NOVEMBER, 1953

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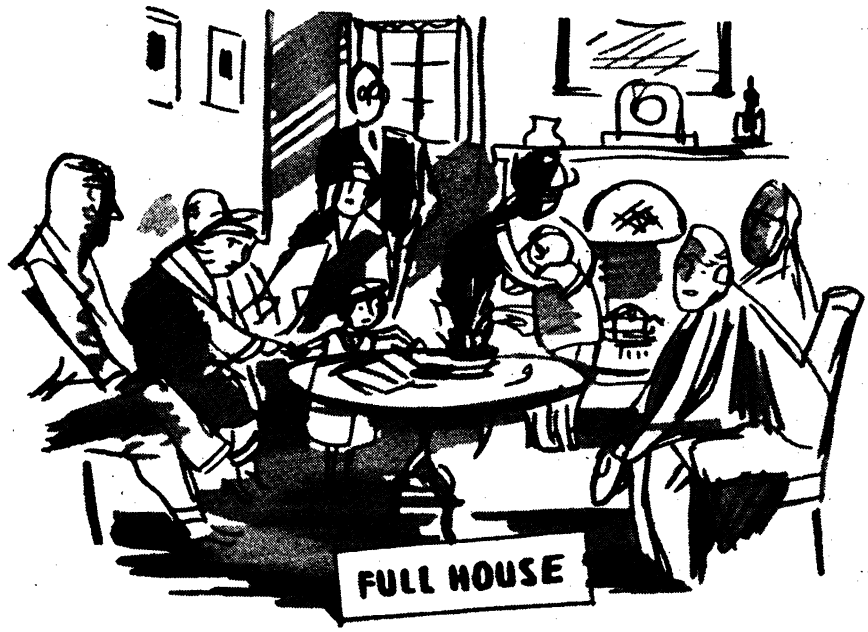

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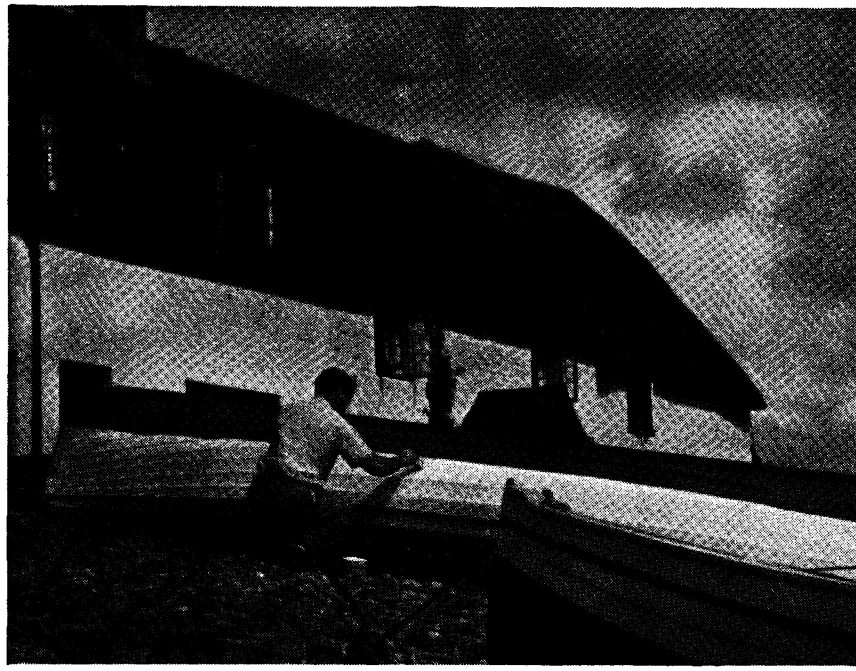

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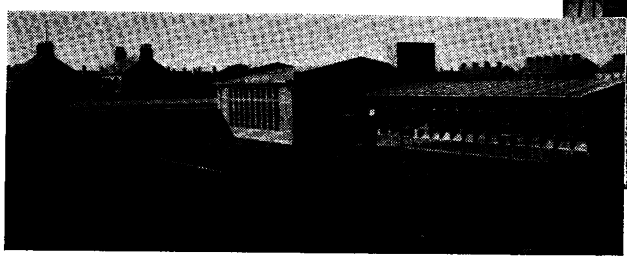

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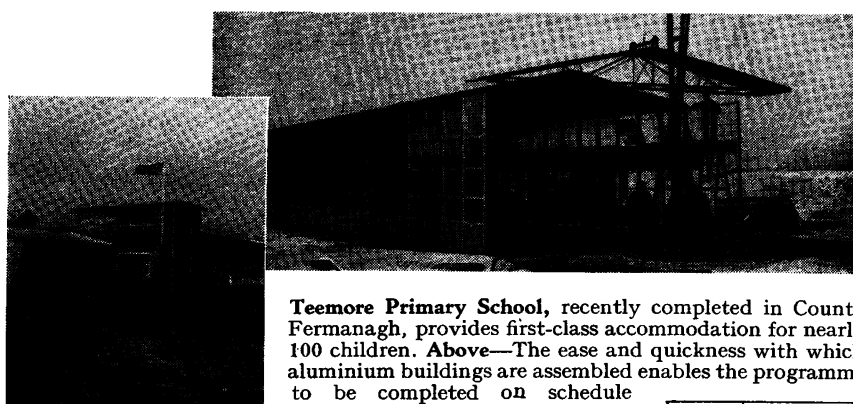

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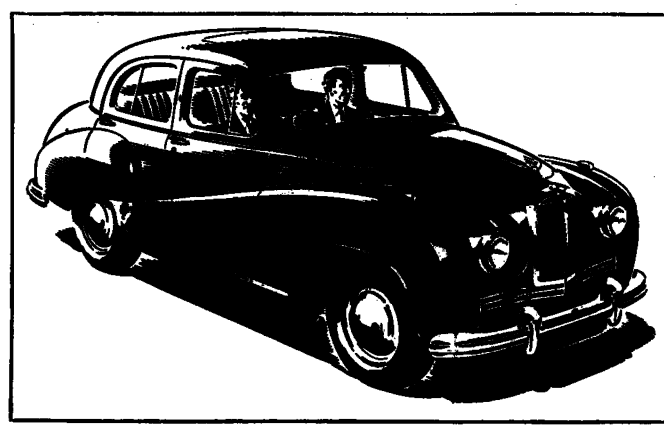

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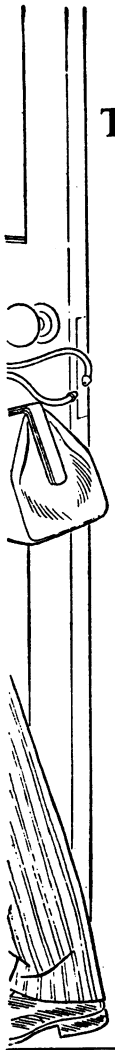

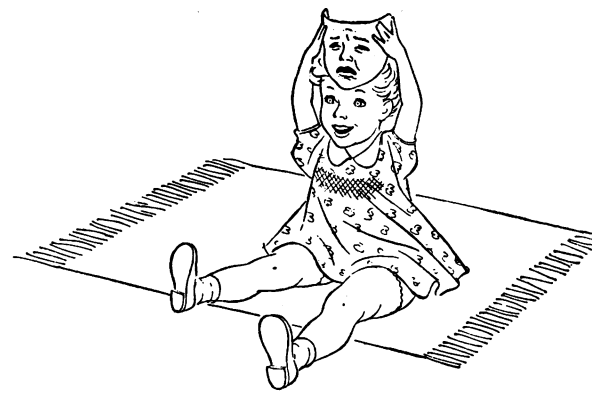

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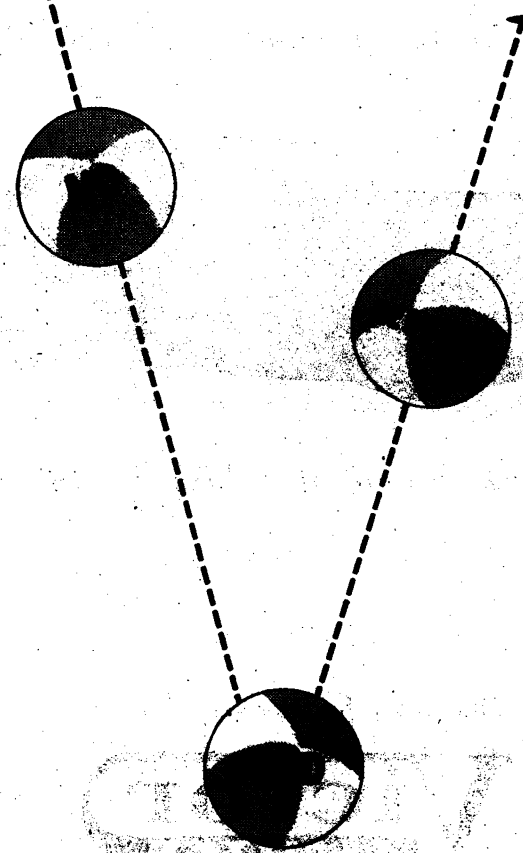

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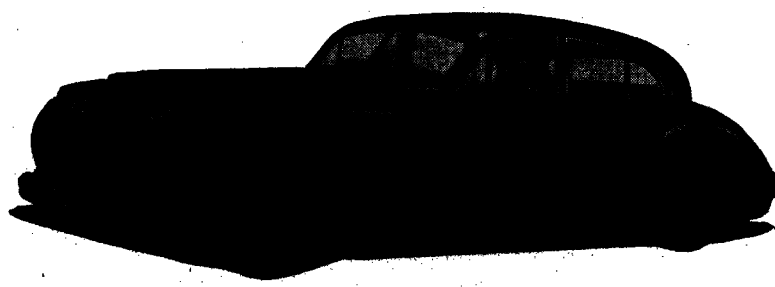

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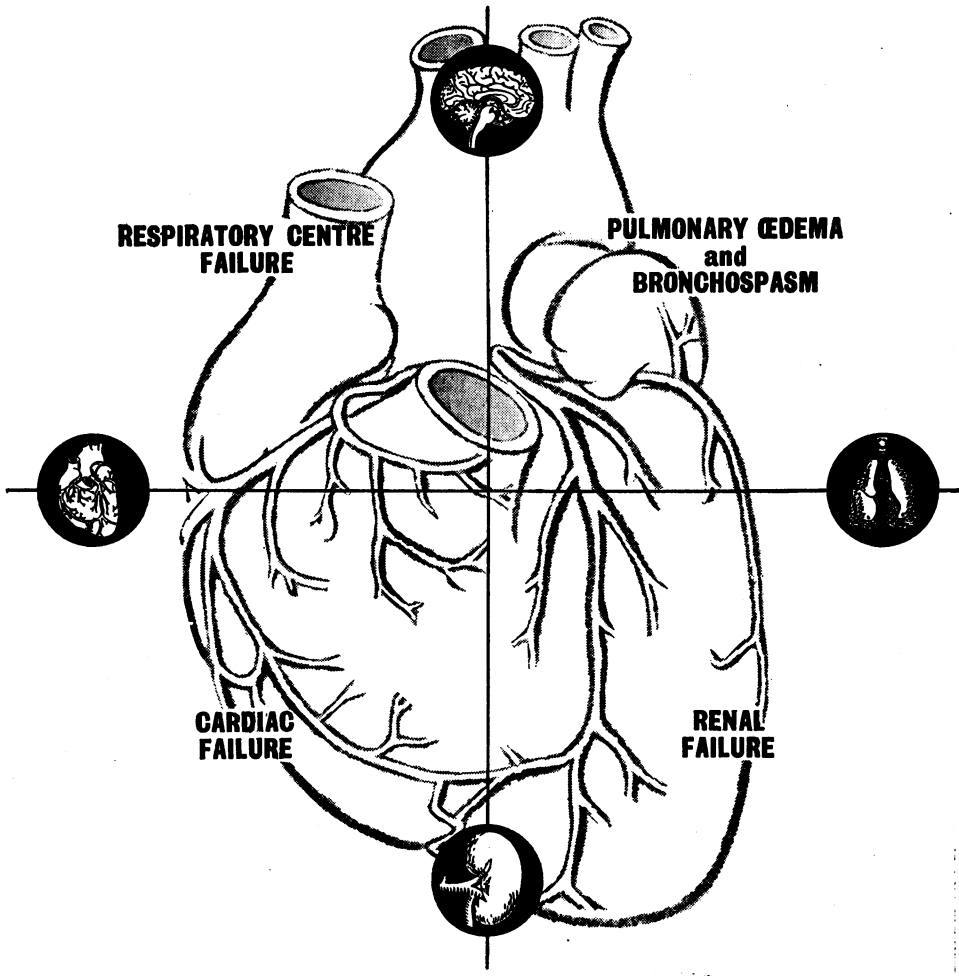

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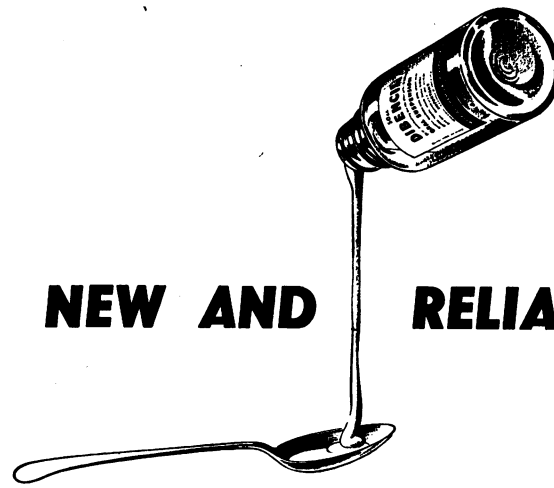

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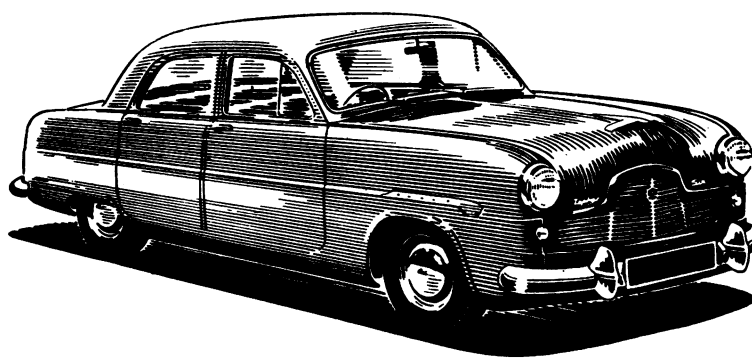

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VOL. XXII

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Joseph Black and Some Aspects of Medicine in the Eighteenth Century

By W. G. FRACKELTON, M D.

Presidential Address to the Ulster Medical Society

THE year 1728 is a notable one in the annals of British medicine, for during it were born two men who later made outstanding contributions to the advancement of medicine and natural science.

The story of the life and work of John Hunter has been recounted in detail by successive generations of Hunterian orators and is well known, but the personality and achievements of Joseph Black are less familiar. Hunter did not make any great discovery, but he took surgery out of the hands of the barber-surgeons and elevated it from a craft to a science. Black made fundamental discoveries in chemistry and physics, opening up vast fields for further exploration in those subjects and laying one of the foundation stones in the building of modern physiology. Both had the experimental outlook and an abhorrence of scholastic dogmatism. Both were great teachers and had the gift of stimulating enthusiasm and affection in their pupils, so that they left after them a band of workers to follow up and extend their observations. These great contemporaries lived through almost three-quarters of the eighteenth century. John Hunter died in 1793 and Joseph Black six years later.

Black has been written about mostly by Scotsmen, who have claimed him for their own. Admittedly the roots were in Scotland but there is no doubt that the tree flourished in Ulster. The family probably came to Ulster from the Scottish Lowlands at the time of the plantation of James I. The earliest authentic record is of a John Black, born in the neighbourhood of Ballymena. He was Joseph's great-grandfather and served as a trooper against Cromwell. Joseph's grandfather was "educated a merchant" by Mr. Pottinger in Belfast and served as supercargo in the West Indies and in various ports of Spain, France, and the

Low Countries. The supercargo's son, John, was born in Belfast and received a good classical education at Ayr and in his native town. He was apprenticed to an uncle, Sir John Eccles, in Dublin, and later settled in Bordeaux in the wine trade. He married an Aberdeen lady, Margaret Gordon, whose family were also settled in Bordeaux in the mercantile line. They had thirteen children, of whom Joseph was the ninth.

John Black was a cultured man and a close friend of the philosopher Montesquieu, who derived much of his knowledge of our constitutional government from the British colony in Bordeaux. Later he returned home to Ulster, settling on a model farm at Ballintaggart in County Armagh, and died at his son George's residence at Castle Place, Belfast, in 1767, having attained the ripe age of eighty-six years.

Joseph's brothers appear to have been successful manufacturers and merchants, and two of them, George and Samuel, were each five times Sovereign of Belfast between the years 1775 and 1789. Another brother, Alexander, had a plate-glass factory at Blackfriar's Bridge, London. There are extant in the Belfast Museum and Art Gallery nine letters from Joseph Black to this brother in London. They are written in a graceful and legible hand, and the phraseology and spelling are modern. Some of these letters, among others, will be referred to later, as they help in the revelation of his personality.

Joseph received his primary education from his mother, who taught all her children to read English, there being no school for the purpose in Bordeaux. At the age of twelve he was sent to live with relations in Belfast to acquire the rudiments of Latin and Greek. His biographer, John Robison, says that he was educated at the local grammar school, and Black himself says that he attended a private school. It is most probable that he attended the Latin school, a foundation by the first Earl of Donegall shortly after the Restoration. Unfortunately the records of the school are not available. It was situated in the rear of the old parish church in High Street, in the corner of the churchyard facing Catherine Street and School Lane, now known as Ann Street and Church Lane respectively. The school existed for about 125 years and was probably closed after the old parish church was demolished in 1774. The area of ground on which it stood is now an open space as a result of the air raids in 1941.

After four years in Belfast Joseph was sent to the University of Glasgow, where his entry as a matriculated student is recorded on 14th November, 1746. It runs, "Josephus Black filius natu quartus Johannis Black Mercatoris in urbe Bordeaux in Gallia, ex urbe de Belfast in Hibernia."

The advent of the eighteenth century heralded an era of prosperity for the Lowlands of Scotland. Agriculture flourished and new industries were established. The political scene was tranquil, for the Lowlands had held aloof from the rising of '45 and had reaffirmed their loyalty to the House of Hanover as soon as Prince Charles Edward had marched south of the Border. The Jacobite cause had received its death-blow on Culloden Moor six months before Joseph Black entered the University of Glasgow.

At the time of the Union Glasgow had been a country town of 18,500 people, an outpost against the lawlessness of the Highlands. By the end of the century it had attained a population of 80,000 and was a flourishing centre of commerce and trans-Atlantic trade. With increasing material prosperity the narrow outlook and frugal habits of the old Covenanting citizens were discarded for more liberal ways. Nor were the things of the intellect forgotten, and the presence and writings of such men as Adam Smith brought fame to Glasgow's university.

