute amount of an impurity—pro-vitamin D. Some earlier work on ergosterol, a sterol of the fungi obtained from ergot of rye or from yeast, was then recollected, and its identification with this pro-vitamin D was simultaneously announced in 1927 by Rosenhein and Webster in England and by Windhaus and Ness in Germany. Vitamin D prepared by the irradiation of ergosterol is immensely powerful—one ten-thousandth of a milligram daily protecting a rat against rickets.

The results given by these laboratory experiments on animals were completely borne out by clinical experience, and allowed of a reconciliation between the dietetic and environmental views of the causation of rickets. The calcification of bone is influenced by both diet and sunshine : diet does so by virtue of its content of vitamin D, while sunshine produces vitamin D in the skin from ergosterol. Many observations which previously could not be co-ordinated are thus now seen to be consistent, and to this end clinical observation, animal experimentation, chemistry, and spectroscopy have all combined.

In 1915 McCollum and Davis reported that young rats fed on a purified synthetic diet, to which the fat soluble vitamins A and D had been added, required for normal growth an additional factor which they named water soluble B. This water soluble B was thought to be identical with the antineuritic vitamin discovered by Eijkman in 1897, but it was presently shown that some foods potent in the prevention and cure of the polyneuritis developing in birds living on polished rice were incapable of maintaining their weight and growth. Differences in heat stability, distribution in nature, and solubility in alcohol made possible the separation of the vitamin B complex into B1 and B2. Further work has proved that there are several other components in the complex—B3, B4, B5, and Y. All of these are necessary for growth and health in various animals and birds, and all are contained in fresh yeast.

Vitamin B1 has been prepared in pure form, first by Jansen and Donath in Eijkman's laboratory in 1926. One five-hundredth of a milligram of the crystalline substance given daily is sufficient to protect a pigeon fed on polished rice from polyneuritis. A provisional linear formula—$C_6H_{10}ON_2$—has been assigned to it.

None of the other members of the B complex have been isolated, but very potent preparations have been produced, and it is probably only a question of time.

So far back as 1734, Bachstrom wrote : "For want of proper attention to the history of the scurvy, its causes have been generally, though wrongfully, supposed to be cold in northern climates, sea air, the use of salt meats, etc., whereas this evil is solely owing to a total abstinence from fresh vegetable food and greens; this is alone the true primary cause of the disease."

In 1907 Holst and Frolich showed that if guinea-pigs were deprived of greenstuffs they developed scurvy, and that oats, barley, lentils, etc., in the dry condition, could not prevent it. It was, however, discovered by Furst in 1912 that if these were soaked in water and allowed to germinate they acquired potent anti-scurvy properties. Sometimes it would seem that there is nothing new under the sun, for in 1782 one Charles Curtis quoted a method of cure by "Mr. Young of the Navy" by means of "beans and pease and barley and other seeds brought under the malting or vegetating process and converted into the state of a growing plant with the vital principle in full activity, eaten in this state without any sort of preparation."

This anti-scorbutic factor has been named vitamin C. Although it has been prepared in very concentrated form, nothing which could lay any claim to being the pure substance has yet been produced.

That there is a specific vitamin which is essential for reproduction has only been realized for the last fifteen years. It was first drawn attention to in 1920 by Conklin, who noticed that rats reared on whole milk, though growing well and in good health, were usually sterile. It was found that this sterility was corrected by an unknown substance present in fresh lettuce leaves and wheat embryo. It was named vitamin E by Sure in 1925, and in 1931 was prepared in a pure form. It is quite possible that it may be found to play an important part in the treatment of cases of human sterility.

Immunology.

A question which has recently begun to attract the attention of biochemists is the chemical basis of the specificity of immunological reactions. There must undoubtedly be some chemical differences in the antigens which give rise to these reactions and in the antibodies which they produce. Take, for example, the serum of a rabbit previously inoculated with human serum. It reacts with human serum to a high dilution, but hardly at all to the serum of the ape, and not to that of any other mammal.