The "old College," as the university was then called, fronted the long and narrow High Street, the central portion of the building being the Senate Hall. At either side of the main building were the professors' houses, which faced the college green or quadrangle, and had in addition a back entrance from the street. The general architecture of the town was mean and irregular. The upper stories of the houses, with gable-ends towards the street, were entered by outside staircases, and in the triangular space between these and the houses the citizens were accustomed to keep pigs. The condition of the streets and the unsavoury atmosphere must have resembled those of a western Irish town on a fair day.

In a note about his studies Black says :—

"I attended all the lectures on the languages and philosophy in a regular succession. Being then required by my father to choose a profession or employment, I chose that of medicine, the elements of which I began immediately to study by attending the lectures of the Professor of Anatomy and of Dr. Cullen, who was at that time Professor of Medicine at Glasgow. Dr. Cullen began also at this time to give lectures on chemistry, which had never before been taught in the University of Glasgow, and finding that I might be useful to him in that undertaking, he employed me as his assistant in the laboratory, and treated me with the same confidence and friendship and direction in my studies as if I had been one of his own children. In this situation I lived three years."

The Dr. Cullen referred to in this note was William Cullen, who, after the great Boerhaave of Leyden, was the most successful clinical teacher of the time. A native of Lanarkshire, he had practised there for a time in partnership with William Hunter. Later he came to Glasgow and acquired a large practice. He was appointed Professor of Medicine and Chemistry in the University. A fluent speaker, he was the first to deliver lectures in the vernacular instead of in Latin. A close friendship, which was maintained throughout their lives, grew up between Cullen and Black, and later when Cullen had occupied the chair of chemistry in Edinburgh for some time, he resigned it in favour of Black. In Edinburgh Cullen held the posts of Professor of the Practice of Medicine and of the Institutes of Medicine, or, as this would now be called, Physiology. His portrait suggests a serene and kindly disposition, and it is said that his gifts of infinite patience and unruffled temper added to his success.

In 1750 Joseph Black transferred to Edinburgh to complete his medical studies. He took up residence with his cousin, James Russell, Professor of Natural Philosophy, who was also engaged in the practice of surgery. One of his

contemporaries in the medical school was Oliver Goldsmith, whose biographer states that he was fond of chemistry and was remembered favourably by the celebrated Black.

Some impressions of a medical student's life in Edinburgh in the eighteenth century are recorded by William Drennan, the Belfast physician and United Irishman, in letters to his sister in Belfast. He writes as follows in November, 1777 :—

"I have fixed on the classes necessary for me to attend. I rise a little after six in the morning. I strike my flint, blow my tinder, and light my match; and after preparing for my classes, at about 8 o'clock, if it be a good morning, I give stretch to my legs for half an hour in the meadow which lies near my lodging—when I return I take my academical breakfast of bread and milk and then issue out to the labours of the day. From nine till one I am tossed about with the wind of doctrine through the different parts of the university; from 9 till 10 at the practice; from 10 to 11 at chemistry, my second attendance at both; from 11 till 12 at the Materia Medica; from 12 till 1 at the infirmary from which I derive much more benefit than when last here. Yet still it is a disagreeable place to me, and I never enter it without thinking of those lines of Milton—

'Despair
Tended the sick, busiest from couch to couch,
And over them triumphant Death his dart
Shook, but delayed to strike.'

From one until three I make it a rule to walk and chew the cud of what I have heard, and either soar to the sublime Calton, where as Johnson expresses it, I can see the dusty world look dim below or pace along with my fellow-mortals in the meadow or the park."

Concerning the status of the medical student he writes :—

"It is greatly the fashion here to despise the students. A student of medicine is a term of contempt, but an *Irish* student of medicine is the very highest complication of disgrace."

The examination for the Doctorate comprised a thesis written in Latin and three viva voce examinations also conducted in that language. There do not appear to have been any clinical or practical tests. Drennan says that "the students generally apply to a fellow in this university, one Brown, who spawns young physicians and surgeons, in order to speak Latin, and get a thesis written by his instructions." Evidently the examiners did not favour this procedure, for Drennan had to repudiate before the Faculty Dr. Gregory's insinuation that his thesis was written by Mr. Brown. Drennan remarks :—"If he (i.e., Dr. Gregory) had known the Irish spirit better he would have known that it was incapable of submitting in such a manner to any Scotchman upon earth."

Black says that he attended the lectures of Dr. Munro, Senior, and the other medical professors in Edinburgh. The Doctor Munro referred to here was Alexander

Munro, the first of the so-called Munro Dynasty. For three generations and over a period of 126 years they taught anatomy in Edinburgh. All three had the Christian name Alexander and were distinguished as Primus, Secundus and Tertius. Alexander Munro Primus had studied under Boerhaave and was a distinguished teacher in anatomy and also in surgery, in which he had a large practice. Munro Secundus, in spite of the handicap of a brilliant parent, was even more famous as an anatomist. It was he who described the foramen of Munro. Munro Tertius appears to have been rather indolent and under him the teaching of anatomy languished. It is recorded that he read his grandfather's lectures verbatim, even retaining such phrases as :—"When I was a student at Leyden in 1719."

The years of student life drew to a close and Black presented his thesis, for which, it is needless to say, he did not require the assistance of any "Mr. Brown." On 1st June, 1754, he writes to his father :—

"I am not yet installed into the order of the great wig, but have gone through all the examinations, and nothing is wanting but the ceremony and that has been put off by the Professors to wait for some others that are to be promoted along with me six days hence.

"In my last letter to you I proposed to go immediately to London to spend some time in the Hospitals there. I am now advised to put that off and remain here yet a while longer; and I must own the reasons for it are very strong and quite unanswerable by me unless you disapprove of them. The following are the chief of them. I have now studied the Theory of Medicine and have likewise been taught everything upon the Practice which can be learned in a College. I have also seen some real Practice and have even practised a little myself. But all this is not enough. I should be thoroughly acquainted with the real Practice and this is a thing very different from what can be learned in a College; thus, for instance, we are taught by our Professors that if a sick person breaths with great difficulty, one thing must be done; if his respiration is yet more laborious, another. But how shall we judge of the nice degrees of laborious breathing unless from a dayly and familiar acquaintance with, and study of the appearances and looks of Patients. Most young Physicians neglect this essential part of their art in their education and very often acquire it when they come to Practice at the expense of their Patients' safety. I have not had time this last winter to apply to it sufficiently; tho I had the opportunities, my attention was too much taken up with some of the Colleges, preparing my Thesis and recalling to my mind everything I had learned, on account of the examinations. If I go to London to acquire this part of medicine, I may see a good deal of Practice, but I am a stranger there, and have no acquaintance whom I can venture to trust so much or be so familiar with as to trouble him with all my questions and doubts. On the contrary here, medicine is allowed on all hands to be in a very flourishing condition. It is practised in the most rational and simple manner. I have the happiness to be lodged with a Gentleman, who is justly esteemed by all his Brethren, who has extensive Practice both as a Physician and Surgeon and, tho no Doctor himself, yet the oldest of

them are not ashamed to consult with him in private. Besides this he is my intimate and familiar friend and is willing upon every occasion to teach me as far as he knows himself.

"When I am well instructed in a method of Practice here, a very short time in London will be sufficient; for then I need only observe the different manner of doing the same thing there, which I shall soon be master of."

Even in the eighteenth century it would seem that the Edinburgh doctor had a staunch loyalty to his school and did not concede pre-eminence to any other place.

The title of Black's thesis was *"De humore acido a cibis orto et de Magnesia"* (Concerning the origin of the acid liquid from foods and magnesia.) It does not, as the title might suggest, conceal a lost solution of the problem of peptic ulceration, but deals with the subject of renal and vesical calculi.

The surgical operation of lithotomy was an unpleasant ordeal, even though it could be performed by such an expert as William Cheselden in one minute, and a treatment which obviated it would be welcomed by the patient. So a search was in progress for what were called lithonotryptic drugs. Hitherto the substances employed had been the strong alkalis, the lye of the soap-boilers, and it is not to be wondered at that surgeons sought a less necrosing liquid. Robert Whytt, a professor of medicine in Edinburgh, attempted to dissolve bladder stones by injecting into the bladder a mixture of lime water and soap.

Interest in the subject had been stimulated some years previously by the statements of Sir Robert Walpole and his brother, Horace, who suffered from "the stone" and claimed to have received benefit from a medicine invented by a Mrs. Joanna Stephens. For a consideration of £5,000 Mrs. Stephens revealed her secret, and the details of her treatment were published in the "London Gazette" of 19th June, 1739, as follows :—

"My Medicines are a Powder, a Decoction and Pills. The powder consists of egg shells and snails, both calcined. The decoction is made by boiling some herbs (together with a Ball, which consists of Soap, Swines-cresses, burnt to a blackness, and honey) in water. The Pills consist of Snails calcined, Wild Carrot seeds, Burdock Seeds, Ashen Keys, Hips and Hawes, all burnt to a blackness, Soap and Honey."

Naturally the profession did not approve of this gross polypharmacy and during Black's student days there was much discussion on the subject.

Black's research began in an attempt to produce a milder alkali from Epsom salts. His classical experiments are well known and will only be described briefly. He commenced by studying the different forms of lime. Limestone, when heated in a fire, became activated, and this quicklime, when placed in water, generated much heat, and was transformed into slaked lime. The limestone was supposed to have absorbed phlogiston from the fire and later to have lost it to the water. Black heated a weighed quantity of marble and found that in the process it lost weight, thus giving the first blow to the phlogiston theory. He next showed that if slaked lime be treated with a mild alkali, such as sodium carbonate, it is changed again to chalk, while the mild alkali becomes caustic alkali.

In modern nomenclature the changes are:—

1. $CaCO_3 = CaO + CO_2$.
2. $CaO + H_2O = Ca\ (OH)_2$.
3. $Ca(OH)_2 + Na_2CO_3 = CaCO_3 + 2\ NaOH$.

Black realized that when chalk or marble was heated, a gas which he called fixed air was released. He was able to collect the gas, which we know as carbon dioxide, and to study its properties. He was also able to show that carbon dioxide was a normal constituent of the air because quicklime was changed into ordinary chalk, albeit tardily, by exposure to air. This was the first atmospheric gas to be isolated and described. The discovery heralded the dawn of a new era in chemical investigation, and so Black is often given the title—Father of Pneumatic Chemistry.

Much of Black's success was due to his accuracy in weighing. The experiments quoted are the first example of a reversible chemical reaction. A certain weight of chalk is taken in experiment 1 and the same weight is recovered at the end of experiment 3. In the words of Sir William Ramsay, "his proof that the change of a complex compound to simpler compounds, and the building up of a complex compound from simpler ones, can be followed successfully by the use of the balance, has had for its consequence the whole development of chemistry." On this score he has been called the Father of Quantitative Chemistry.

Truly, Joseph Black's thesis has a strong claim to be the most important ever presented for a doctorate in medicine.

Its contents were made known more widely a year or so later, when it was read in English before the Philosophical Society of Edinburgh under the title:— "Experiments on Magnesia, Quicklime, and other Alkaline Substances." Henry Brougham described this paper as "incontestably the most beautiful example of strict inductive investigation since the 'Optics' of Sir Isaac Newton."

Surely here is a story as romantic as any in the history of science. To alleviate a distressing ailment investigations are undertaken and lead to a discovery in pure science, apparently remote from the original plan. Some would say that this was a gift from medicine to chemistry. Does it not rather illustrate the indivisible unity of all scientific endeavour, and was not the "gift" repaid later with interest in the elucidation of those "nice degrees of laborious breathing" about which the young doctor had written to his father?

As regards his discovery Black was fortunate in another respect. There was none to claim priority. There was, however, a great deal of opposition to his views, especially from the German schools, and Black spent several years in refuting their arguments. The phlogiston theory did not die easily. He considered his experiments a complete expression of his opinions and did not make any others. It was not till 1767 that a Viennese chemist, Jacquin, performed the simple experiment of passing the gas expelled from heated marble into lime water, thus transforming the lime to chalk again. This finally silenced the critics.

After receiving his doctorate in medicine Black appears to have practised his profession in Edinburgh for two years. At the end of this period his old teacher

and friend, William Cullen, was invited to take the chair of chemistry in Edinburgh, and Black was offered the chair of anatomy and a lectureship in chemistry at Glasgow. He was diffident about his ability to teach the former subject and soon effected an exchange of the chair for that of the Institutes of Medicine. His biographer, John Robison, who succeeded Black as Professor of Chemistry in the University of Glasgow and who edited his lectures in chemistry, says there are no remains of his medical lectures to be found among his papers. He followed a celebrated lecturer, who, Robison says, had exhibited "brilliant prospects of systematic knowledge" to his students. Black, however, kept on the firm ground of established principles, declining to travel with the systematists in their attempts to form an all-comprehending doctrine. Robison says that it does not appear that he ever satisfied himself with his method of treating those subjects and he did not encourage conversation on them. He would have been at one with another distinguished Ulsterman and Honorary Fellow of this Society, Sir Almroth Wright, who some thirty years ago in this room impressed on his hearers that medicine must advance by *passus scientificus* and not by *saltus empiricus*.

Apart from his work at the University Black practised as a physician in Glasgow and its environs. He took his practice seriously and was always anxious about his patients' welfare. Robison says, "He was in particular a favourite with the ladies. I could not but remark that they regarded themselves as honoured by the attentions of Dr. Black; for these were not indiscriminately bestowed, but exclusively paid to those who evinced a superiority in mental acomplishments, or propriety of demeanour, and in grace and elegance of manners." However, he remained unmarried all his days, perhaps a mild disappointment to his father, who wrote later on :—"As for our Hippocratic Joseph his affections are about Edinburgh and absorbed in his dear Mistress Philosophical Enquiry as an alchymist."

It was in Glasgow that Joseph Black established a firm friendship with the philosopher Adam Smith, famous for his "Enquiry into the Nature and Causes of the Wealth of Nations." The friendship lasted throughout their lives. Each recognised certain sterling qualities in the other, and an oft-quoted saying of Adam Smith was "that no man had less nonsense in his head than Joseph Black."

During this period Black conducted the other piece of research for which he is famous—the enquiry into the nature of heat. He had been attracted to the problem by an observation of Cullen that ether boiled when the atmospheric pressure was lowered. Cullen had merely recorded the phenomenon and had not offered an explanation. In a series of simple and conclusive experiments Black discovered the property, which he named "latent heat" in solids and liquids. He investigated especially the changes in heat distribution during the transition of ice to water and of water to steam.

In these researches he had the assistance of a rather remarkable young man who was employed as a technician at the university. His name was James Watt. A delicate child, Watt had not received an ordinary school education, but from early childhood he had shown evidence of mathematical genius. The story is told that one day a visitor, calling at his father's home, found young James, aged six years,

sprawling on the floor on which he had drawn many intersecting chalk lines. The visitor reproached the father for allowing his son so to waste his time, when he should have been at school, but had to recant the hasty judgment on receiving the explanation that the boy was solving an abstruse problem in geometry.

Watt was employed at the university as a maker of instruments of precision and it was part of his duty to set up the apparatus for experiments in the class of Natural Philosophy. The department possessed a model of a primitive form of steam engine, Newcomen's, which was used for demonstration to the class. It went out of order and was given to Watt to repair. He investigated the machine thoroughly and noted its defects. He was aware of Dr. Black's researches into heat, saw the possible applications to his own problem and entered into collaboration with the professor. The association was a very happy one, and in his lectures Black never failed to acknowledge the help he had received from Watt. The latter applied the results of their joint experiments to the design of his condenser, which was his main contribution to the improvement of the steam engine. Black, the most selfless of men, derived as much pleasure from the young technician's subsequent success and prosperity as if they had been his own. Robison says of Watt's engine, "Its immense superiority, in respect of power and economy, offered to the busy part of society a most certain and powerful first mover for all machinery; and thus attracted the attention of all those engaged in the great business of making money. It was this, more than all the love of knowledge, so boldly claimed by the eighteenth century, that spread the knowledge of the doctrine of latent heat and the name of Dr. Black."

In the year 1766 William Cullen transferred from the chair of chemistry in the University of Edinburgh to that of medicine, and Black was appointed to succeed him.

On returning to Edinburgh he found the lines were fallen to him in pleasant places. The old city had recovered from the depression of the early years of the century, when by the Act of Union, she had been deprived of the chief function of a capital, government. Those were dark days, when men said the glory had departed. Grass grew between the cobblestones of the Royal Mile. Yet by the mid-century all this was changed, for Edinburgh had experienced an intellectual revival which had placed her in the van of European culture. Her philosophers and the great teachers of her medical school were known all over the civilised world. It was said that you could stand at the Mercat Cross of Edinburgh and, within an hour, shake by the hand fifty men of genius.

Black was welcomed into this select company, which included his old friend, Adam Smith. However, his closest friend from henceforth was to be James Hutton, the geologist, whose work, "The Theory of the Earth," revolutionized the study of geology and laid the foundations of modern views on the subject. Two years Black's senior, he had been first of all a law student but changed to medicine, graduating at Leyden in 1749. Seldom did a day pass without these friends meeting. Though alike in their love of scientific accuracy and adherence to fact, Hutton's jovial temperament was a foil for Black's seriousness. Hutton was now

the only person near him to whom Black communicated his views on scientific matters, though he carried on a regular correspondence in such with his friend Watt, who at this time was living in Birmingham.

To digress, it seems strange to us now that so many men of science in the eighteenth century were primarily doctors of medicine. In those days medicine was the main gateway to all branches of natural science. In Black's time at Glasgow all the chairs in these subjects, as well as that in mathematics, were held by graduates in medicine.

After his return to Edinburgh Black did not engage in any further serious research work. There were two reasons for this. First, he considered that his primary duty was to instruct the large number of students whom the growing reputation of the Edinburgh medical school now brought to his classes. The general standard of their education was low, and the lecturer had perforce to present his subject in a simple and direct manner. He scorned the tricks of the showman, and, in spite of difficulties, became a favourite lecturer. Robison says of his students, "They were not only instructed but (they knew now how) pleased."

As the years passed he was fond of relating to his classes his early difficulties and how they were overcome. His labour was not in vain, for he trained many who later rose to eminence in the scientific world. One of his pupils, Daniel Rutherford, was the discoverer of nitrogen. It is interesting to note that Rutherford had a nephew who is even better known, Sir Walter Scott.

In the correspondence columns of our medical journals we are still treated occasionally to discussions on the relative importance of art and science in medicine. In the eighteenth century many thinkers did not rank chemistry as a science but regarded it as an offspring of the art of pharmacy. In his introductory lecture on the "Definition of Chemistry" Black states his opinion on the subject simply and adduces the practice of medicine as an illustration. He says : "The physician who only practises what he has learned, treats his patients as we say *secundum artem*, and gives himself no further trouble, should be reckoned an artist; but when he bestows uncommon attention and study upon the diseases he has occasion to treat, endeavours to understand them better than ordinary, or to improve the method of curing them, he, in so far, is certainly one of the most useful philosophers—a medical philosopher." Black applied the term "philosopher" to "any man who endeavours to acquire knowledge, or thinks and reasons upon any useful subject." For him a plain farmer, if he studied the construction of his plough and attempted to improve its function, had more title to be called a philosopher than many men of great learning who never proposed a new thought of their own.

The second reason for Black's failure to prosecute his researches was the state of his health. Never robust, the long hours in his laboratory and the mental exertion involved tended to induce febrile illness often accompanied by hæmoptysis, and this hæmoptysis was severe on more than one occasion.

At this time the university buildings were in a state of decay. Principal Robertson said they resembled almshouses rather than the courts of a seat of

learning. Until the year 1780 all classes of society had lived in the dark, many-storied houses in the wynds and closes off the High Street and the Canongate. After that year the New Town with its spacious crescents and stately buildings began to spread forth beyond Princes Street. The foundation stone of New College was laid in 1789 and Black presented a memorial to the trustees on the strong claim of the professor of chemistry to a house contiguous to his laboratory. In the course of his plea he says, "And supposing the Professor of Chemistry should be allowed this advantage over the Professors of Medicine, he need not on this account be an object of envy; his office is much more laborious than theirs who have only an hour of teaching daily; it is also attended by considerable expense for fewel, furnaces, glass and materials. The time he must necessarily bestow on his laboratory prevents him in some measure from courting the world and giving those attentions which procure favour and employment as a physician." Unfortunately he did not succeed in convincing the trustees and he did not live to occupy the new classrooms and laboratory.

All through his working life Black continued to practise as a physician, and though the extent of his practice had to be limited by his other commitments, his advice in their illnesses was sought by his many friends. His old students also wrote to him for advice on matters medical, and one of the honours conferred on him was that of Physician to His Majesty King George the Third in Scotland. A high tribute described him as "a physician of good repute, in a place where the character of a physician implies no common degree of liberality, propriety and dignity of manners, as well as of learning and skill."

Other honours came to him. He was elected an honorary member of the Imperial Academy of Sciences at St. Petersburg and also of the Royal Academy of Sciences at Paris. This last honour was a graceful recognition of his work by the great French chemist, Lavoisier.

Black disliked publishing papers on his work, and, though invited frequently, he never could be persuaded to address either of these learned societies. He preferred the homely gatherings in the Old Town, the small evening party with his friends rather than the more formal social occasion. A lover of good conversation, he sedulously avoided speaking on subjects in which he was acknowledged an expert, preferring to let others choose the topic and then to contribute his own observations. Being well informed on most subjects he was at ease in the company of all men, whether scholars or men of action.

A shrewd judge of character, though himself without guile, he was not deceived by insincerity or ostentation in others. For example, in a letter to his brother Alexander in London on some problems in the manufacture of plate glass he discusses the work of one Dantic, and says, "He shews that he has had much experience in the manufacturing of glass and he has also some genius but he is too much of a Projector and uses too much declamation."

Black also acted the part of adviser to his brothers on occasion. He writes again to Alexander about brother James, who appears to have been the lame dog of the

family, suffering ill-health and receiving regular financial aid from Joseph. James may have been a speculator, for he is advised that "Projects and schemes are dangerous even to men of great fortune; to those who have little they are certain ruin, both by exhausting that little and by debauching the mind from the habits of sober industry and close attention to business which when acquired are a sure means of thriving."

His tastes were simple, verging on frugality, and some said he was parsimonious. The evidence for this imputation is slender and depends on his habit of weighing the guineas which he received from his students in payment of their fees. However, this was probably a necessary precaution in the days of a nobler coinage than ours, when it was worth while for a rogue to indulge in a little coin-clipping. We have his cousin Dr. Ferguson's word that he kept a table equal to, if not above, his position, and that his purse was ever open to his friend.

For thirty years life continued uneventfully in agreeable surroundings until his strength began to fail. The walks with his friends in the meadows were gradually curtailed and finally even conversation fatigued him. He husbanded his reserves and did not suffer any acute illness, though the recurrences of hæmoptysis became more frequent. Robison says:—"He thus spun his thread of life to the last fibre; and even this does not seem to have broken but merely ended." He delivered his last course of lectures in the session of 1796-7.

He dreaded a long illness on account of the trouble and distress this would give to his friends, and his wish was gratified. On a November afternoon in the year 1799, as he sat partaking of his usual simple meal, his servant entered the room to inform him that someone had called. Seeing him perfectly still, the cup steadied on his knee, the servant thought him to be asleep but on looking closer found that he was dead. A friend said it was "as if an experiment had been required to show to his friends the facility with which he departed."

He rests in the old Greyfriars Churchyard, the burial place of many men famous in Scotland's history.

A physician of good repute, an acceptable teacher, a wise counsellor, a faithful and unselfish friend—for these qualities alone Joseph Black, of Ulster lineage, is worthy of our remembrance; but he has an even higher claim to fame for he fitted the key-piece in a section of that jig-saw puzzle, intricate and still incomplete, the scientist's portrait of Nature.

I wish to thank Mr. A. H. George of the Belfast Museum and Art Gallery for the loan of Joseph Black's letters from the museum and for his help in suggesting local sources of information about the Black family.

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REVIEW

PICTORIAL INTRODUCTION TO NEUROLOGICAL SURGERY. By G. F. Rowbotham and D. P. Hammersley. (Pp. 108 + viii; figures 81. 21s.). Edinburgh: E. and S. Livingstone. 1953.

THIS book is a lavishly illustrated introduction to operative neurosurgical technique. It opens with precise instructions on the preparation of the operative field; then, in following chapters, the surgery of the scalp, skull, and brain are successively described, and finally there is a chapter on the surgical treatment of injuries of the head.

The book was apparently compiled at the request of the author's former pupils—in general or special branches of surgery, and is intended to help surgeons in peripheral areas where there is no congregation of specialists but where traumatic intracranial work has to be done. The scope of the work has, however, been widened beyond the author's original intention, and such matters as cortical excision are fully dealt with. Even the admirable section on head injuries is over-elaborated —there are four pages of illustrations on the repair of cerebrospinal fluid fistulæ—and two pages on extradural hæmatoma straddling the transverse sinus, a condition of the greatest rarity. On the other hand, some elementary matters have been overlooked, and in the section on compound injuries of the frontal sinus, no instructions are given for dealing with the sinus itself.

These criticisms do not detract from one's admiration for the clarity and artistry of the production. It is a beautifully documented account of traumatic neurological surgery as carried out in Newcastle. It falls, however, between two stools; while obviously not intended for the practising neurological surgeon, it is unnecessarily elaborate for the general surgeon forced by circumstances to operate on the acutely head injured. A. R. T.

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Aspects of Human Heredity in Health and Disease

By J. S. LOUGHRIDGE, M.D., B.Sc., F.R.C.S.(ENG.)

Opening Address Royal Victoria Hospital, 8th October, 1953

To the younger members of the Medical School this annual convocation is only one more incident to be endured in an overcrowded curriculum. To the undergraduate with so many new experiences and so much new knowledge continually forced upon him, the retrospect of even one year appears a long way off; and similarly the events to be of a year ahead are in the dim and distant future. However, after graduation and a year or two spent in residential posts, the passing of time takes on an increasing tempo which becomes greater with each and every year. But to the older members of the hospital staff this address has come to mean something more. For each year brings fresh duties, responsibilities, and interests, and the amount of time to sit back and think annually becomes less. So much so, that year follows year with an unrealized rapidity, and it is by such recurring annual events as this morning's meeting that the senior staff mark off each year from its successor.

Since the last annual meeting three new members have been elected to the Medical Staff Committee. It is therefore my pleasant duty to introduce Mr. R. I. Wilson, Mr. S. R. Sinclair, and Dr. J. Martin Beare. We sincerely hope that they will long be spared to make their contribution to the relief of pain and sickness and, no less importantly, to hold and to pass on the torch to you, the next generation.

In welcoming you to your first year of hospital studies, we have in mind, as you have, the feeling that this is the real introduction to your life-long vocation. Hitherto you have lived in and absorbed an atmosphere of academic calm with systematic classes in the structure and working of the human body. From to-day you are going to meet a new and very different world—that of disease—and disease not only as it is found in the scientific study of pathology, in a bottle on the museum shelf, but disease as it occurs in the living and sensitive human being, with all his instinctive dread of pain and discomfort, his fear of death, his pathetic faith in irrational and unscientific modes of treatment and the many other psychological traits which divide the sick from the healthy.

I would ask you then throughout the whole of your medical career, no matter how difficult the diagnosis may be, no matter how technical the treatment, no matter how interesting or unusual the pathology, I would ask you to remember that you are not treating just a disease, that you are not just a sculptor modelling a statue, or a dissector of living tissue, but you are a physician called in by the

patient at a crisis in his existence and that it is your privilege as well as your duty to treat your patient as a whole, to treat his mind as well as his diseased body.

The burden of learning which will descend upon you in the next few years will almost be more than you can bear. You will experience that weariness of the flesh of which Solomon complained and with so little reason in comparison with the present-day student of medicine. However, with the passing of years and with increasing knowledge, many of you will find yourselves attracted to one of the many specialities into which modern medicine is divided. But as all parts are members of one body, your interest in one part will always be the richer and more fruitful if you gain and retain a knowledge of medicine in all its parts.

Not only must you keep your medical knowledge wide, but it will be an advantage to keep in touch with recent advances in cognate sciences, for you are the heirs of all the ages and of all the sciences.

The scientific approach is probably more discussed than understood and it is difficult for us to appreciate the intellectual effort which has been expended in acquiring each and every bit of scientific knowledge.

And though I have emphasized the concept of the patient as a whole, you will find that pure science has much to offer in the diagnosis and treatment of disease, that much progress has been made, and doubtless more knowledge will continue to be made, in relief of sickness and suffering, and in postponing that inevitable day when we must shuffle off this mortal coil.

Thus it may be that, on your first visit to a medical ward, you will see a patient with, say, the type of anæmia first described by Addison; and after a few weeks' treatment with liver extract you will see that patient, who until some years ago was doomed to death, restored to full health and strength. This recurring miracle of treatment is the direct result of a disinterested inquiry into finding those articles of diet which most readily restored to normal the blood content of an animal whose hæmaglobin had been artificially reduced.

Again in a surgical operating theatre you will see operations performed with a margin of safety undreamt of even ten years ago. Of the factors increasing that margin of safety, not the least are the new drugs available to the anæsthetist. One of these is the active principle of the arrow poison used for centuries by the South American Indians to kill game for food or to paralyse their enemy. Chemically purified and scientifically controlled, it is now a means of saving life by facilitating surgical procedures.

Or yet again in another year or two you will be admitted to the maternity wards, where you might find one baby picked out of a hundred and see its red blood cells removed from its circulation to be replaced by those of a total stranger but of the same blood group. The saving of the life of that baby, predestined to death by the hereditary incompatibilities of its parents, follows directly from a study of blood groups in man and rhesus monkey.

These are three instances of every-day practice, and though they may lose something of the dramatic by their daily repetition, yet they can claim to be modern

life-saving miracles which have arisen, not from any wishful thinking, but from long continued and disinterested search for truth in pure science.

We have all different abilities for remembering facts or for arriving at logical conclusions. It does not matter so much what views you hold but in how you hold them. Instead of holding them dogmatically, you should hold them tentatively, never forgetting that new evidence may at any time lead to their abandonment. Do not accept new suggestions merely on the grounds of novelty, but analyse them critically and in the light of basic principles or proved results. Be especially careful in adopting new lines of treatment, bearing in mind that nothing is more difficult to establish than a fact in therapeutics.

There have been two periods in the history of Europe which have been remarkable for their enthusiastic curiosity about the facts of Nature, for the rapid acquisition of new knowledge and for the ability to show their observations as examples of general principles which reign throughout the natural order of things. We all know something of the extraordinary flowering of the classical Greek civilization in science and philosophy—in certain parts of which their work has not been improved upon to this day. The Greek genius was philosophical, lucid, and logical; it was interested in generalities, and showed clear thinking and bold reasoning. The Greeks not only began scientific medicine, but they provided the basic elements of anatomy, physiology, and pathology. It is from the Greeks that we get most of our medical terms. Only the Greeks among all the nations of antiquity practised a system of medicine based not on theory and superstition, but on the observation of clinical facts accumulated systematically as time went on. Nor did they ever forget that disease was a departure from the normal.

Thus Herophilos—he who first described the torcular Herophili, the wine press, the confluens of the sinuses in modern prosaic anatomical nomenclature—wrote in the third century B.C. : "Science and Art have equally nothing to show that strength is incapable of effort, Wealth useless and Eloquence powerless if Health be wanting."

This efflorescence of Greek science was short-lived and was followed by a long period of stagnation. Indeed, it has been affirmed that during the period extending from the end of the first to the end of the fourteenth century no radical advance was made in technology.

It is our privilege and our responsibility that we are living in the second of the two periods in history, when there has been a disinterested search for knowledge, when there have been men "pre-eminent in elucidating the laws of Nature and in applying them to the service of man."

In contrast to the Reformation, which was a popular uprising, and the wars of religion which drenched Europe in blood for a century and a half, the beginnings of science were simmering quietly in the minds of a few of the intellectuals, such as Copernicus, who introduced a new conception of the universe, and Vesalius, who is rightly regarded as the father of modern anatomy because he went for his anatomical facts, not to the writings of the authorities, but to the subjects in the dissecting room. Both typify the new mode of thought which is now accepted,

namely, the establishment of general principles in relation to what William James called "irreducible and stubborn facts." As Whitehead has said, "It is this union of a passionate interest in detailed facts with equal devotion to abstract generalization which forms the novelty in our present society." We might here say, in parentheses, that the main business of universities is to transmit this tradition as a widespread inheritance from generation to generation.

Thus by the end of the Middle Ages, a new mentality is revealed with invention stimulating thought and thought stimulating invention; for in the year 1500 Europe knew less than Archimedes, who died 212 B.C. Yet, in 1700, Newton's "Principia" had been written and the world was well started on the modern epoch.

If the sixteenth century saw the first definite beginning of the scientific approach, the following century was marked by an outburst of literary and scientific genius —the like of which had not been seen from the days of Greek thought at its apogee. "Hamlet" was published in 1604; Bacon's "Advancement of Learning" and Cervantes' "Don Quixote" in 1605. By 1616 Harvey put physiology on a firm foundation by his demonstration of the circulation of the blood, and Newton was born in the year that Galileo died (1642) at the time that Descartes published his "Meditations." It has been claimed that the combined labours of four men— Galileo, Newton, Descartes, and Hughens (who suggested the wave theory of light)—have the right to be considered as the greatest single intellectual success which mankind has achieved, for their work compressed into one logical picture a concept which extends from the limits of the stellar universe, on the one hand, to the dimensions of a wave-length of light on the other.

The nineteenth century shows the flood-gates of knowledge and technology to have been opened wide by men, who, with a new consciousness of power and of a mission, were attacking unknown problems in every branch of learning from the decipherment of Egyptian hieroglyphics to the discovery of a new element in the sun. In medicine it saw the introduction of anæsthesia, the discoveries of Pasteur and their application by Lister. The birth of one new branch of biology was announced in the middle of the century, but ignored and forgotten until the end of the century, and its significance is not yet appreciated. I refer to the theory of heredity as founded and explained by Mendel. The origin and nature of life and the mystery of reproduction and the similarity of one generation to the next has always been a challenge to the enquiring mind. It has only been during the past fifty years that the processes of reproduction and heredity have been demonstrated and understood; and in so doing they have led us to understand the evolution of life, infection and disease, and the nature of race and class and the development of society. It is not easy for us to appreciate the difficulties experienced by the first enquirers after truth in this field. The great problems of spontaneous generation, of virgin birth, of the relative influence of the male and female in heredity, of the inheritance of acquired characters were still being settled by invoking magic or superstition. It is worth recalling that the path which led to our present conceptions of these problems was opened up by the invention of the microscope, which was made a serviceable instrument in 1650. It proved so useful a key that within ten

years Swammerdam had been able to see the red blood corpuscles, and Malphigii the blood circulating in the capillaries of the lungs and had thereby supplied the missing link in Harvey's theory of the circulation of the blood.

In 1672 de Graaf observed the follicles in the ovary, which have been known by his name ever since, and just three years later, in the same Dutch town of Delft, Antony van Leeuwenhoeck recognised spermatozoa. But another one hundred and fifty years were to elapse before Von Baer recognised the ovum within the Graafian follicle, and it was only in the second half of the nineteenth century that the nuclei of ovum and sperm were seen to fuse, and the movement of the chromosomes observed and analysed.

When talking of the ovum the late Professor Walmsley told his class that the thought that each individual started life as a microscopic ovum should make them philosophical, but I cannot say that I was aware that his anatomy class showed any evidence of being more philosophy conscious. I can assure you that I shall not therefore be disappointed if you fail to be impressed by the statement that the 40,000,000 sperms which carry one-half of the heredity of Britain—and all that that heredity stands for—go into a space no larger than the head of a pin. Perhaps I should hasten to add that the distaff half of heredity is a bigger half, not necessarily on genetical grounds the better half.

Important as these observations were, the centre of the biological stage was held in the mid-nineteenth century by the doctrine of evolution, of which the world was made suddenly and painfully conscious by the publication of Darwin's book on the "Origin of Species." Darwin had been a world traveller and world observer, and had come to accept the idea of change of species from his observation of plants and animals chiefly in the New World. He had noticed that plants and animals in South America were nearly all of different species from the Old World, though families and genera were common to both. Moreover, in small islands like the Galapagos, each island had its own species—ten species for ten islands—while the vast continental land mass of South America might have only one species. All this was hard to explain as the result of a special creation.

Two years after his return home from South America, an English clergyman, Malthus, pointed out that more children are born than ever live to become parents, and this idea, coupled with the knowledge that farmers and breeders had been continually altering various races of domesticated plants and animals, gave Darwin the idea of natural selection.

These were the facts that pushed Darwin over the edge from believing in the fixity of species to believing in their variability, for in its simplest terms that is what evolution means—that a species is not fixed for all time but is capable of variation.

However, all theories of origin and variation in species, and all workers on the problem, including Darwin, were handicapped by a lack of knowledge of the mechanism of heredity. It was actually while Darwin was writing his famous book that Gregor Mendel took the first significant step in elucidating a problem

which had hitherto baffled all attempts at solution. He was successful, as have been all the great experimenters, because he asked the right questions under the right conditions.

It is interesting to compare Darwin and Mendel. As we have seen, Darwin was a world traveller; he was interested in generalizations of long-term processes. His mind was contemplative; he was no experimentalist, but his book achieved an immediate and widespread publicity which no doubt was increased by the violent protests which it evoked among the theologians. On the other hand, Mendel was fixed at one spot. His world was his monastery. He was an abbot, reared in an atmosphere of scholastic philosophy. Mendel used the microscope; Darwin did not. His mind was analytic, and his bent was experimental. Moreover, his work was published in the Proceedings of the Brunn Natural History Society, where it lay unread and aroused neither interest nor antagonism, yet it contains the seeds of ideas more significant for theology than anything in Darwinism.