An amazingly high degree of specificity is shown by the antibodies produced by bacteria. If you examine the serum of a pneumonia patient you will find that it does not react to other organisms like typhoid or paratyphoid, but it will also fail to give a reaction with any other type of pneumococcus than that infecting the patient. Even the most optimistic biochemist might scarcely expect to find in chemistry the explanation of an infinity of such specific reactions, but recent research in this branch has produced such promising results that great advances have already been made. The future doubtless holds even greater discoveries. It is on pneumococci that most of the work has been done. In antigenic structure this organism consists of a nucleoprotein common to all pneumococci, and different carbohydrates which are type-specific. It has been possible to analyse the carbohydrates, though not as yet to determine their exact formulæ. They seem to be polysaccharides, however. A very interesting thing happened in the investigation of the type-specific carbohydrate of a Friedlander's bacillus isolated from a chance infection in a guinea-pig. Its chemical structure and physical properties were noticed to be remarkably similar to that of type II pneumococcus, and suggested to Heidelberger and Avery, who were working with it, the experiment of cross precipitation tests. Much to their surprise they found that the Friedlander substance gave a precipitate with anti-pneumococcus type II serum up to a dilution of one in two million, and also that an anti-serum prepared from this Friedlander bacillus gave a precipitate with pneumococcus type II substance. On the other hand, no such reaction occurred with type I and type III pneumococci, which are chemically different. A development of this was that it was found that mice, which are extremely susceptible to infection with pneumococci, could be protected against type II by injection of anti-Friedlander serum just as well or even better than by anti-pneumococcus type II serum.

Laidlaw and Dudley have isolated from tubercle bacilli a specific carbohydrate analagous to those obtained from pneumococci, and recently Lancefield has done the same for a streptococcus viridans. Lancefield has also obtained from this

organism a relatively non-specific nucleoprotein similar to that obtained from the pneumococci, and which gives rise to an antibody which reacts wth nucleoprotein of related species. It is likely that these two types of substances, a non-specific nucleoprotein and a highly specific carbohydrate, constitute the antigenic mosaic of most organisms. There is a considerable amount of evidence to show that these peculiar carbohydrates are the real fundamentals in immunological reactions and are the elements which determine their specificity. As Pryde remarks, "That nature should have selected carbohydrates for this rôle is perhaps not surprising when we bear in mind the numerous possible ways in which two simple sugar molecules may be linked together, each one distinct from the others. Thus there are at least twenty-eight ways in which two molecules of D-glucose may combine with each other. If you take, say, twelve molecules of glucose and combine them in every possible way, the number of carbohydrates which would be formed would be somewhere about one million million million. When we consider the possibilities offered by two or more different sugars, the number becomes an infinity."

Chemotherapy.

In chemotherapy the biochemist and pharmacologist have collaborated in the attempt to produce antiseptic substances which, when introduced into the blood-stream, may destroy infecting organisms. The danger is that they may at the same time destroy the host, and the investigations have resolved themselves into finding substances which have a selective toxicity for the organisms concerned. Research in the subject had its beginnings in observations by Ehrlich in 1890, while working on the selective staining action of organic dyestuffs on certain bacteria. At the beginning a great variety of substances was used, but most of them were found to be either innocuous to the infecting organism or too toxic to the host, and their use discontinued. Many discoveries have been made, however, so that we have now synthetic compounds almost specific for several diseases previously hopelessly intractable. For example, in syphilis, salvarsan, discovered by Ehrlich in 1912; in sleepy sickness, "Bayer 205" and "Fourneau 309" (which are probably one and the same thing), tryparsamide, and salvarsan; in amœbic dysentery, emetine.

The interesting thing is that these drugs, while very toxic to their respective organisms *in vivo*, are almost or altogether non-toxic *in vitro*. Conversely, substances very toxic in the test-tube may be quite inert when injected. The exact mechanism of their action is not so simple as had at first been supposed by Ehrlich, and for some time very ingenious experiments have been going on in attempts to elucidate the matter. Some fascinatingly interesting facts have come to light in their course.