The theory of evolution is academic because the time processes necessary involve such long periods of geological time, of which historical time and, much more, the allotted span of a human life are such infinitesimal fractions, but it stirred up the feelings of the man in the street in no uncertain way. It is difficult for us, a century later, to realize the excitement and tension in the public mind which followed the publication of his book. It probably reached its peak at the famous meeting of the British Association with the controversy between the Bishop of Oxford and T. H. Huxley. What a contrast with the recognition of the first facts of Mendelism, which was born in the quiet of a monastery garden in 1865, and the importance of which is only now slowly and reluctantly being recognised.

You are all aware of Mendel's ratios and his conception of segregated characters which do not fuse but are free to reappear in the third or the thirtieth generation. But Mendel also recognised, slowly it is true, but none the less vividly, because it was at variance with his scholastic training, that this segregation of factors—or genes, as they are now called—gave a deterministic interpretation to heredity. It is only with the last few years that the revolutionary nature of Mendel's "elements which determine" have been appreciated. Mendel's conclusion was derived from a carefully designed experiment. The work of Weissmann and other Germans supplied the cytological foundation to Mendel's work by demonstrating the presence and numbers of chromosomes and their reduction to half at germ cell formation. A further and important advance was made by another Catholic priest called Janssens, who saw under the microscope that the chromosomes, after pairing, are held together at certain points called chiasmata when the chromosomes break, cross over and reunite. This is a fundamental and generally accepted principle in genetics, and explains the greatest stumbling block in the popular conception of heredity, which assumes that children of the same parents have the same heredity; but this is not so, because a rearrangement of the order of the genes in crossing over creates a new genotype just as a rearrangement of the letters of the alphabet forms a new word. It is a Mendelian paradox that brothers differ by heredity and because of heredity.

When the late Sir William Bateson was lecturing to the troops in 1917 on heredity a Scottish soldier said to him : "Sir, what you have been telling us is nothing but scientific Calvinism." Bateson reported the remark as "something strange and novel—a flash of illiterate inspiration." But all the workers of Europe and America on heredity for the previous fifteen years had been so engrossed in their experiments and ratios that they did not notice this main principle of Mendelism—only the soldier saw the implication.

The medical profession, of course, from the earliest times, has had some knowledge of heredity as it applied to man and some of his diseases, but the common use of the terms congenital and familial indicates that the doctors' idea of inheritance were as hazy and obscure as those of the biologist. It has been recently remarked that human genetics was a harmless occupation pursued by doctors who knew no genetics or by geneticists who knew no medicine; but as each group learns more of the other's work that gibe will cease to have point.

The discovery of new and more complicated principles in heredity has served only to strengthen and confirm the conclusion that the genetics of man is essentially like those of other organisms. Nearly every basic law and principle of modern genetics has been observed in man, and indeed some, such as sex-linked inheritance, were first derived from him as material. The difficulty of the genetic analysis in man has arisen not only from the large number of factors involved and the absence of pure lines, but also because of the few non-pathogenic variations in man which show a simple Mendelian characteristic; and it is only single genes which show this simple relationship. The only recognised single gene differences in man, which are relatively frequent and are apparently non-lethal in their effects, are three in number, being the genes for blood group antigens, taste deficiency for certain chemicals and colour blindness.

The earlier studies in human heredity dealt with individual families, and were largely concerned with obvious abnormalities. The newer types of twin and twin family studies show signs of being a fruitful approach to the less simple examples of Mendelian inheritance. Already such work has seen its application in the clinical detection of genetic carriers of disease, in the solution of immunological problems such as hæmolytic disease of the new-born and in medico-legal problems such as that of disputed paternity. Further, it is now realised that the very earliest signs of a disease, so often unrecognisable, are to be found more frequently in relatives of a patient with open manifestations of that disease. Thus new and earlier facilities for diagnosis and treatment are provided. Less obviously, genetics plays a part in infectious diseases, both as regards the host and the parasite. One of the most remarkable differences between races is the varying degree of resistance to a given disease. We remember that infection is a struggle between the patient and the infecting organism, and that the reaction of the organism, like that of the host, is within limits which are genetically controlled. When infection is carried to a fresh community the result can be devastating, as in the case of tuberculosis among North American Indians, or measles in the Fiji Islands. Not all diseases

are exported with civilization, some are imported; probably the best example is the introduction of syphilis into Europe by Columbus and his sailors. The initial virulence of syphilis and for the next fifty years indicates that it was fresh seed sown on fresh soil.

The infecting micro-organism in adopting a life of parasitic ease becomes less resistant to other environmental factors, including anti-bacterial drugs. The number of resistant organisms which have appeared in recent years indicates that, in the treatment of infections, it is necessary to aim at curing the patient, without developing resistant strains of organisms.

Though medicine has supplied many of the known data of human inheritance to the science of genetics, the effect of genetics on medicine has not been as great as it could and should be. One of the most notable and fortunate exceptions to this remark is that of the blood groups, the existence of which was discovered by Landsteiner in 1901.

It might not be inappropriate to mention here that this knowledge of blood groups is applied constantly in every hospital for preparing blood for transfusion in surgical and obstetrical patients. The routine use of blood for those who have been severely injured or who are undergoing major operations has come to pass, largely through the agency of two world wars, and has proved invaluable in saving innumerable lives by making the patient safe for surgery and surgery safe for the patient. It is only those medical and nursing personnel who are in daily touch with such cases who are in a position to appreciate fully what the constant supply of new blood means to the desperately ill. I know I am speaking on behalf of both doctors and patients when I pay tribute to the blood donors throughout the country and to the members of the Blood Transfusion Service who collect and type the blood ready for use.

Every successful blood transfusion and every baby saved despite Rh incompatible parents bear witness to the practical value of this item of applied genetics. Anyone who has seen the tragic consequences of a transfusion of blood from a donor of an unsuitable group requires no further proof of the reality and importance of blood typing. It is a vindication of Mendelism and a salutary thought that the blood from one's own parent or offspring may be fatal when transfused, though that of a person of a different race and colour but of the correct group can be life-saving. Yet in the Southern United States of America, so strong is the racial feeling between black and white that any doctor who transfuses a white patient with the blood of a black donor is laying himself open to strongest legal action. It affords one of the best examples how far astray the human mind can be led by ignorance and bigotry.

As we have seen, the inheritance of normal or non-lethal factors by single genes in man is confined to blood group antigens, colour blindness and taste deficiency for certain uncommon chemicals; in contrast, many pathological processes obey the simple Mendelian rules of single gene defects; of these there are more than one hundred known in each of three groups affecting the skin, the eye and the

skeleton, and there are about a score concerned with diseases of the blood, of the muscles, of metabolism and of the nervous system. As the biochemical explanations are more fundamental than anatomical, it is of interest to note that many metabolic disorders have long been recognised and described, particularly in that remarkable book of Garrod's, *Inborn Errors of Metabolism*, with special reference to albinism, alcaptonuria and cystinuria and the other disorders associated with definite compounds excreted in the urine. Garrod has rightly been called the Father of Chemical Genetics.

You may reasonably ask of what practical use is the study of heredity in the practice of medicine, and of the many answers perhaps the most important is the advice which you will be able to give to sufferers from inherited disease. Many of these know that heredity is a factor in their trouble and will come to you for advice as to whether they should marry; if they marry, should they have children, and if there are children, what are the chances of the children inheriting the disease in question. How important this may be is shown by the report in the "British Medical Journal" some time ago of a family of four, three of whom had that very malignant tumour glioma of the retina. The father of these children had had a successful operation for the same condition when a child. Such case reports raise questions of the greatest ethical importance. Again, in diabetes, there is sufficient evidence to show that in a fair percentage heredity is a factor. Formerly diabetic children did not live to grow up. Now the young diabetic lives to produce children, raising a problem both for himself and the eugenist. The term eugenics was introduced by Sir Francis Galton, and, as his pupil, Karl Pearson, pointed out: "The word *eugenics* has the double sense of the English *well bred,* goodness of nature and goodness of nurture." There is much confusion about the practice of eugenics and it may be that the enthusiasm of some eugenists has outrun our existing knowledge. Sir F. Galton himself said: "Natural selection rests upon excessive production and wholesale destruction; eugenics on bringing no more into the world than can be properly cared for and those only of the best stock." The importance of eugenics has been enhanced by the progressive adoption of the practice of birth control, which is biologically a recent and racially harmful development.

The study of blood groups and metabolic errors belong to the laboratory and the appropriate techniques cannot be applied to the great mass of clinical material, and other methods have to be devised. One of these is the study of twins. Two-egg twins may be as different as Jacob and Esau, but one-egg twins have long been known for their similarity. The device of comparing the properties of twins was discovered by Galton, and in his *Inquiries into Human Faculty* his research proves the vastly preponderating effects of nature over nurture. The resemblance of one-egg twins extends far beyond their appearance; their susceptibility to disease is similar, e.g., recently identical twins were admitted to this hospital on successive days and each suffering from a perforated duodenal ulcer; identical twins have one and the same blood group, and their capacity for mutual transplantation of

skin grafts is unique. A German investigator, Lange, studied the criminal tendencies and records of identical twins. He investigated thirteen pairs of one-egg twins in which one of the pairs was a criminal. In ten out of the thirteen instances, the other was a criminal too. Lange called his book *Crime as Destiny*. Further, Lange found that his pairs of twins often rose or fell in the social scale with respect to their families, but the twins always rose or fell together. Lange's work has an important bearing on the study of heredity in general as well as on the heredity of crime, because it helps to sort out what is important in the environment from what is inherited. Thus we can see the force of the Second Commandment in visiting the iniquity of the father unto the third and fourth generation, though we may query the notion of vengeance when heredity and environment play such an important part in wrongdoing. The evidence from these criminal twins show that deterrence and reformation are of limited scope in treatment of criminals.

Although it is now over eighty years since Galton discovered the value of one-egg twins, the importance of this field has not yet been really recognised and a vast field of enquiry is awaiting exploration, e.g., the failure of transplants from one person to another is due primarily to chemical differences which are specific to the individual, and the chief differences may become manifest in allergic reactions to the inhalation of pollen or the ingestion of eggs, or the handling of primulas. The relative importance of inheritance and environment in cases of allergy can most readily be deciphered in the study of twins. Another field for twin studies is education. Absence of opportunities or an unfavourable environment will prevent the proper development of the genetic potentialities, for we know that a child deaf from birth will have a less well-developed level of intelligence. Thus many of our efforts in the three great fields of health, education and prevention of crime will be altered for the better when we are in a position to study and evaluate the similarities and difference of large numbers of twins.

Already we have learned sufficient from the similarity of twins to enlarge and emphasize the genetic control and determination of those properties and characters which go to make the individual. These include our general form and character, our height and the structure and quality of all our tissues, our endocrine systems, our temperaments and social habits—whether solitary or fond of company, affectionate or the reverse. Also included are our intelligence, our memory, facilities for imagination and reasoning and therefore our educability, our susceptibility to disease, whether infectious or not, and last, but by no means least, our sex, male or female, depending on whether the ovum selects an X or Y. In all these respects our properties are limited and prescribed in the fertilized egg; they are inherited in every cell of the body and are carried in them from conception till death. The genes which determine these qualities mediate through chemical changes, physiological processes, and anatomical structures. While this means a sentence of predestination, it is also the index of individuality. As Darwin pointed out, the mother recognises her own offspring, from among millions, whether she is a human mother, or a ewe or a mare, and each of us is also conscious of his or her individuality.

It is this determination which maintains our individuality, our peculiarities and our dispositions from the cradle to the grave and provides each with his own degree of self-esteem and pride. This, of course, has long been known and has given rise to such proverbs as "the child is father of the man" and "what is bred in the bone comes out in the flesh."

It is to the credit of the Church that it has always known and emphasized the importance of the individual. The recognition of individuality is also the basis of the working of the law and the practice of medicine. Indeed it is the primary cause of our existence as doctors, for if it were not for the tremendous problem of individual diversity the patient himself could cull from a text-book both his diagnosis and his treatment.

There are many aspects of individuality; it accounts for the different impressions which two persons have of the same scene; they see the world through different eyes and speak in different voices, even when of the same dialect.

The increase in individuality which follows adolescence accounts for that intolerance of each other's company, of brothers and sisters who played and romped together as children and for the estrangement which may develop between parent and offspring, between the parent's desire and child's inclination. Sir Edmund Gosse's *Father and Son*, with its revealing sub-title—"A Study of Two Temperaments"—is but one of many biographies of great minds which deals sympathetically with this problem.

Perhaps the most striking contrast in the past three centuries is man's reaction to man, is his tolerance of the other fellow's point of view. Indeed, this tolerance, though often incomplete and variable, has been a basic factor in the growth and strength of European civilization. The appreciation of the need for tolerance was emphasized by John Milton in his Areopagitica, which he calls a speech for the liberty of unlicensed printing. The need for preservation of freedom of thought, and that means freedom of speech, is as great now as ever, not only in Europe, but even more strikingly in the United States, the traditional home of political freedom. For history shows that intolerance has never paid. After the revocation of the Edict of Nantes, France intensified her persecution of the Hugenots. Her subsequent loss was Ulster's gain. During the last war Germany might have been first in the field with atomic bomb had Hitler not expelled his Jewish physicists.

In spite of Linnæus putting all men into the one species *homo sapiens*, many observers have considered that the different races of mankind are distinct species. Darwin had difficulty in explaining the origin of the different races; he said : "Since not one of the external differences between races of man is of any direct or special service to him, there remains one important agency, namely, sexual selection. All over the world beauty plays an important part in sexual attraction, but as the standard of beauty varies, so does the appearance of the different races. Darwin's theory is as plausible to-day as when it was first written. The underlying explanation, however, is changed by one fact of which Darwin was unaware—namely, the Mendelian ratio of chromosome propagation. By the halving of the chromosome

number at meiosis and its restoration at fertilization, an unexpected juggling of the chromosomes occurs; for in a population that is fixed in regard to numbers, each pair will beget on an average two offspring. Hence in this population one quarter of the chromosomes will be lost in every generation, one quarter will be doubled. The loss or the doubling is by chance. This Mendelian ratio is the most important of all, for it is the Mendelism of race. For natural and sexual selection by permitting the survival of some offspring and not of others determines which quarter will be doubled and which will be lost. Nobody could realize, before this chromosome shuffling was seen under the microscope and was demonstrated by breeding, with what tremendous stakes selection could play. This process of selection acts not merely on genes, chromosomes and individuals, it acts also on the group of individuals which form a stable community. This community forms of its chromosomes a pool from which individuals are begotten and into which they return their genes in begetting. The importance of the community in this respect was another of Francis Galton's discoveries when he described colour blindness among the Quakers, a group to which he himself belonged. He wrote :—

> "I may take this opportunity of remarking on the well-known hereditary character of colour blindness in connection with the fact that it is nearly twice as prevalent among the Quakers as among the rest of the community. Nearly every Quaker is descended on both sides solely from members of a group of men and women who segregated themselves from the rest of the world five or six generations ago; one of their strangest opinions being that the fine arts were worldly snares, and their most conspicuous practice being to dress in drabs."

We now know that colour blindness is controlled by a single gene. What is true for one gene in the Quakers is true of all genes in all communities.

These remarks of Galton's form the first genetical analysis of civilization, an analysis which now shows that the genetically fixed capacities of the individual influence his beliefs and social behaviour; that these, in turn, influence the groups in which the individuals will mate, and that the mating group selects and concentrates the genetic capacities of the individuals within the group. Thus the formation of a mating group by people who are mutually attracted and culturally and genetically alike has a cumulative effect, because amongst human beings, as opposed to all other living organisms, the group forms an important part of the environment. It has not always been realized that a whole community working for generations is needed to make a culture which is adapted to the nature of the individuals of that community and which will give that stable and harmonious relation to his environment which is characteristic of each of the historical civilizations. In this connection language has become a powerful agent in determining the size and nature of the genetic pools within which the genes and characters of the group are recombined.

The history of Britain during the past millennium has been determined largely by the succession of conquests which ceased with the invasion of the Normans in 1066. The nine hundred years which have elapsed since these have allowed of the

coming together of the characteristics of the earlier races to form a stable genetic pool from which has sprung the Englishman of to-day and his culture. The United States is now going through the same genetic process as Britain did in the eleventh century, for the great influx of various races and cultures is now in the process of active genetic recombination. As the genetic pool works towards equilibrium, a rejuvenation and increased vigour may be expected in its inhabitants, quite apart from the benefits arising from its natural resources or scientific advances. Accordingly, we are witnesses of perhaps the greatest experiment in the development of human races which the world has yet seen. Though scattered over half a continent, the absence of political frontiers and the constant mixing allowed by the rapid and easy facilities of modern transport puts the population of the United States in a position to maintain its vigour and uniformity for generations.

History has many examples of stable civilization, the most notable, perhaps, being the Ancient Egyptians, who formed a more or less closed genetic community for 3,500 years; China, for a similar time, but on a much grander scale, has maintained its own uniform culture. It may be that this country and the United States will exist in the millennium to come, but the greatest risk for non-survival is not from any likely natural catastrophe, but from the hand of man, through the agency of the atomic bomb. A high explosive shell will blast a body, but the atomic bomb, acting on the chromosomes of the radio-sensitive germ cells, will blast human heredity itself for all time.

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Clinical and Therapeutic Aspects of Thrombocytopenic Purpura

By M. G. NELSON, M.D., M.R.C.P.

Royal Victoria Hospital, Belfast

THE title Morbus Maculosis Werlhofii for the severe form of purpura hæmorrhagica is derived from the fact that the first clear and accurate clinical account of this condition was made by Werlhof in 1775. However, over two centuries earlier, a Portuguese called Amatus Lusitanus described in one of his works, under the title of Morbus Pulicaris Absque Febre, the case of a boy with undoubted acute hæmorrhagic purpura who had a spontaneous recovery. Indeed, little can be added to-day to these earlier clinical descriptions which are full of the fruits of keen observation and reflect the scholarship of their age.

The disease is characterised by the presence of petechial hæmorrhages in the skin—compared by one earlier worker to "flea bitings." These are more commonly seen in the limbs but may also occur on the trunk. These minute hæmorrhages may spread to produce purpuric spots or coalesce to form extensive superficial ecchymoses. Associated lesions are commonly seen in the buccal mucosa where they assume the characters of blood filled blisters. These manifestations are associated with free bleeding from mucous surfaces with epistaxis, hæmaturia, hæmatemesis or persistent oozing from the gums. In women profuse uterine bleeding is not uncommon and may be the presenting sign and reason for the patient's hospitalisation, as it has been in two of our cases.

It was not until late in the nineteenth century that Bizzozero (1882) noted the relationship of blood platelets to clot formation and this was quickly followed by the observation in some cases of purpura of a diminished number of circulating blood platelets. Thus, the understanding of the function of blood platelets preceded any knowledge as to their origin, which was the subject of considerable dispute until Wright (1910) clearly demonstrated platelets budding off from the megakaryocytes of the bone marrow.