It is in protozoal diseases that chemotherapy has yielded most striking results, and the search for chemical substances specifically toxic to pathogenic bacteria has not been so fruitful. Optochin, an artificial cinchona derivative first used by Morgenroth in 1911 in conjunction with specific anti-pneumococcal serum, is said to give results much better than would be obtained by summation of their two individual effects. In tuberculosis, sanocrysin, a gold-salt introduced by Mollgaard in 1924, undoubtedly has a specific action on tissues infected by tubercle bacilli,

and the general opinion seems to be that it has a definite curative action on the disease.

Various drugs like acriflavine and mercurochrome have been used in cases of septicæmia, and occasional miraculous cures reported, but it is doubtful whether these have not been examples of *post hoc propter hoc*. We seem to be making progress, however, and although we have not as yet attained Ehrlich's ideal—*therapia sterilisans magna*, more and more potent remedies are being produced. As yet we have no knowledge of how these internal antiseptics really act, and when we once begin to discover this mechanism we may expect much more rapid advance. The first streaks of dawn will have begun to shine in the darkness through which we now grope.

Although a great deal has been done in attempts to solve certain questions, the answers have not yet been given; for example, the composition of insulin and other endocrine secretions, and of some of the vitamins and how they may be produced synthetically. In problems of this kind the solution often evades one, and endless work is done finding out little odds and ends. Ultimately some one makes a lucky discovery and releases a flood of light. In the growth of every science there are periods, sometimes very long periods, when there is no forward movement. Then comes suddenly a discovery opening up a new point of view, followed, it may be, by an advance which completely changes existing beliefs, and progress becomes the order of the day, each step forward paving the way for yet another. One such discovery which stands out as a landmark is Wohler's production of urea—an organic substance from inorganic material. This epoch-making discovery did away with the prevalent belief in the existence of a vital force as a necessity for the production of substances which enter into the structure of living organisms. This was the beginning. Synthesis has gone steadily forward, and the chemical structures of organic substances of the greatest complexity have been made clear, though many still remain to be revealed. But the mysterious so-called vital force has been eliminated, and there seems to be no obstacle to the ultimate discovery of the chemical structure of any and every organic substance that plays a part in the process of life. In this way it may be possible one day to answer the question of what life really is. The outworks of that problem have already been reached.

Life is like a star. At first sight a star is just a curious fact. Then by means of the telescope we discover that it is a body with inequalities and irregularities of surface—its physical features; later by the spectroscope we determine the different elements composing it; by mathematical calculations we answer many abstruse questions regarding it. Ultimately we may find out what it really is.

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dential address (published elsewhere in this number of the Journal), thanked Professor Wilson for the capable and dignified manner in which he had filled the chair during the last session. "We owe him," he said, "our best thanks also for his generous hospitality on various occasions here and at Donaghadee, where many of us spent a most enjoyable day. I am sure you will allow me to include in our thanks Mrs. Wilson and the members of their musical family, who helped to make his 'At Home' such a wonderful success. It gives me the greatest possible pleasure to propose this vote of thanks."

Dr. Hunter then referred in the following terms to the loss the Society had sustained during the past session in the deaths of four of its Fellows.

On 11th December, 1933, this Society lost one of its most distinguished as well as one of its warmest supporters by the lamented death of Sir William Whitla. It was due to his great kindness and bountiful generosity that this building was erected, equipped, and presented to the Ulster Medical Society for its permanent home, and by his last wish he made it possible for this Society to reside here practically rent free. To mark their appreciation of these great gifts, your Council decided to honour and perpetuate his memory by calling this handsome building the "Whitla Medical Institute." In addition to these deeds of generous benefaction, Sir William will always be remembered as the author of two books which made his name famous in medical circles throughout the world. Edition after edition of his "Materia Medica" and his "Dictionary of Treatment" were printed, as they seemed to fill a long-felt want among practitioners, medical students, and dispensing chemists. His third medical book was a "Dictionary of Medicine," in two volumes, a copy of which he presented to every member who attended the B.M.A. meeting held in Belfast in 1909, of which he was that year the worthy president. To the older members Sir William was a remarkable and fascinating personality. Many will readily remember his distinguished professional appearance as he drove through the streets of the city in an open victoria, behind a pair of high-stepping, fast-trotting bays, wearing a silk hat and a startling red tie. As long as his health permitted he was a regular attender at our meetings, an active member in its deliberations, and was remarkable for his wisdom and shrewdness. Twice he was honoured by being elected president, first in 1886-7 and again in 1901-2, and he was also made an Honorary Fellow. Sir William was really a great man of wonderful vision, who never did anything mean, or ever looked for praise or renown. As is well known, he was deeply religious, and took the keenest interest in and was a generous supporter of many philanthropic movements. Widely travelled and highly cultured, he was a charming companion to his intimate friends. His ability as a clinical teacher and his wide knowledge of all the latest methods of medical treatment made him a worthy successor to the famous James Cuming, the distinguished professor and teacher of clinical medicine in the old Royal Hospital. In conclusion, to quote from the words of an old friend of his—"a great man," a very great man has gone to his long rest, a rest for which he earnestly desired, and for which he patiently waited. William Whitla has not lived in vain.

The news of the death of Andrew Fullerton on the 22nd May of this year was

received with deep regret and sorrow, and filled all our hearts with the sense of irreparable loss. His death deprived this Society of one who was a regular attender at its meetings, who took the keenest interest in its management and was always ready to take part with kindly criticism on any subject in debate. A member since 1896, he filled the office of president in 1919-20. Ten years later he delivered the fourth Campbell Oration, taking as his subject, "The Progress of Urology," a line of research and work which had won for him an international reputation.

Andrew Fullerton had a most persevering spirit, which enabled him to overcome the uphill work of his earlier career and in his later years to surmount his indifferent health.

For thirty years he held appointments on the surgical staffs of the Belfast Hospital for Sick Children and the Royal Victoria Hospital, serving these institutions with unwearying energy and skill, gaining for himself the affection of his colleagues and the unshakeable confidence of all who knew him. In spite of large private and hospital practice he found time to write some seventy-seven papers on the surgery of the urinary tract. His brilliant work on this subject made his name famous, and numerous distinctions were conferred on him. In 1922 he was elected an Honorary Fellow of the American College of Surgeons. In 1924 he succeeded Professor Sinclair in the Chair of Surgery in Queen's University, but perhaps none gave him greater pleasure than his election as president of the Royal College of Surgeons in Ireland, being the first surgeon resident outside Dublin to hold this office, and in the following year he was re-elected. In 1915 he was invited to become a consulting surgeon to the British Expeditionary Force in France, with the rank of Colonel, and his record of service there not only confirmed the wisdom of this appointment, but brought a wider recognition of the Belfast School of Surgery. For his valuable service he was rewarded with the C.M.G. and the C.B., and was three times mentioned in despatches. His energy and his enthusiasm seemed to have endowed him with perpetual youth. His inherent simplicity and honesty rendered him incapable of guile. He had the gift of making friends, and with him friendship was lifelong. He was a keen golfer, and we were all delighted when the Royal County Down Club elected him captain last year. Very seldom was he absent from the annual golfing meeting of this Society. We shall certainly miss his cheery word and his winning personality, and it is no exaggeration to say that his name and work will long be remembered by his patients, students, and colleagues alike.

It was with surprise and regret that we learned of the death of Doctor John A. Milroy, the Professor of Biochemistry at Queen's University. A highly distinguished graduate of Edinburgh University, he came to Belfast in 1902 as lecturer of physiology; he then joined this Society and attended many of our meetings, taking a keen interest in its discussions. We were accustomed to hear him expounding his views rather shyly, it is true, but with a quiet assurance that won our heartiest admiration. Of a kindly and unassuming nature, he was held in the highest esteem and affection by all with whom he came in contact. His valuable scientific contributions to the various journals of biochemistry and of physiology were distinguished by the extreme care and accuracy with which they were written. His death leaves

a vacancy at Queen's and in scientific circles which will be difficult to fill, and this Society has lost a good friend whose modesty and charm will always remain a pleasing memory.