Further study of the relationship of circulating blood platelets to the presence of clinical purpura received intensive study which revealed that there were two major kinds of purpura. In the first of these the number of circulating blood platelets is normal. This is called non-thrombocytopenic purpura and in this type the bleeding is almost certainly due to a disturbance of the walls of blood vessels. In the second type the number of circulating blood platelets is reduced. This is called thrombocytopenic purpura and in this type the bleeding is clearly related to the diminished number of circulating blood platelets although an associated vascular defect cannot be entirely excluded.

Purpura with a decrease in the circulating blood platelets can be produced in a number of ways. It is often secondary to other diseases, particularly those diseases of the hæmopoietic system, which are associated with marrow replacement and consequent reduction in the number or interference with the function of the parent megakaryocytes. Thrombocytopenic purpura may also be caused by the damaging effect of hæmatotoxic drugs on the megakaryocytes of the bone marrow. Because of the ætiology, this type is known as 'secondary thrombocytopenic purpura.' In other cases, however, no known cause for the thrombocytopenia can be discovered and these are classified as 'primary' or 'idiopathic thrombocytopenic purpura.'

Idiopathic Thrombocytopenic Purpura.

The mechanism for the production of thrombocytopenia in this type of purpura has been the subject of controversy. The theories can be broadly classified into those which envisage increased peripheral destruction or utilisation of platelets and those which regard the reduced platelet count in the peripheral blood as being the result of diminished platelet formation in the bone marrow. Kaznelson (1916) postulated an accelerated phagocytosis of platelets by the spleen and introduced splenectomy for treatment. This theory of excessive destruction of platelets in the reticulo-endothelial system is supported by Wiseman, Doan and Wilson (1940). An alternative method of producing a diminution of circulating blood platelets by peripheral utilisation was suggested by Tidy (1926). He considered that the primary defect lay in the capillary endothelium and that excessive numbers of platelets were used in plugging vascular breaches.

The opposing theory of diminished platelet formation has many adherents since Frank (1925) first suggested that the peripheral thrombocytopenia was due to reduced platelet formation from megakaryocytes under the influence of the spleen. This led Troland and Lee (1938) and many others to attempt to produce thrombocytopenia in experimental animals, using splenic extracts. These experiments produced very variable results. Indirect support for this theory of Frank was adduced by Dameshek and Miller (1946), who demonstrated the presence of a marked hyperplasia and maturation arrest of the megakaryocytes in the bone marrow of untreated cases of chronic purpura. The restoration of the megakaryocytic pattern to normal following splenectomy led these authors to postulate the presence of a splenic inhibitory substance which caused arrest of megakaryocytic maturation.

The theory of peripheral platelet destruction has once again come into prominence following the work of Evans et al. (1951), who put forward evidence of an auto-immune mechanism in thrombocytopenic purpura similar to that responsible for the erythrocytic destruction in acquired hæmolytic anæmia. This has been supported by Harrington and his co-workers (1951), who have demonstrated an anti-platelet immune body in the serum of some patients with thrombocytopenic purpura. Such a serum is capable of producing

thrombocytopenia and clinical purpura when injected intravenously into normal individuals.

From the diagnostic point of view idiopathic thrombocytopenic purpura is regarded as that group of diseases characterised by a hæmorrhagic diathesis which manifests itself as ready bruising or free bleeding from mucous surfaces. Hæmorrhages may also occur into the skin producing petechiæ, purpuric spots or ecchymoses. The bleeding time is prolonged, the capillaries are unduly fragile and, although the clotting time is normal, the clot fails to retract normally. The platelet count is usually less than 100,000 per c.mm. but no evident cause for the thrombocytopenia can be found. There may be slight anæmia but severe anæmia is uncommon, and whatever its degree it is always explicable by the severity of the blood loss. Enlargement of the spleen is so uncommon in primary thrombocytopenic purpura that it can be used as a clinical differential diagnostic sign from purpura secondary to diseases of the reticulo-endothelial system.

Acute Idiopathic Thrombocytopenic Purpura.

Although all cases of idiopathic thrombocytopenic purpura satisfy the above general diagnostic criteria, two distinct clinical varieties of this disease occur (Hirsch and Dameshek, 1951). These differ in onset, clinical course, treatment and prognosis. The first of these is acute thrombocytopenic purpura which is well illustrated by the following case :—

Case 1.—A 41-year-old woman with no family history of bleeding had never suffered from any tendency to hæmorrhage during her lifetime and had not taken any drugs. One day she slipped and fell, bruising her left leg. This bruise spread to produce an extensive ecchymosis. Within four hours both her legs became covered with numerous small blue spots and further large spontaneous bruises appeared. Severe epistaxis and vaginal hæmorrhage then developed and she was immediately admitted to hospital. On examination there was generalised and extensive purpura of the skin of all four limbs, chest, and abdomen. This was most marked around the ankles and was associated with several large ecchymoses. Purpuric spots and blood-filled blisters were present on the buccal mucosa. Bleeding occurred from the nose and the vagina and catheter specimen of urine contained visible macroscopic blood.

The hæmoglobin was 74% Haldane = 10.9 gms./100 ml.; erythrocytes 3.74×10^6 per c.mm.; leucocytes 3,100 per c.mm.; platelets 90,000 per c.mm.; bleeding time grossly prolonged; clotting time normal; clot retraction poor. While in hospital the epistaxis continued despite local hæmostatic measures and further crops of purpuric spots appeared. Two days after admission, when the platelet count had fallen further to 52,000 per c.mm., the patient received one pint (570 mls.) of fresh compatible whole blood. The bleeding immediately ceased from all mucous surfaces and the purpuric rash subsided. Ten days after the onset the patient had recovered completely; the platelets had risen to 280,000 per c.mm.; the bleeding time was normal and the clot retraction good.

In this case the onset was sudden and dramatic in a patient with no previous history of bleeding or ready bruising. Following an injury the patient noticed a shower of purpuric spots on the legs which spread to involve the trunk and upper limbs. These purpuric spots coalesced to form large ecchymoses. Bleeding occurred from mucous surfaces with gross epistaxis and menorrhagia. Examination of the blood showed a low platelet count which fell at one time to 52,000 per c.mm., and

a poorly retractile blood clot. The bleeding time was grossly prolonged. The clinical manifestation lasted only a few days and the platelet count returned to normal in ten days, the patient making a complete recovery. As acute thrombocytopenic purpura is a self-limited disease with spontaneous and permanent recovery usually within 4 weeks, treatment consists largely of expectancy. In purpura there is always a danger of cerebral hæmorrhage in patients over 40 years of age and consequently it may be necessary to control the hæmorrhagic episodes by transfusions of fresh (not stored) whole blood. Splenectomy, which always carries an added risk if performed during an acute hæmorrhagic phase, is not usually indicated.

Chronic Idiopathic Thrombocytopenic Purpura.

In chronic thrombocytopenic purpura the onset is gradual and the patient usually gives a history of bleeding or ready bruising for many years with periods of exacerbation and remission. Scattered petechiæ may appear from time to time but true purpura may be entirely lacking. For this reason Hirsch and Dameshek (1951) have suggested that the term purpura should be omitted from the descriptive title of the disease which they suggest should be known as the "chronic" thrombocytopenic state.

In this type of purpura the platelet count is only significantly reduced at periods of relapse and in periods of remission may be normal. This also applies to the other tests used in the diagnosis. On examination of the bone marrow the presence of a megakaryocytic hyperplasia with no evidence of platelet production is the usual but not invariable finding and it was this which led Dameshek and Miller (1946) to postulate an inhibitory effect on the marrow by the spleen in this disease.

Although splenectomy is usually immediately curative of the bleeding tendency, as the normal course of the disease is subject to spontaneous fluctuations, the treatment can only be regarded as successful if no further bleeding has occurred for a period of six months after operation and if the platelet count remains normal for the same period.

The following is an example of a case of chronic thrombocytopenia successfully treated by splenectomy :—

Case 2.—A 22-year-old chemist's assistant had always had severe and prolonged menstrual bleeding since her menarche at 14, although her cycle was regular. She had noticed a tendency to undue hæmorrhage from tooth extractions and superficial wounds but had not noticed spontaneous hæmorrhage or 'spots' on the skin. There was no family history of bleeding and the patient had not been exposed to any toxic drug.

When seen at the outpatient department her hæmoglobin was 75% Haldane = 11.1 gm./100 ml.; platelets 110,000 per c.mm.; bleeding time 6 mins.; coagulation time normal; prothrombin 100%.

One month later she was admitted to hospital for investigation of her menorrhagia and when in hospital she suddenly developed showers of petechiæ on her chest and limbs and bleeding from the gums. The spleen was not enlarged. The bleeding time was 18 mins.; coagulation time normal; platelets 46,000 per c.mm.; capillary fragility increased. Examination of her bone marrow showed a marked megakaryocytic hyperplasia with maturation arrest.

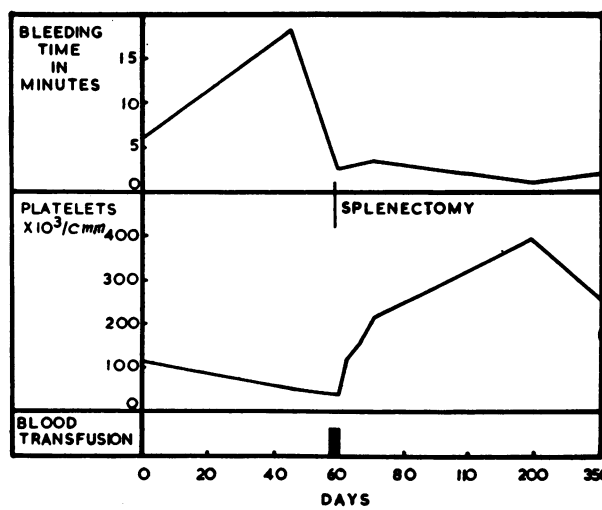
TABLE 1.

	Pre-Splenectomy	Six Months' Post-Splenectomy
Hæmoglobin gm./100 ml.	10.4	14.8
Erythrocytes per c.mm.	3.5	4.8
Leucocytes per c.mm.	11,000	10,750
Platelets per c.mm.	46,000	392,000
Bleeding Time/mins.	18	1′ 30″
Capillary Fragility	Increased	Normal

This shows the hæmatological response to splenectomy in Case 2.

Splenectomy was carried out because of continued profuse vaginal bleeding uncontrolled by blood transfusion and associated with a further fall in the blood platelets. Bleeding at operation was profuse but controllable by local application of topical thrombin. On the fifth post-operative day signs of severe internal hæmorrhage appeared. This responded to transfusion of one pint (570 ml.) of fresh whole blood and convalescence thereafter was uneventful. Since operation the patient has had no further bleeding and has successfully undergone a plastic operation for removal of scars from her face. When seen two years after her splenectomy the hæmoglobin was 95% Haldane = 14.1 g./100 ml.; platelets 270,000 per c.mm.; bleeding time 2 mins.; capillary fragility normal and it would appear that splenectomy has produced marked clinical and hæmatological improvement.

GRAPH 1.



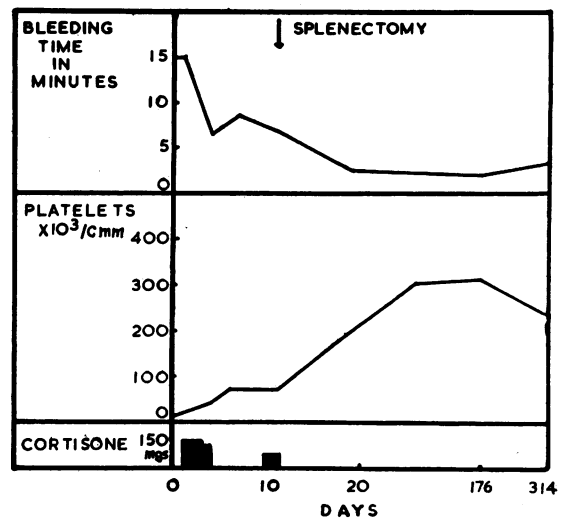
Showing the response of the bleeding time and platelet count to splenectomy in Case 2.

Cortisone and A.C.T.H. in the Management of Idiopathic Thrombocytopenic States.

The treatment of blood disorders with cortisone and A.C.T.H. by a large number of workers has shown that the most encouraging results are obtained in acquired hæmolytic anæmia and chronic idiopathic thrombocytopenic purpura but these

results are variable and often of short duration. In acute idiopathic thrombocytopenic purpura these drugs do not appear to have any significant effect. In chronic idiopathic thrombocytopenic purpura the effect of these hormones is largely on the blood vessels, with an improvement in the capillary resistance and a shortening of the bleeding time. An increase in the circulating blood platelets is less consistently produced. Because of these temporary effects, the use of cortisone and A.C.T.H. in the management of cases of thrombocytopenic purpura has

GRAPH 2.



The effect of cortisone and splenectomy on the bleeding time and platelet count of Case 3 are recorded.

been restricted to the control of acute episodes of bleeding in chronic idiopathic thrombocytopenic purpura and to the pre-operative preparation of patients for splenectomy.

In many cases of idiopathic thrombocytopenic purpura the decision as to whether the case is one of acute thrombocytopenic purpura or an acute exacerbation in a chronic case may present serious difficulty. The following case is such an example. This young girl presented with gross bleeding from mucous surfaces and into the skin. She failed to respond to whole blood transfusions or significantly to cortisone although this may have been due to the short period of its administration. An emergency splenectomy was then carried out which produced a complete clinical and hæmatological remission.

Case 3.—A 12-year-old schoolgirl had noticed bleeding from her gums for some three weeks. This was followed by the appearance of a generalised, fine purpuric rash over the whole body. She had numerous blood-filled blisters on her buccal mucosa and lips. The hæmoglobin was 59% Haldane=8.7 g./100 ml.; leucocytes 8,000 per c.mm.; platelets 50,000 per c.mm.; bleeding time 9 mins.; clotting time normal. A bone marrow biopsy failed to show any significant megakaryocytic hyperplasia but the sample

obtained was not entirely satisfactory. A few days later she had severe gastro-intestinal hæmorrhage with gross melæna and was transfused with 6 pints (3420 ml.) of whole blood. The gastro-intestinal hæmorrhage occurred intermittently for a period of one month; she developed vaginal bleeding and further crops of purpuric spots and required more transfusions of fresh whole blood. She was started on a course of cortisone when her hæmoglobin was 7.5 g./100 ml. = 51% Haldane; platelet count 14,000 per c.mm.; bleeding time more than 15 mins. and received 375 mgm. in 5 days without any clinical response although there was a diminution in the bleeding time.

As the condition of the patient was critical it was decided to remove the spleen. Accordingly pre-operative transfusion of fresh whole and stored blood was given to a total of 10 pints (5700 ml.) and a splenectomy successfully carried out. Two days after the operation the platelet count began to rise and the bleeding time to return to normal and she made an uneventful recovery which has been maintained for the six months that the patient has remained under observation.

TABLE 2.

	Pre-Splenectomy	Six Months' Post-Splenectomy
Hæmoglobin g./100 ml.	7.5	13.0
Leucocytes per c.mm.	19,400	9,650
Platelets per c.mm.	14,000	240,000
Bleeding Time	15 mins.+	2 mins. 12"
Clot Retraction	Poor	Good
Capillary Fragility	Increased	Normal

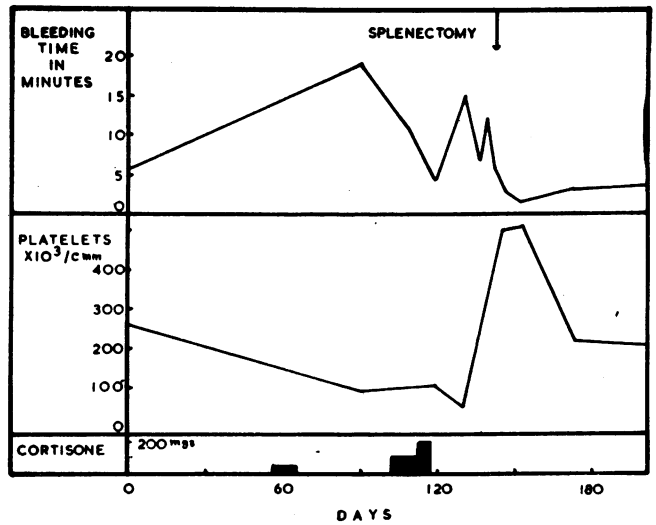
This shows the hæmatological response to splenectomy in Case 3.

In another case of chronic idiopathic thrombocytopenic purpura in a boy of 3 years, cortisone given in a dose of 100 mgm. daily for ten days produced considerable improvement in the bleeding time and platelet count but this effect was only temporary. A second remission was induced with cortisone and splenectomy successfully carried out.

Case 4.—A 3-year-old boy, with no family history of bleeding, first developed a generalised purpuric rash in March, 1952. There was no hæmorrhage from the mucous membranes and no joint involvement. At that time the hæmoglobin was 88% Haldane = 13.0 gm./100 ml.; leucocytes 12,000 per c.mm.; platelets 355,000 per c.mm.; bleeding time 18 mins.; coagulation time normal. The purpura subsided but recurred within two months when it was accompanied by ecchymoses and epistaxis. The bleeding time was still prolonged although the platelet count was normal. The hæmorrhagic diathesis responded to the transfusion of one half pint (285 ml.) of fresh whole blood but this produced only temporary benefit. In July, 1952, because of a recurrence of ecchymosis and epistaxis, the patient was readmitted to hospital. The hæmoglobin was 96% Haldane = 13.6 g./100 ml.; leucocytes 11,900 per c.mm.; platelets 98,000 per c.mm.; bleeding time more than 15 mins. The bone marrow showed no increase in the number of megakaryocytes or evidence of morphological abnormalities. A course of cortisone consisting of 100 mgm. a day for ten days was then given and the dose gradually reduced over a further ten days. This produced considerable improvement in the clinical evidence of bleeding, caused a rise in the platelet count in the peripheral blood and restored the bleeding time to normal. This beneficial effect, however, only lasted 14 days when the platelet count fell to 50,000 per c.mm., the bleeding time again rose to more than 15 mins. and clinical purpura and ecchymoses

reappeared. The boy was prepared for splenectomy by being given a short (5 day) course of cortisone consisting of 175 mgm. daily which again restored the bleeding time to normal. The post-operative course proceeded normally and no further episodes of hæmorrhage have occurred. The platelet count and bleeding time have been restored to normal by the operation and have remained satisfactory for the six months that the child has been observed.

GRAPH 3.



The effect of cortisone and splenectomy on the bleeding time and platelet count of Case 4 are recorded.

SECONDARY THROMBOCYTOPENIC PURPURA.