The death of Doctor James Hunter Gillespie as a result of a motor accident in England on the 25th February, 1934, removed from our membership a young man who, if he had been spared to have specialized in radiology in this city, as had been his intention, would no doubt have won fame and renown for his medical school. The son of a much esteemed Fellow of this Society, he received his early education at Campbell College, where he first showed that interest in electrical subjects which finally led him to choose radiology as a career. At Queen's University he proved himself a very brilliant student, winning many prizes and scholarships, and graduating with honours in 1930. Later, in 1933, he was awarded his B.Sc. with honours and his M.D. with gold medal for a thesis, much of the work for which had been carried out with the electrocardiograph and the Matthews oscillograph. He was working for his D.M.R.E. in London when the fatal accident occurred, and there is no doubt but that the promise of a brilliant future which his student days presaged would have been amply fulfilled.

To the relatives of these deceased members we tender our respectful sympathy.

The second meeting of the session was held on 1st November in theWhitla Medical Institute, Dr. S. R. Hunter, the president, in the chair. Dr. Eileen M. Hickey read a paper on "Medical and Surgical Practice in Belfast Fifty Years Ago." This paper is published elsewhere in this number of the Journal. A discussion was then raised on the question of inaugurating a Tuberculosis sub-section of the Society. This was proposed by Dr. Brooke, and seconded by Dr. Gillespie. The secretary, Dr. Montgomery, stated that the Council was ready to accept the sub-section if the members of the Society decided on its formation. A lively discussion ensued, in which Doctors McCollum, McNabb, Boyd Campbell, and Kean supported the motion, and Professor W. J. Wilson with Doctors Allen, Montgomery, and Clearkin in opposition. Several other members took part in the discussion, but it was not clear from their remarks whether they supported the motion or were in opposition to it. The motion was finally put to the Society and meeting, and it was rejected by a large majority.

The third meeting of the session was held on 15th November, with the president, Dr. S. R. Hunter, in the chair. Six short papers were read by Dr. S. B. Boyd Campbell, Mr. G. R. B. Purce and Dr. B. R. Clarke, Dr. J. T. Lewis, Dr. R. Marshall, Mr. J. S. Loughridge, and Dr. F. P. Montgomery. These papers appear elsewhere in this number of the Journal.

The fourth meeting of the session was held in the Whitla Medical Institute on 22nd November, the president, Dr. S. R. Hunter, in the chair. Professor J. Preston Maxwell, M.D., F.R.C.S.Eng., of the Union Medical College, Pekin, addressed the Society on the subject, "Thirty-Five Years' Medical Work in China." The thanks of the Society were expressed to Professor Maxwell by several members.

H. Hilton Stewart,
Hon. Editorial Secretary.

18 Malone Road, Belfast.

BRITISH MEDICAL ASSOCIATION
TYRONE DIVISION

A MEETING of the Tyrone Division, British Medical Association, was held in the Tyrone County Hospital, Omagh, on Thursday, 6th December, at 4.30 p.m.

Those present were: Doctors Leary (chairman), Eaton, Lagan, W. Lyle, L. A. Lyle, Gillespie, Murnaghan, Warnock, Chambers, Collins, Johnston, Ekin, O'Brian, and Martin (hon. secretary).

Dr. Eaton proposed that it be recorded in our minutes the high appreciation which the members of the medical profession, especially those of the Tyrone Division, held of our past chairman, the late Dr. McAllister, who took such an active part in our Divisional meetings. Dr. Murnaghan supported this, and it was passed in silence, all members standing.

Dr. Eaton proposed, and Dr. Murnaghan seconded, that Dr. W. Lyle be appointed our representative on the Representative Body.—Passed.

Dr. Eaton proposed, and Dr. Murnaghan seconded, that Dr. Leary be appointed our representative (deputy) on the Representative Body.—Passed.

The secretary was instructed to write the Fermanagh Division, and ask them to appoint a deputy representative on the Representative Body and notify head office of same.

Dr. Leary, on behalf of the Tyrone Division, extended a welcome to the two new members—Dr. Ekin and Dr. O'Brian.

Dr. Gillespie proposed, Dr. Martin seconded, and the motion was passed:—"That the following resolution be sent to the Ministry of Home Affairs: 'That a preparation of ipecachuana, preferably the tincture, be placed on the prescribed list of medicines.' "

Dr. Martin suggested that we hold four meetings during the coming year, and that each member be sent a fixture card. After some discussion the following dates of meetings were agreed upon:—

(1) 24th January, 1935, in Tyrone County Hospital, at 4.30 p.m.:
Special Lecture on Gynæcology by Dr. C. H. G. Macafee.

(2) 21st March, 1935, in Tyrone County Hospital, at 4.30 p.m.:
Annual General Meeting; Election of Office-bearers.

(3) 30th May, 1935, in the Tyrone and Fermanagh Mental Hospital, at 4.30 p.m.

(4) 18th October, 1935, in Tyrone County Hospital, at 4.30 p.m.:
Special Lecture on Common Bone Diseases by Ian Fraser, F.R.C.S.Eng.

Dr. Gillespie proposed and Dr. Warnock seconded the following resolution:—"That we, the Tyrone Division of the B.M.A., call again the attention of the Council of the Belfast Branch to the very inadequate fee for certifying persons of unsound mind, and to the fact that no fee can be paid if the doctor cannot satisfy himself that the patient is certifiable." The secretary was instructed to forward a copy of the above resolution to the Branch Council.

J. M. MARTIN,
Hon. Secretary.

Holmedene, Clougher, Co. Tyrone.

LISBURN AND DISTRICT MEDICAL GUILD

THE last meeting of the Guild was held at Dr. Boyd's of Hillsborough, who kindly provided tea for the members. After the minutes had been read and signed, Mr. Macafee of Belfast was introduced to read a paper entitled "Acute Abdominal Conditions in the Female." This paper was of a purely clinical nature, and many useful points were brought forward in the differential diagnosis of such common conditions as ruptured ectopia, pregnancy, acute appendicitis, acute salpingitis, as well as uterine infections, and ovarian cysts and uterine fibroids which had undergone torsion.

A vote of thanks was proposed by Dr. W. M. Hunter, and seconded by Dr. Colquhoun, to Mr. Macafee for an extremely interesting and valuable paper.

J. W. PEATT,
Hon. Secretary.

Railway Street, Lisburn.

BRITISH MEDICAL ASSOCIATION
NORTH-EAST ULSTER DIVISION

THE Division met in the Café, Coleraine, on Friday, 12th October. There was a fair attendance, and Dr. Hunter entertained the members to tea before the meeting.

The minutes of the previous meeting were read and passed. The chairman, Dr. Allison (Coleraine), then gave his address on "Some Observations on Medical Practice." He dealt with the relationship which should exist between doctor and patient and between members of the profession. Dr. Allison gave much sound advice on the conduct of medical practice, and related many interesting and amusing incidents which had happened during his long experience.

Dr. Bateman proposed and Dr. Gordon seconded a vote of thanks to Dr. Allison for his most interesting and helpful paper.

The usual silver collection for medical charities was taken.

At the meeting on Friday, 16th November, the main business was a paper by Mr. G. D. F. McFadden on "Modern Methods in the Treatment of Fractures." We hope to publish this paper in our next issue.

J. M. HUNTER,
Hon. Secretary.

36 Eglinton Terrace, Portrush.

REVIEWS

AIDS TO EMBRYOLOGY. By Richard H. Hunter, M.D., M.Ch., Ph.D., M.R.I.A. Second Edition. 1934. London: Baillière, Tindall & Cox. pp. 172, figs. 39. Price 3s. 6d.

The policy of the publishers of the Students' Aid Series has been to keep these little books up-to-date, and to issue new and revised editions as frequently as possible. In keeping with this policy a second edition of the "Aids to Embryology" has just been published. The success of the first edition has prompted its author to retain the general form of the original edition, and by revising and shortening certain sections, of interest mainly to the student of pure science, many new features have been added, and a number of additional diagrams have been included, while at the same time keeping the book no larger than the first edition. A short account of the development of the carotid sinus is given for the first time in any small book, and the sections devoted to the female genital tract, and to the myelination of the central nervous system, have been completely re-written, while the newer views on the development of the face, the thyroid gland, the branchial sinuses, and other regions have been incorporated. The book is based on the short series of lectures on Human Embryology delivered before the class preparing for the second professional examination in medicine at Queen's University, Belfast.