In secondary thrombocytopenic purpura a decrease in the circulating blood platelets may be produced as the result of the effect of hæmototoxic drugs, and among such drugs are the organic arsenicals. The appearance of purpura during the therapy of syphilis with organic arsenicals may occur with dramatic suddenness and subside spontaneously once the drug is withdrawn, as the following case which was previously reported (Nelson, 1952) illustrates.

Case 5.—A 30-year-old woman with secondary sero-positive syphilis had been treated with 3 mega units of penicillin followed over a period of somewhat less than a year by 3 g. of bismuth metal, 0.86 g. of mapharsan and 7.2 g. of neoarsphenamine when she suddenly noted the development of a black spotted 'rash' on her body and bleeding from her gums. On admission to hospital an extensive petechial rash was present over the face, arms and legs, being most extensive on the limbs. She was bleeding from the gum margins and numerous blood-filled vesicles were seen in her mouth. She had no hæmoptysis, hæmaturia, hæmatemesis or melæna. Her spleen was not palpable and there were no hæmorrhages in the optic fundi. A capillary fragility test was positive. The hæmoglobin was 12.0 g./100 ml. = 81% Haldane; erythrocytes 4.30×10^6 per c.mm.; leucocytes 5,700 per c.mm.; platelets 54,000 per c.mm.; prothrombin 100%; bleeding time greatly increased—25 mins.; clotting time normal. Examination of a specimen of bone marrow obtained by needle biopsy showed a normal cellular marrow with some reduction in the total number of megakaryocytes rather than a megakaryocytic hyperplasia with maturation arrest.

TABLE 3.

	During bleeding episode		After spontaneous recovery
Hæmoglobin g./100 ml. - -	12.0	...	17.0
Erythrocytes × 10^6 per c.mm. -	4.30	...	5.95
Leucocytes per c.mm. - -	5,700	...	5,700
Platelets per c.mm. - - -	54,000	...	240,000
Bleeding Time—mins. - - -	25	...	3
Capillary Fragility - - -	Increased	...	Normal

The spontaneous hæmatological recovery following drug withdrawal in Case 5 are recorded in this table.

On the day following admission the patient had a slight hæmatemesis and melæna but the purpuric rash began to fade and she made a complete and spontaneous recovery.

This case illustrates the phenomenon of the reduction in the number of circulating blood platelets with the development of purpura and spontaneous mucosal hæmorrhages as the result of exposure to a hæmatotoxic drug. This toxic action affected only one cell system in the marrow, viz., the megakaryocytes. Both the granulocytic and erythrocytic precursors were unaffected. There was no gross anæmia or leucopenia in the peripheral blood and, once exposure to the toxic drug ceased, a rapid rise in the platelet count occurred with spontaneous recovery.

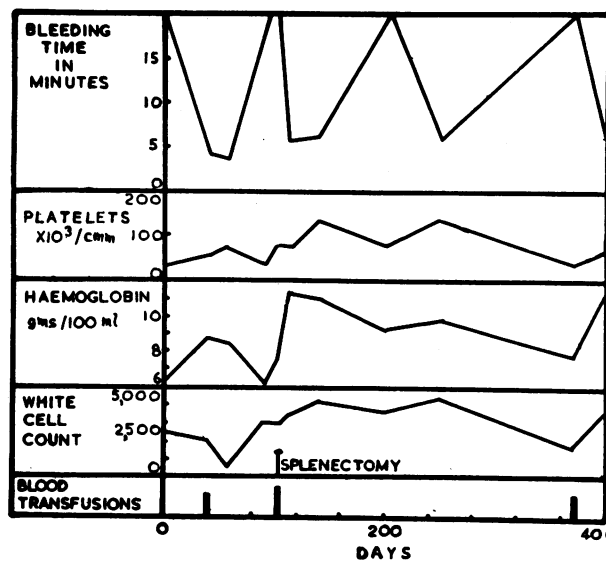
In patients with syphilis, who are treated by organic arsenicals and who develop thrombocytopenic purpura associated with peripheral pancytopenia, i.e., thrombocytopenia with severe anæmia and leukopenia, the marrow may be so damaged that recovery may not occur even with strenuous treatment with dimercaprol (Nelson, 1952).

The appearance of spontaneous bleeding or skin purpura may herald the development of an aplastic or primary refractory anæmia. In certain cases the hæmorrhagic diathesis may so dominate the picture as to raise the possibility of a diagnosis of primary idiopathic thrombocytopenic purpura. However, the presence of a persistent anæmia not explicable by blood loss and a granulocytopenia should arouse suspicion. The absence of primitive white cells in the peripheral blood and examination of the bone marrow will exclude the hæmorrhagic onset of a subleukæmic leukæmia. The bone marrow in chronic refractory anæmia may be cellular or even hyperplastic and is not necessarily aplastic. It is for this reason that the term 'primary refractory anæmia' is preferred for this group rather than aplastic anæmia where the peripheral pancytopenia is associated with a grossly acellular marrow.

Case 6.—A 22-year-old married woman had noticed, over a period of some ten months, that her menstrual loss had become increasingly heavy. She became weak and listless and was admitted to hospital, where she received a transfusion of eight pints (4560 ml.) of whole blood. The heavy menstrual loss continued and she developed frequent attacks of epistaxis which required her readmission to hospital. There was no enlargement of spleen or lymph nodes. Her hæmoglobin was 41% Haldane = 6.1 g./100 ml.; erythrocytes 1.84×10^6 per c.mm.; P.C.V. = 18%; M.C.V. = 100 cu; leucocytes 2,530 per c.mm.; platelets 35,000 per c.mm.; bleeding time 20 mins.;

clotting time normal; prothrombin concentration 100%; capillary fragility increased. The marrow obtained by needle biopsy was examined on three occasions and showed a cellular marrow with a normoblastic erythropoiesis. Megakaryocytes were inconspicuous in the marrow but showed normal morphology. Because of the peripheral pancytopenia and cellular marrow a diagnosis of primary refractory anæmia was made. However, as the hæmorrhagic diathesis continued despite fresh blood transfusions a splenectomy was carried out as a purely empirical measure in the hope of controlling the hæmorrhage. Since this operation her menstrual loss has been less heavy and no further bleeding has occurred from other sites. However, her platelet count is still low, her bleeding time intermittently prolonged and her anæmia and leucopenia still present.

GRAPH 4.



This graph shows the hæmatological changes which resulted from splenectomy in a case of primary refractory anæmia. The spontaneous fluctuations in the bleeding time occurring independently of the platelet count are particularly noticeable.

DISCUSSION.

Blood transfusion occupies pride of place in the treatment of purpura not only as a general supportive measure to combat shock and blood loss but also as an efficient hæmostatic. As platelets disintegrate rapidly in contact with glass surfaces freshly drawn whole blood is preferable to banked blood. The more recent experiments carried out on blood withdrawn through silicone-coated tubing and stored in silicone-coated glassware have shown that this reduces greatly the rate of platelet distintegration. This technique offers the hope of transfusing a more platelet-rich blood in the future. Indeed the therapeutic value of this form of treatment in thrombocytopenia and thrombopathia has already been reported (van Creveld et al. 1953), and in our hands has been most effective in controlling hæmorrhage and raising the platelet count.

If the hæmorrhage is due to a platelet deficiency produced by the effect of hæmatotoxic drugs acting on the megakaryocytes in the bone marrow, the outcome of drug withdrawal or elimination will largely depend on the degree and extent of damage to the immature cells in the marrow. When the megakaryocytes only are damaged, a pure thrombocytopenic purpura is produced without severe anæmia or leucopenia. Such cases have a prompt and spontaneous clinical and hæmatological recovery once the toxic drug is removed. When the marrow damage is extensive so that the megakaryocytes, the primitive granulocytes and the red cell precursors are all found to be affected, the hæmorrhagic diathesis is associated with severe anæmia and granulocytopenia and recovery is unlikely (Nelson, 1952). The prognosis in cases of purpura due to hæmatotoxic drugs therefore depends on the damage to the whole hæmopoietic system and the outcome can be inferred, to some extent, from an examination of the peripheral blood and bone marrow.

Purpura may complicate a number of diseases affecting the hæmopoietic system, where it is often a terminal manifestation. However, in some cases of refractory or aplastic anæmia the presence of purpura may be the presenting and predominating sign (Case 6). In the absence of any sure knowledge as to the ætiology of primary refractory anæmia and the lack of response to any of the known hæmopoietic drugs these cases are usually maintained with blood transfusions. Although splenectomy has been carried out in some cases of primary refractory anæmia, the results have not been encouraging. It is only in cases with an active cellular marrow that splenectomy is likely to be followed by beneficial results. Here it is postulated that the spleen is exerting some inhibitory effect on the marrow which is relieved by splenectomy. In one case of primary refractory anæmia presenting as a hæmorrhagic diathesis the effect of removal of the spleen was to produce immediate cessation of the bleeding tendency with a temporary restoration of the bleeding time which has since shown frequent remissions and relapses. The low platelet, erythrocyte and leucocyte counts have persisted but the hæmoglobin has, for a limited period, been fairly satisfactorily maintained so that the patient has only required a blood transfusion once in the twelve months since her operation. This case also clearly demonstrated the lack of correlation which can exist between the bleeding time and the platelet count. In purpura it has been shown that the bleeding time is paralleled by the capillary fragility but not by the platelet count, and that both bleeding time and capillary fragility are increased during periods of active bleeding with associated skin purpura. The only tests which can be correlated with any degree of accuracy with the platelet count are the clot retraction and rate of prothrombin consumption. This is one of the facts which suggests that the low platelet count is not entirely responsible for the hæmorrhagic manifestations which may have an underlying vascular origin.

Acute idiopathic thrombocytopenic purpura has such a dramatic presentation and bleeding may be so profuse that the unwary may be trapped into carrying out an emergency splenectomy which carries an undue risk, if carried out under such

circumstances. The management of these cases resolves itself into the control of the acute bleeding episode and the practice of a policy of watchful expectancy to see if spontaneous recovery occurs. Control of this bleeding can most readily be achieved by the transfusion of fresh (not stored) whole blood. The value of cortisone or A.C.T.H. in acute thrombocytopenic purpura is dubious, as some workers have been unable to detect any clinical or hæmatological difference in the course of patients treated with A.C.T.H. and cortisone and other patients left untreated. Because splenectomy is followed by clinical improvement in the bleeding tendency and a rise in the platelet count, the decision to carry out this operation in a case of acute thrombocytopenic purpura may be forced by the developments in the individual case which is not showing signs of spontaneous recovery. Under these circumstances the presence of uncontrollable hæmorrhage threatening life or of severe bleeding, particularly in patients over 40 years of age where there is the ever-present risk of cerebral hæmorrhage, are two possible indications for splenectomy.

Splenectomy in chronic thrombocytopenic purpura is the elective form of treatment and is followed by permanent recovery in a high percentage of cases. The decision here is the timing of the operation, for the risk is less if the operation is carried out once the acute hæmorrhagic episode has subsided. Here a pre-operative course of cortisone or A.C.T.H. is most useful in helping to restore the bleeding time to normal and to control the hæmorrhagic manifestations. This effect is maximal about the seventh day of administration and consequently the operation can be performed at a time when the risk of both operative and post-operative hæmorrhage is reduced to a minimum.

The appropriate treatment of an individual case of idiopathic thrombocytopenic purpura may present a problem of considerable difficulty to the physician or surgeon. The major difficulty is to know whether the case is one of acute thrombocytopenic purpura or an acute episode in a chronic case. The most helpful points are (1) In chronic purpura there is a previous history of bleeding or ready bruising which is not obtained in acute purpura. (2) The clinical manifestations in acute purpura are those of severe bleeding with widespread gross purpura and ecchymoses, while in an acute exacerbation of chronic purpura the skin manifestations usually consist of petechiæ, localised to the legs rather than generalised purpura. (3) The hæmatological changes in acute purpura are more marked than in chronic purpura.

The differential diagnosis is important and not merely academic. It is the differential diagnosis between an acute self-limited disease in which the danger from splenectomy is great and a chronic persistent disorder in which, at the moment, splenectomy carries the only hope of complete cure. It is a problem which taxes to the full the judgement and skill of the physician.

Summary.

Idiopathic thrombocytopenic purpura occurs in two clinical forms.

Acute idiopathic thrombocytopenic purpura is a self-limited disease in which

control of severe hæmorrhage can be achieved by the transfusion of fresh whole blood while awaiting spontaneous recovery.

Chronic idiopathic thrombocytopenic purpura is a disease liable to fluctuating remissions and relapses. In relapse the acute bleeding episode may be controlled by transfusion of fresh whole blood or cortisone therapy. If the bleeding is uncontrollable, threatening vital structures or is persistently recurrent, splenectomy is indicated.

In secondary thrombocytopenic purpura due to hæmatotoxic drugs, recovery is prompt following withdrawal of the drug. If the hæmatotoxic drug has produced severe marrow damage with peripheral pancytopenia the prognosis is poor.

In one case of primary refractory anæmia with a secondary thrombocytopenic purpura splenectomy has relieved the bleeding tendency without affecting significantly the underlying disease process.

It gives me great pleasure to acknowledge my indebtedness to the many physicians who afforded me the opportunity of seeing cases which were under their care and to Mr. A. Lamont for his technical assistance.

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The Assessment of Cases for Mitral Valvotomy and the Results of Operation

By J. F. PANTRIDGE, M.C., M.D., M.R.C.P.(LOND.)
Physician, Royal Victoria Hospital
T. B. SMILEY, M.C., F.R.C.S., and E. W. HENRY, M.D.
Thoracic Surgeon Registrar

IN certain cases of inactive rheumatic heart disease when the lesion is predominantly mitral stenosis dramatic results may be obtained from surgical relief of the valvular obstruction (Bailey, 1949; Glover, et al., 1950; Baker, et al., 1950, 1952). Unfortunately, not all cases of mitral stenosis will benefit from operative interference. The major difficulty associated with the surgical treatment of rheumatic heart disease is that of deciding in which case, and at what stage in the course of the disease, operative interference is required. The responsibility for this decision is borne by the physician. In some cases it will be easy to determine whether or not benefit will be obtained from operation; in others it may be a matter of considerable difficulty.

The object of this communication is to discuss the selection of patients for mitral valvotomy and to report 121 cases, 105 of whom were selected for this operation by one of us (J.F.P.).

Mitral valvotomy is obviously indicated if a patient is becoming progressively incapacitated and the condition is one of "pure" mitral stenosis, i.e., mitral stenosis uncomplicated by significant mitral incompetence or aortic valvular involvement.

It is apparent that by no means all patients with "pure" mitral stenosis are sufficiently incapacitated to require operation. The proper selection of cases requires therefore :—

(a) Information regarding the effects of mitral valvular obstruction on the circulation.

(b) A clinical classification of patients suffering from the disease.

THE PULMONARY CIRCULATION IN MITRAL STENOSIS.

The effect of mitral stenosis on the circulation may be predicted from simple hydraulic principles. When an orifice is narrowed an increase in the pressure gradient across this orifice will be required if the rate of flow is to be maintained, and any increase in the rate of flow will require a further increase in the pressure gradient. Mitral stenosis is associated with a rise in left auricular pressure and with further elevation of this pressure when blood flow is increased as by exertion.

The rise in pressure in the left auricle is necessarily followed by a rise in pulmonary vascular pressure. The pressure in the venous side of the pulmonary circulation may be measured by introducing a cardiac catheter into one of the pulmonary arteries and advancing it till it is made to block a small pulmonary

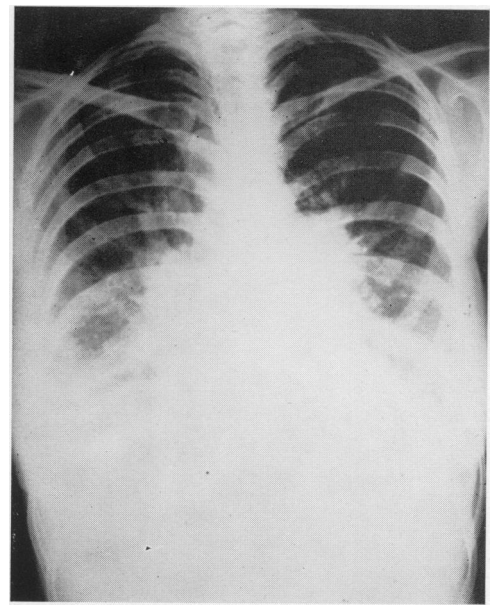

Fig. 1

Mitral stenosis in pregnancy. Chest film before operation showing gross pulmonary congestion.

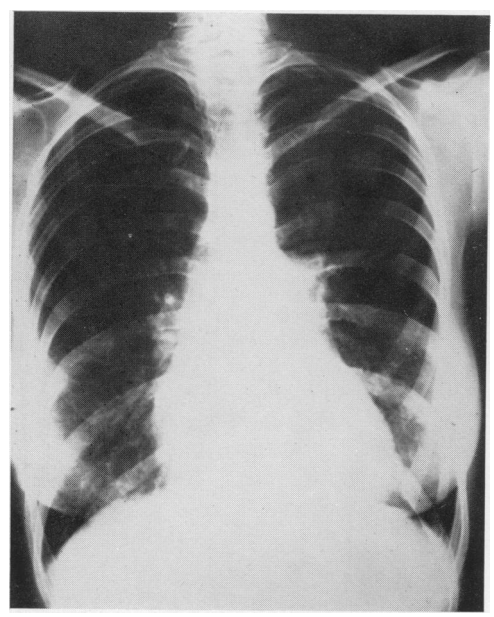

Fig. 2

Chest film after operation. Hilar vascularity is almost normal.