ILLUSTRATIONS OF REGIONAL ANATOMY. By E. B. Jamison, M.D. 1934. Edinburgh: E. & S. Livingstone. Price 30s. net.

As a teacher of human anatomy there is probably no better known personality than Dr. E. B. Jamison, and there is probably no anatomist living to-day with a more detailed knowledge of his subject. The illustrations of regional anatomy which he has just published are up to the high standard which one would expect from such a teacher. They are accurate and detailed, yet at the same time clear and readily understood. They should have a wide circulation amongst students, as they will form an invaluable help in revision, and in evening study away from the dissecting-room. They are published in five sections—Central Nervous System, Head and Neck, Abdomen, Pelvis, Thorax, each of which may be purchased separately. All are printed in colours. We regret that Dr. Jamison has not included sections on the upper and lower limbs. The anatomy of these parts is just as important to the student as that of the other regions, in the trying days of the examination.

A MANUAL OF PRACTICAL ANATOMY. By T. Walmsley, M.D., F.R.S.E. Part I: The Upper and Lower Limbs. Second Edition. 1934. London: Longmans, Green & Co. pp. 376, figs. 117, plates 7. Price 12s. 6d. net.

It is with pleasure we note the passing into further editions of any textbooks published by members of the staff of the Belfast Medical School. It is, therefore, with sincerity that we congratulate Professor Walmsley on the publication of the second edition of his Manual of Practical Anatomy (Vol. I). The present edition is considerably enlarged, and includes a somewhat lengthy introduction to the general study of anatomy. This introduction should be of considerable help to students, in enabling them to realize that anatomy is not merely the study of dead bodies to satisfy the academic whims of university teachers, but rather that such a study is a means whereby a knowledge of the structure of the living body may be obtained. We are glad to see that this outlook is maintained throughout the book. Methods used in the examination of the living body are given after each dissection, and in addition there are given exercises in the making of measurements used in clinical practice. Such a study of the living body should be of great value in preparing students for their work in hospital wards, and for this reason, apart from its usefulness as a guide to dissection, the book should have a wide circulation.

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MELANCHOLIA IN EVERYDAY PRACTICE. By Edwin L. Hopewell Ash, M.D. London: John Bale, Sons & Danielsson, Ltd. pp. 136. Price 7s. 6d. net.

THERE are few more hopeless complaints to treat than melancholia, and therefore any new contribution to the subject is always welcome.

The author from his twenty-five years' experience has come to the conclusion that the less typical forms are often not fully understood. The first chapters, therefore, describe the conditions, and some cases are quoted as examples.

Next in order come chapters on diagnosis and differential diagnosis, and here the author shows clearly the distinctions between such disorders as mania, dementia præcox, and paranoia.

Treatment is apparently of very doubtful value in the condition, and consequently includes almost all the armentarium of the physician. No details are forthcoming, but endocrines, many forms of electricity, and psychotherapy are advised.

One would like to have been told what value these individual treatments had, and when to use each. The book must, therefore, have a more diagnostic than therapeutic value.

CLINICAL SCIENCE. By Sir Thomas Lewis. London: Shaw & Sons, Ltd., 1934. 12s.

IN recent times we have availed ourselves to so wide an extent of the help of laboratory workers that the true importance of the clinician in the field of medical research is in danger of being forgotten. Sir Thomas Lewis's latest book, "Clinical Science," comes at an opportune moment to restore our balance and to remind us that progress in medicine may still come from the study of the patient at the bedside.

The greater part of the book is devoted to accounts of the investigations of the author and his associates of the problem of the circulatory system. The difficulties that arose during these investigations are pointed out, the steps taken to deal with these difficulties are described, and there is a full summing-up of the present position with regard to each problem.

The book has been written in the hope of encouraging young men to undertake clinical science as a life-work. It should certainly be placed in the hands of every young man with character enough to appreciate it. It will encourage older men to persevere with a science that is often misunderstood and the importance of which is rarely appreciated.

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