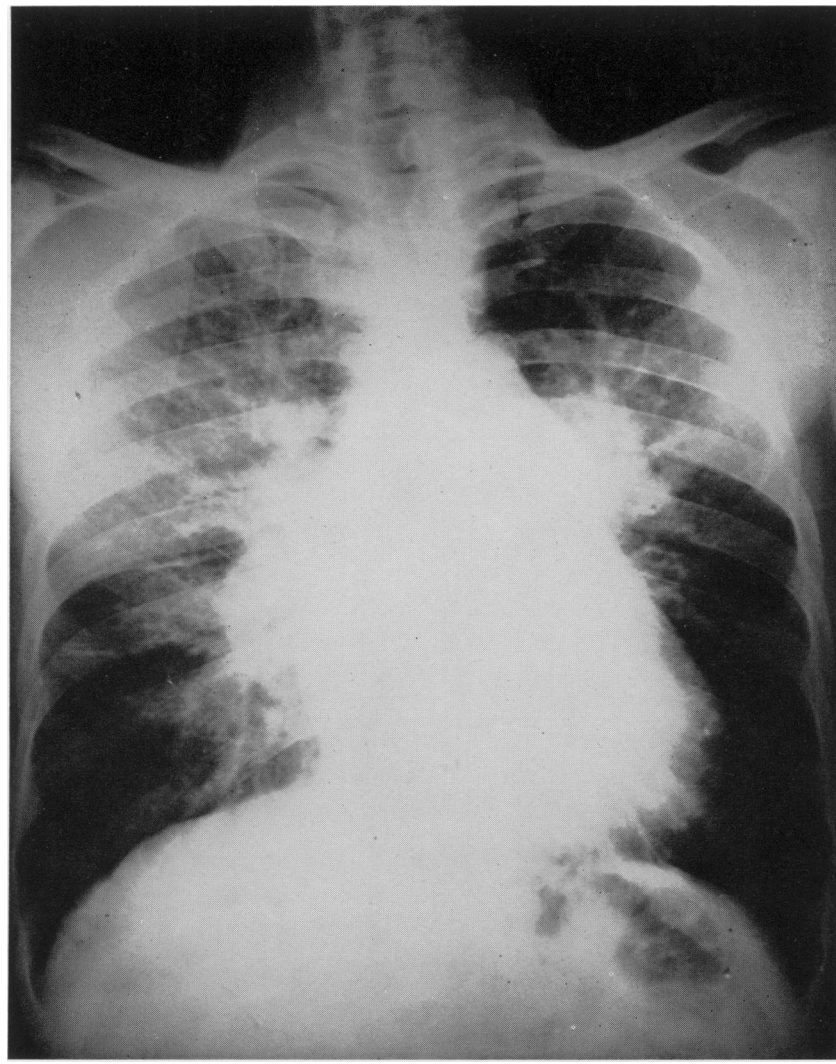

Fig. 3

W. G. (Case 49). Chest film before operation showing gross pulmonary engorgement.

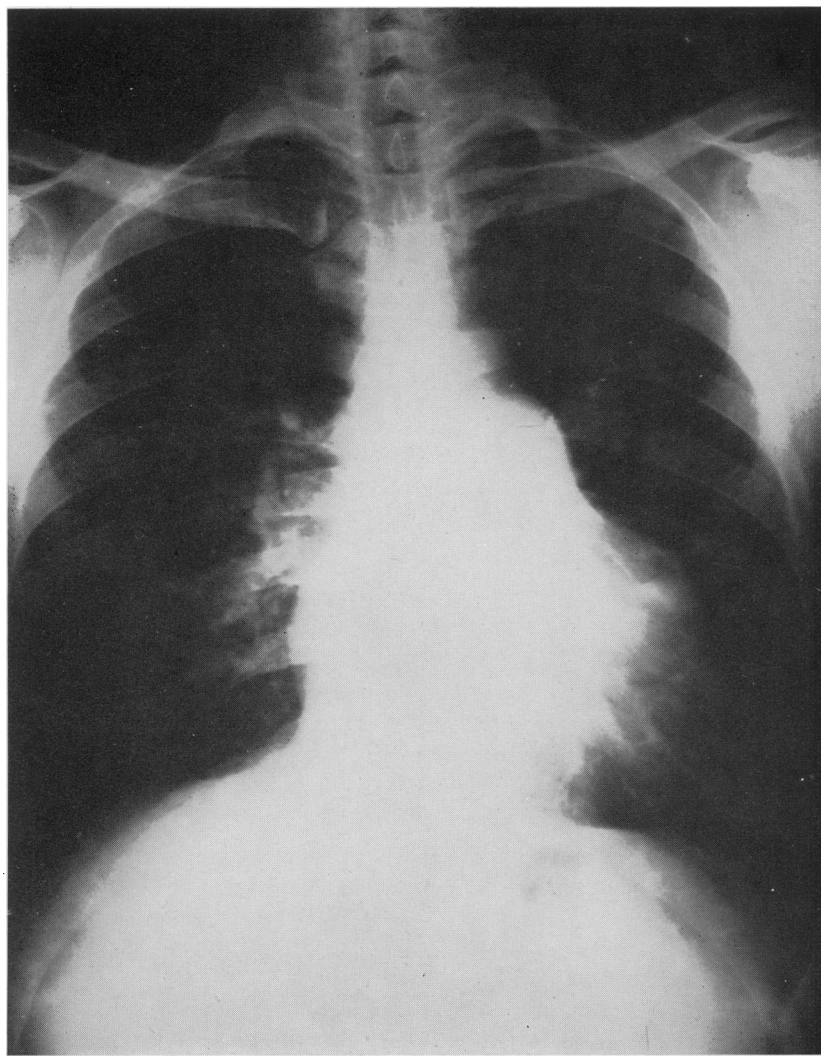

Fig. 4

W. G. (Case 49). Chest film after operation : lung fields are clear. Cardiac outline shows little change.

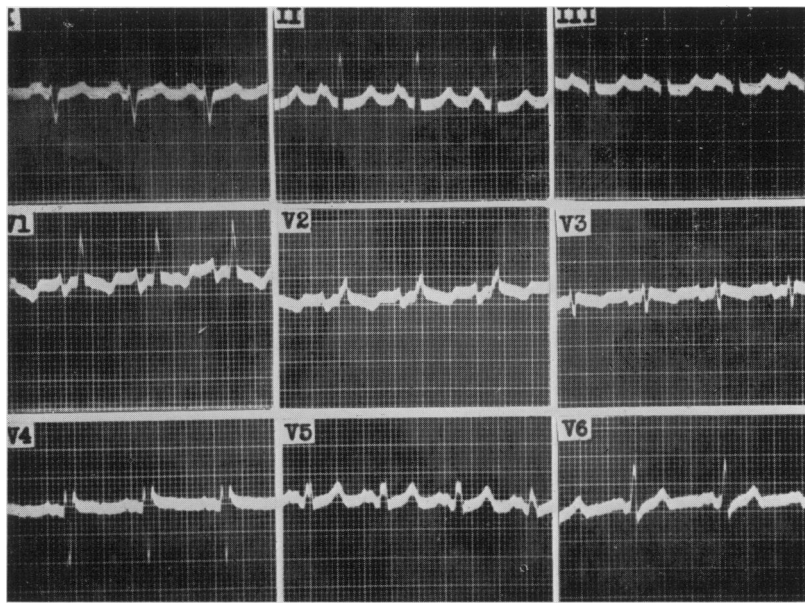

Fig. 5

A. C. (Case 68). Pre-operative E.C.G. shows gross right ventricular hypertrophy.

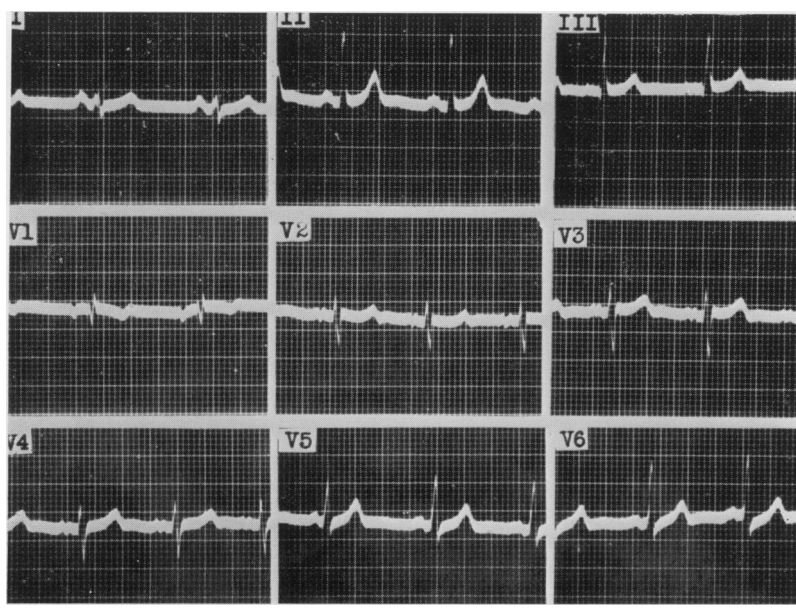

Fig. 6

A. C. (Case 68). Post-operative E.C.G. shows that the signs of right ventricular hypertrophy have entirely gone.

vessel (Hellems, et al., 1948; Lagerlof and Werko, 1949). It is probable that the pressure recorded at this point, the pulmonary capillary venous pressure, closely approximates the left auricular pressure (Dow and Gorlin, 1950; Epps and Adler, 1953). Pulmonary œdema is likely to occur when the pulmonary capillary venous pressure exceeds the plasma colloid osmotic pressure (30 mm. Hg.). Gorlin and Gorlin (1951) placed the pulmonary œdema threshold at 35 mm. Hg. and indicated the close relationship which must exist between the mitral valve area, the rate of blood flow through the valve, and the pulmonary capillary venous pressure. Thus when the valve area is normal (4 to 6 cm^2.), the rate of blood flow may be increased to as much as 700 cc. per sec. (adequate for the most strenuous activity), without significant rise in the left auricular or pulmonary capillary venous pressure. When the area is narrowed to 2.5 cm^2. flow rates exceeding 400 cc. (required by strenuous activity) will cause a rise of pulmonary capillary venous pressure to 35 mm. of Hg. or more and therefore give rise to pulmonary œdema. Flow rates exceeding 250 cc. per sec. cannot be tolerated if the area is reduced to 1.5 cm^2. When the area is less than 1 cm^2. flow rates of 150 cc. cannot be maintained without a rise of pulmonary capillary venous pressure above 35 mm. Hg. Patients with severe mitral stenosis (valve area 1 cm^2. or less) are therefore likely to have pulmonary œdema at rest.

A rise in pulmonary venous pressure is followed by a rise in pulmonary artery pressure. However, in some 25 per cent. of cases of mitral stenosis the rise in pulmonary artery pressure is disproportionately great. This disproportionate rise in pulmonary artery pressure is due to increased pulmonary arteriolar resistance. How much of this increase in arteriolar resistance is due to structural changes in the arteriolar wall and how much to vasoconstriction is not known. Its effect is to prevent a marked rise in pulmonary venous pressure and hence to "protect" the patient from pulmonary œdema.

Despite the fact that in some circumstances the protective increase in pulmonary vascular resistance may temporarily fail permitting flooding of the capillaries and pulmonary œdema, patients with mitral stenosis may, on the basis of the presence or absence of an increase in pulmonary vascular resistance, be classified as "protected" or "unprotected." Unprotected mitral stenosis is associated with symptoms and signs referable to pulmonary venous engorgement—hæmoptysis, nocturnal dyspnœa, and recurrent attacks of pulmonary œdema. Patients with "protected" mitral stenosis tend to avoid these manifestations of pulmonary congestion but may be no less disabled since the circulatory obstruction in the pulmonary arterioles results in their inability to increase the cardiac output on activity. "Protected" mitral stenosis gives rise to clinical, radiological, and sometimes electrocardiographic evidence of right ventricular hypertrophy. Eventually congestive heart failure results from failure of the hypertrophied right ventricle.

Clinical Classification of Patients with Mitral Stenosis.

A suggested classification is :—

Group 1.—Asymptomatic mitral stenosis. The characteristic mitral diastolic

murmur is present but disability is negligible. Rise in pulmonary vascular pressure is minimal.

Group 2.—The disability is moderate but not increasing. Patients are able to do their ordinary duties without discomfort. Cardiac catheterization shows a slight rise in pulmonary vascular pressure at rest and a moderate rise on exertion.

Group 3.—There is evidence of increasing disability. "Unprotected" patients in this group will have symptoms and signs of pulmonary congestion, history of hæmoptysis, marked diminution in exercise tolerance, perhaps nocturnal dyspnœa, and moist sounds at the lung bases. Cardiac catheterization will show a considerable rise in pulmonary capillary venous pressure without marked rise in the pulmonary artery pressure. "Protected" patients in this group will have gross impairment of exercise tolerance due to a low fixed cardiac output. There will be clinical evidence of right ventricular hypertrophy, prominent "a" waves in the jugular pulse, a heaving right ventricular outflow tract felt to left of the sternum, the Graham Steele murmur of pulmonary incompetence, and accentuation of the second component of the split pulmonary second sound. X-ray screening will confirm the presence of right ventricular enlargement and show a prominent pulmonary conus. The electrocardiogram may show a præcordial lead pattern characteristic of right ventricular hypertrophy. Cardiac catheterization will show a marked increase in the gradient between the pulmonary artery pressure and the pulmonary capillary venous pressure. When first seen, "protected" patients in this group may show signs of early right ventricular failure.

Group 4.—Patients in this group are completely incapacitated because of intractable pulmonary congestion or intractable right heart failure.

Cases in group 1 obviously do not require surgical intervention. Cases in group 2 may require operation if the degree of static disability is great. It has, however, been our policy to defer operation when it is entirely clear that the disability is not progressive. The possibility of improvement in operative technique cannot be overlooked, so that much may be gained by waiting a few years. The condition of patients in this group is, however, carefully reviewed at three to six monthly intervals to ensure that the earliest evidence of progression of the disease is recognised. When doubt exists as to whether a patient should be placed in group 2 or 3, the pulmonary vascular pressures recorded by cardiac catheterization will be decisive. Groups 3 and 4 are those which, in the absence of contraindications, are selected for operation.

Contraindications to Operation.

1. Active infection, due either to active rheumatism or subacute bacterial endocarditis, is an obvious contraindication to operation. Unfortunately it is impossible, with the clinical and laboratory methods at present available, to exclude with certainty smouldering rheumatic activity. Inquiry regarding recent joint or limb pains, electrocardiographic investigation, erythrocyte sedimentation rate, and white cell count may give no indication of rheumatic activity, and yet Aschoff nodules may be found in the biopsy of the left auricular appendage removed at operation

(McKeown, 1953). It has been shown, however, that the incidence of unsuspected rheumatic activity, which in some series has been as high as 45 per cent., progressively declines with age, being 89 per cent. in the age group 20-25 and 14 per cent. in the age group 45-50 (McNeely, et al., 1953).

2. Aortic valvular involvement, if associated with clinical, radiological or electrocardiographic evidence of left ventricular enlargement, is, as a rule, a contraindication to mitral valvotomy. An early diastolic murmur heard along the left side of the sternum in patients with mitral stenosis and marked pulmonary hypertension—the Graham Steele murmur of pulmonary incompetence—should not be confused with the murmur of aortic incompetence. An aortic diastolic murmur associated with the peripheral signs of aortic reflux—a Corrigan pulse—and raised pulse pressure is an unfavourable sign. However, if the patient's condition is precarious because of the pulmonary congestive features associated with tight mitral stenosis, aortic valvular involvement, unless obviously very considerable, is not regarded as a bar to operation.

A double aortic murmur was present in nine cases (7.5 per cent.) in this series. In two of these it was associated with the peripheral signs of aortic incompetence and with slight to moderate left ventricular enlargement. In both improvement after mitral valvotomy has been remarkable. Two cases with a double aortic murmur, but without change in the peripheral pulse or left ventricular enlargement, failed to improve following operation. In neither of these can the poor result be attributed to the aortic lesion.

3. Predominant mitral incompetence is a contraindication to the present operation of mitral valvotomy. Mitral stenosis, complicated by slight to moderate incompetence, may, however, be successfully dealt with by operation. It may, in fact, be noted that the amount of mitral reflux diminishes when the adherent commissures are freed.

The great difficulty in the selection of patients for valvotomy is to predict the condition of the valve when the signs produced by the mitral lesion are neither those of "pure" stenosis or "pure" incompetence. In this connection it is of value to keep in mind the signs produced by "pure" stenosis as opposed to those produced by "pure" incompetence.

The characteristic findings in "pure" mitral stenosis are a low-pitched mitral diastolic murmur, maximal in presystole and ending in a slapping first heart sound, the absence of a murmur in systole and the presence of a third heart sound in early diastole, the opening snap of the stenosed valve. This opening snap is maximal inside the apex, but when loud may be widely conducted. It is high-pitched, of short duration, and closely resembles in character the normal second heart sound. It is best heard in expiration. It is to be distinguished from the second component of the split pulmonary second sound which is accentuated in the presence of pulmonary hypertension and is best heard in the pulmonary area. Splitting of the pulmonary second sound is maximal during inspiration. When the condition is "pure" mitral stenosis there will be no clinical, radiological, or

electrocardiographic evidence of left ventricular enlargement. However, in some cases of protected stenosis with marked pulmonary hypertension displacement of the left ventricle by the grossly enlarged right ventricle may result in erroneous radiological evidence of left ventricular enlargement. In these cases the electrocardiogram is of great value, since it will usually show a right ventricular hypertrophy pattern in the præcordial leads with displacement of the transitional zone towards the left.

Pure mitral incompetence is usually associated with a loud mitral systolic murmur often maximal in late systole and conducted to the axilla or as far as the left scapula and with absence of accentuation of the mitral first heart sound. A third heart sound is frequently heard in diastole, and differs from the opening snap of the mitral valve in that it is later in diastole, is of longer duration, of lower pitch, and is confined to the apex. It is thought to be due to rapid ventricular filling (Brigden and Leathem, 1953). A mid-diastolic murmur may be audible. There will be radiological and in many cases electrocardiographic evidence of left ventricular enlargement. X-ray screening will usually show obvious systolic expansion of the left auricle in both right oblique and antero-posterior views.

When the character of the mitral valvular lesion is in doubt, the signs of stenosis are weighed against those of incompetence as indicated in Table I.

TABLE I.

RECOGNITION OF MITRAL STENOSIS AND INCOMPETENCE.

SIGN.	STENOSIS.	INCOMPETENOE.
Accentuated or slapping mitral first heart sound.	Usually present.	Uncommon.
Mitral opening snap.	Common.	Rarely, if ever, occurs.
Mitral systolic murmur.	Not usually loud or notably conducted.	Often loud and conducted to axilla.
Radiological evidence of		
(a) left ventricular enlargement.	Absent unless there is a complicating condition, e.g., hypertension or an aortic valvular lesion.	Left ventricular enlargement usually evident.
(b) left auricular systole expansion on screening.	Backward movement of barium filled œsophagus may be present in right oblique position.	Systolic expansion usually present in both oblique and antero-posterior views.
Electrocardiogram.	May show evidence of right ventricular enlargement.	May show evidence of left ventricular enlargement.
Pulmonary vascular pressure determined by cardiac catheterization.	Marked pulmonary hypertension common.	Marked pulmonary hypertension distinctly uncommon.

It was found that if the first heart sound was slapping, the opening snap audible, and left ventricular enlargement absent, the mitral lesion was predominantly stenosis, irrespective of the character of the mitral systolic murmur.

However, the accentuation of the first heart sound and the opening snap may both be abolished by calcification of the mitral valve. Absence of these features is not therefore conclusive evidence of mitral incompetence. Further, when right ventricular enlargement is considerable determination of the size of the left ventricle may in some cases be difficult.

For these reasons great care must be taken to avoid an erroneous diagnosis of predominant incompetence and hence to refuse the patient the chance of benefit from operation. If this possibility is constantly in the physician's mind the reverse mistake will occasionally be made and an unexpected degree of mitral incompetence may be discovered at operation.

Predominant mitral incompetence was found at operation in five of the 121 cases in this series. It was present in two of 105 cases assessed by one of us (J.F.P.).

The first of these two patients (E.M.) showed a mitral diastolic murmur, slapping mitral first heart sound, and a grade III mitral systolic murmur conducted to the axilla. The mitral opening snap was absent. There was slight left ventricular enlargement on X-ray screening.

The second case (A.M.), a male aged 43 years, was first seen nine months before operation because of hæmoptyses. There was a mitral diastolic murmur but no accentuation of the mitral first heart sound and no mitral opening snap. There was no mitral systolic murmur. An aortic diastolic murmur was audible but the peripheral pulse and pulse pressure were normal. X-ray screening showed gross right ventricular enlargement and apparent considerable enlargement of the left ventricle. The præcordial leads of the electrocardiogram showed a right ventricular hypertrophy pattern with shift of the transitional zone to the left as far as V 6. The radiological appearance of left ventricular enlargement was therefore thought to be more apparent than real. The electrocardiogram in this case is of interest since it has been stated that a right ventricular hypertrophy pattern in mitral valvular disease is always associated with predominant stenosis (Frazer and Turner, 1953).

It is true that both these cases were regarded as unsuitable for operation at the initial assessment. Subsequently operation was agreed to in the hope that sufficient stenosis was present to enable operative interference to arrest the rapid downhill course. Needless to say, we hold that if there is doubt about the relative degree of stenosis and incompetence and the patient is pursuing a rapidly downhill course it is better to risk the possibility of a useless operation than to deny the patient the chance, however remote, of benefit from surgery.

Factors Increasing Operative Mortality.

1. The presence of auricular fibrillation undoubtedly increases the mortality but is certainly not a contraindication to operation. The risk is that of systemic embolism from dislodged auricular thrombi. A history of or evidence of previous

systemic emboli is now regarded by some as an indication for mitral valvotomy since removal of the left auricular appendage and decrease in the pooling of blood in the left auricle diminish the tendency toward the formation of left auricular thrombi (Griffiths, et al., 1953). It is of interest that unsuspected rheumatic activity is less common when auricular fibrillation is present (McNeely, et al., 1953).

2. Extreme severity of the effects of mitral obstruction does not contraindicate mitral valvotomy. It is true that if the signs of congestive cardiac defeat or gross pulmonary congestion show no response to medical therapy, the operative mortality is considerably increased. However, some of our most gratifying results have been in patients who at the time of operation were virtually moribund.

3. Age. In view of the high incidence of undetected rheumatic activity and because of the possibility of recrudescent activity, patients below the age of 20 are not submitted for valvotomy if operation can be delayed without risk to life. The youngest patient in this series was aged 16 at the time of operation, which was performed because of frequent exsanguinating hæmoptysis. Despite the absence of clinical and laboratory evidence of rheumatic activity left auricular biopsy showed evidence of virulent rheumatic infection.

The majority of patients submitted for mitral valvotomy have been in the fourth decade. Our oldest case was aged 55. The mortality is said to increase over the age of 50, although in a recent report the mortality for valvotomy in 35 patients between 50 and 61 years was 8.5 per cent. (Janton, et al., 1953).

Mitral Valvotomy in Pregnancy.

The operation was performed in three patients during pregnancy. It was performed in two during the sixth month as an alternative to termination by abdominal hysterotomy. Both patients suffered from tight mitral stenosis with intractable pulmonary œdema. Valvotomy was eminently successful in both. In one pregnancy continued normally and a live child was obtained; the other, however, came into labour soon after operation. A third patient, moribund because of pulmonary œdema, had an emergency valvotomy in the thirty-second week. During the operation the patient was kept almost vertical by tilting the table. Dramatic improvement was apparent immediately after the valvular split. Convalescence was uneventful apart from premature labour in the first post-operative day. The child survived. The radiological appearances before and after valvotomy are shown in Figs. 1 and 2.

Pre-operative Therapy.

Congestive heart failure is treated on the usual lines of digitalisation and diuretic therapy, till maximal improvement is obtained. In the absence of evidence of right ventricular failure digitalis is not used unless auricular fibrillation is present.

Instruction in breathing exercises is given by a competent physiotherapist for a few days before operation so that deep breathing and expectoration of mucus in the immediate post-operative period is less difficult to encourage.

Quinidine is given one hour before operation with the object of diminishing myocardial irritability.

Operative Complications.

Prolonged cardiac arrest occurred in one case in which valvotomy was done for intractable pulmonary œdema. The circulation was maintained by cardiac massage. Ventricular fibrillation incident on cardiac massage was abolished by electrical stimulation of the ventricles. Uneventful recovery followed and the patient is now, two and a half years after operation, in full employment as a motor engineer.

Three patients died from cardiac arrest, two at operation and the third two months after operation from gross cerebral damage.

Two patients with auricular fibrillation and left auricular thrombi had systemic emboli. In one a saddle embolus was removed from the aortic bifurcation two hours after operation. The other developed a hemiplegia and aphasia in the second post-operative day. Both made a good recovery. Ventricular tachycardia appeared on one occasion. This was quickly abolished by intravenous quinidine. In two cases profound hypotension occurred immediately after the valve was split. This showed an immediate response to noradrenaline given by drip and calcium chloride by injection into the left auricle.

There were two deaths from sudden circulatory failure in the immediate post-operative period. In one post-mortem demonstrated a small tear of doubtful significance in the anterior cusp of the mitral valve.

Post-operative Auricular Fibrillation.

It was found that auricular fibrillation, if present before operation, always persisted after operation. In addition, a considerable number of patients in normal sinus rhythm before operation developed auricular fibrillation in the immediate post-operative period. In these cases the rapid heart action was controlled by digitalis. It was frequently possible to establish sinus rhythm with quinidine prior to discharge from hospital. However, 15 per cent. of patients with normal sinus rhythm before operation show persistent auricular fibrillation since operation.

Results.

The operative mortality has been 5 per cent.—six deaths in 121 cases. The deaths occurred early in the series. There has been no death in the last 75 cases. Mr. J. A. W. Bingham performed the operation in five of these. In 57 cases operation was performed more than one year ago, in 25 more than two years ago. Four patients have died since operation from causes unrelated to valvotomy. One who had been markedly improved died two and a half years after operation from massive cerebral embolism. Another in whom separation of the valve commissures was impossible died two years after operation from pulmonary œdema complicating pregnancy. A third, unimproved by valvotomy, died fourteen months after operation from congestive cardiac failure. The fourth apparently had had a successful valvotomy but died suddenly eight months after operation while playing cricket.

The results shown below have been assessed by careful questioning regarding exercise tolerance and by comparison of the clinical, radiological, and electrocardiographic signs before and after operation.

Excellent	51	
Improved	19	
Slightly improved	8	
Not improved	12	
Operative deaths	6	
Post-operative deaths	4	
	100	
Too recent for assessment (operation within last three months)	21	
TOTAL	121	
Operative mortality—First 46 cases	13%	Total 5%
Last 75 cases	Nil	

ILLUSTRATIVE CASES.

Case 49.—W. G., a male aged 38. Admitted to hospital 24th July, 1952. Completely incapacitated because of exertional dyspnœa and recurrent hæmoptysis. There had been orthopnœa for some months. Examination showed pure mitral stenosis—a mitral diastolic murmur, slapping first heart sound, and well-marked mitral opening snap. A loud Graham Steele murmur was audible along the left sternal margin. X-ray screen (Fig. 3) showed a considerable increase in hilar vascularity, gross prominence of the pulmonary conus, some right ventricular enlargement, moderate enlargement of the left auricle and a hypoplastic aorta. Cardiac catheterization showed that the mean pressure in the main pulmonary artery was 125.5 cm. saline.

Mitral valvotomy was performed on 5th August, 1952. The valve was cartilagenous with some calcification at the medial commissure. Splitting occurred readily at both commissures. When reviewed six months after operation, he reported that the exercise tolerance was completely unimpaired. The auscultatory signs of mitral stenosis were unchanged. X-ray screening, however, showed a normal hilar vascularity and a diminution in prominence of the pulmonary conus (Fig. 4). When seen fifteen months after operation he stated that he was at full work as a dock labourer. Cardiac catheterization at this time showed, in comparison with the pre-operative state, a marked fall in pulmonary vascular pressure, the main pulmonary artery pressure at rest being 43.5 cm. saline and the pulmonary capillary venous pressure 15.5 cm. saline.

Case 68.—A. C., a female aged 30. Admitted to hospital in January, 1953, because of extreme exertional dyspnœa of two years' duration and recent marked nocturnal dyspnœa.

Examination showed pure mitral stenosis, there being a prolonged mitral diastolic murmur with presystolic accentuation, a slapping mitral first heart sound, and a clearly audible mitral opening snap. Crepitations were present at the lung bases. X-ray screening showed a gross increase in hilar vascularity, considerable right ventricular enlargement, a prominent pulmonary conus, and moderate enlargement of the left auricle. The left ventricle was not enlarged. The electrocardiogram showed a marked right ventricular hypertrophy pattern in the præcordial leads (Fig. 5). Cardiac catheterization showed the mean main pulmonary artery pressure to be 109 cm. saline and pulmonary capillary venous pressure 50.5 cm. saline.

Mitral valvotomy was performed on 30th January, 1953. Both commissures were readily split. Convalescence was uneventful. When reviewed on 31st March, 1953, she had already walked three miles. The mitral diastolic murmur had almost entirely gone. The first heart sound was, however, slapping and mitral opening snap still audible. Cardiac catheterization repeated in October, 1953, showed almost normal pulmonary vascular pressure at rest—main pulmonary artery = 25.5 cm. saline and pulmonary capillary venous pressure = 8 cm. The electrocardiogram recorded at this time showed that the right ventricular hypertrophy pattern in the præcordial leads had entirely disappeared (Fig. 6).

Assessment of the degree of improvement following valvotomy is frequently less easy than in the cases described above. Patients' subjective impressions regarding improvement vary. Some are hesitant to admit improvement. Others make exaggerated claims of well being. Thus after operation one patient rejoiced at his ability to get around better when, in fact, owing to the impossibility of gaining access to the left auricle, valvotomy had not been performed.

The auscultatory signs of mitral stenosis may be little affected by operation. Improvement in the radiological signs is in some cases disappointing. Indubitable electrocardiographic evidence of right ventricular enlargement is very frequently absent in mitral stenosis, a change in the electrocardiogram after operation is therefore uncommon. For these reasons an objective assessment of the results of a relatively recently introduced surgical procedure appeared to one of us (J.F.P.) to be advisable. Such an objective assessment is obtained by comparing the pre-operative and post-operative pulmonary vascular pressures as determined by cardiac catheterization.

This comparison has been made in 34 cases in the series. The result is shown in Table 2. It will be noted that there is a broad correlation between the clinical result and the post-operative fall in pulmonary vascular pressure. A marked fall in pulmonary pressures is seen in 20 of the 34 cases. In some cases, however, there is a disparity between the clinical impression of improvement and the objective evidence. Thus in Cases 5 and 12, classified as slightly improved, no fall in pulmonary pressures is noted. The fall in pulmonary capillary venous pressure in Case 24 is insignificant, yet the clinical result is regarded as excellent. It will also be noted that of 26 cases in which the result is regarded as excellent only 9 (35 per cent.) show post-operative resting pulmonary vascular pressures which approach normal.

Summary.

The assessment of patients for mitral valvotomy is discussed. The operation has been performed in 121 cases with an operative mortality of 5 per cent. Seventy per cent. of patients who have been followed up for more than three months show a worthwhile clinical improvement. In 51 per cent. the result is on clinical estimation excellent. There is, however, in some cases a disparity between clinical improvement and post-operative fall in pulmonary vascular pressures. Less than 35 per cent. of cases whose clinical result is regarded as excellent have a post-operative hæmodynamic state which approaches normal. It is nevertheless apparent

that the operation of mitral valvotomy will, in the majority of cases, convert high-grade mitral stenosis to a stenosis of much lesser degree.

TABLE 2.

		PRE-OPERATIVE		POST-OPERATIVE			
No.	Case	Mean P.A. Pressure	P.C.V.P.	Mean P.A. Pressure	P.C.V.P.	Duration Follow-up Month	Clinical Classification
5	R.B.	44.5	—	58	35	35	SI
7	J.N.	62.5	—	54	—	34	I
8	J.W.	41.5	—	27.5	—	33	I
12	G.W.	41.5 (76)	—	40.5	21	32	SI
15	M.McK.	41 (70.5)	—	31 (54.5)	21.5	29	E
17	M.D.	43.5 (62.5)	28	31.5	13	29	E
19	K.McM.	51.5 (86.5)	35.5	41 (63)	21.5	27	SI
22	M.McI.	69	66	36 (48)	25.5	25	E
23	M.B.T.	93	89.5	39	18	24	E
24	K.K.	35.5 (66)	23 (38.5)	26 (42)	19	24	E
26	J.B.	71.5 (100)	48.5	29 (42)	14	24	E
28	J.S.	48 (70.5)	31.5	25 (34.5)	10.5	23	E
30	J.M.	88.5	58	35.5	24.5	23	E
31	M.M.	54 (83)	38	23.5 (51.5)	16.5	22	E
32	A.F.	110	—	48.5	15	22	E
33	M.McM.	43 (78)	35	29	20.5	21	E
34	D.McC.	80.5 (98)	40	25.5 (41.5)	4	21	E
36	W.C.	72	—	36.5	16	20	E
38	H.S.	88.6	60	30 (35)	10	19	E
39	A.S.	52.5	—	33.5	16	18	E
41	J.M.	49	25	32.5	16	18	I
47	S.M.	54	45.5	26.5 (35)	15	18	E
49	W.G.	125.5	—	43.5	15.5	15	E
54	J.S.	43.5 (73)	34.5	32.5	21.5	13	E
58	E.S.	52.5	44	34.5	30	12	I
63	M.McD.	45	35	27	19.5	11	E
65	M.B.	37	26.5	22 (30.5)	11	11	E
68	A.C.	109	50.5	25.5	8	11	E
78	H.R.	56 (90)	34.5	24 (48)	13	8	E
79	L.C.	59	40	15.5	5	8	E
81	R.P.	71	45	43.5	28	7	E
87	C.F.	106	45	36.5	10	6	E
91	A.D.	49.5	38.5	37.5	25.5	6	I
94	Y.M.	51	34.5	23	10.5	6	E

P.A. = Pulmonary artery. Normal maximum mean pressure—20 cm. saline.
P.C.V.P. = Pulmonary capillary venous pressure. Normal maximum—12 cm. saline.
SI = Slightly improved.
I = Improved.
E = Excellent.

Mean pressures were recorded, with a saline manometer, at rest and in some cases after two minutes' exercise. The figures in brackets ( ) indicate the pressure on exercise. The reference point was the sternal angle.

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REVIEW

MEDICINE: The Patient and His Disease. By A. E. Clark-Kennedy, M.D., F.R.C.P. Volume 1. Second Edition. (Pp. 410 + xiv. 25s.). Edinburgh: E. and S. Livingstone. 1953.

IN this unusual book Dr. Clark-Kennedy has undertaken a formidable task which may be expressed as the integration of the normal physiological and psychological reactions of human beings with the many variations of both sets of reactions which occur in the presence of disease. This is the second edition and may be said to represent his maturing views on a subject which has absorbed his interest during a lifetime of study and teaching of physiology and medicine. The titles of the chapters indicate how widespread is his canvas. Chapter 1, on Body and Mind, is subdivided into sections on Energy and Matter, Life, Organic Evolution, Heredity, Development, Constitution, Consciousness and Mind. The succeeding chapters present to us a wide and humane consideration of Symptoms, Symptoms and Signs, Heredity and Environment, Reactions of Body and Mind, and finally The Nature of Disease, each divided into appropriate sections. In such a work as this there are bound to be certain uneven phases of emphasis and each reader will have his own ideas about where the stresses should have been placed; but its outstanding value is that it presents Medicine as the greatest of the "Humanities"—the proper study of mankind. The patient is more to this physician than is his disease. Here you will not find sick human beings described as clinical material nor is it implied that all the ills that human flesh is heir to are likely to be expressed in mille-equivalents. Dr. Clark-Kennedy expresses his thanks to various friends and colleagues who have helped him. Among them the present reviewer is glad to see the name of his former house physician, Professor J. D. Boyd; but this is not the only reason why he recommends this interesting book.

R. M.

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R. M.

A Report on the Cases of Acute Poliomyelitis treated in the Northern Ireland Fever Hospital in 1952

By F. Lenore J. Robinson, M.D., D.C.H.

Senior House Officer, Northern Ireland Fever Hospital, Purdysburn, Belfast

In the year ending on the 31st December, 1952, there were one hundred and twelve cases of acute poliomyelitis admitted to the Northern Ireland Fever Hospital. One hundred and eleven patients were admitted as suspected cases of poliomyelitis. Of these the diagnosis was correct in seventy-one. In the forty in whom the diagnosis was not confirmed no distinctive condition could be found in twenty-three. Tonsillitis was present in four and pneumonia in three, and there was one case each of meningitis, Flexner dysentery, influenza, scurvy, transverse myelitis, Guillain-Barré syndrome, lumbago, mumps, anæmia, and acidosis. Among patients admitted for other conditions forty-one were found suffering from poliomyelitis. They had been described before admission as meningitis (37 cases) and as dysentery, scarlatina, typhoid, and pyrexia of unknown origin (1 case each).

The seasonal incidence of the infection is shown in the following table.

Table 1.

1952	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter
No. of cases	7	16	72	17

Children were mainly affected, the highest incidence occurring in the 5-10 year group, as shown in Table 2. Before 1947 the maximal incidence was in the under fives (Harries and Mitman, 1951). The higher age incidence now seen has been explained by Horton and Rubenstein (1948), who state that the change is due to alteration in the age distribution of the population, as well as to increased accuracy in the diagnosis of non-paralytic poliomyelitis.

Table 2.

Age in years.	Under 1 year.	1-4	5-9	10-14	15-24	25+	Total
1952	3	20	37	13	24	15	112

Of the one hundred and twelve cases admitted, sixty-two were non-paralytic, forty-five were paralytic, and five had polio encephalitis. In the non-paralytic cases the disease varied from a mild systemic upset where headache lasting one hour or more was the only symptom to the full blown meningeal syndrome.

The forty-five paralytic cases can be sub-divided according to the part of the central nervous system affected (Table 3), but no classification can be adequate because of the overlapping in each group.

TABLE 3.

C.N.S.	No. of cases
Cranial Nerves	14
Spinal	31
Total	45

The majority of patients admitted had symptoms of fever, malaise, headache, irritability, photophobia, muscle pains and meningism. Eight cases had symptoms of upper respiratory tract infection, and eleven had gastro-intestinal disturbances. The abdominal symptoms might be explained by a virus infection of the abdominal glands. Where there was spinal paralysis the legs were twice as commonly affected as were the arms, the extensor muscles of the foot, and the muscles of the shoulder girdle bearing the brunt of the disease. Respiratory paralysis remains the most dreaded complication of poliomyelitis. Six cases with respiratory paralysis required artificial respiration, and of these, three died. The survivors who are still in hospital are males aged 4, 8, and 28 years. All three survivors had extensive spinal paralysis but no bulbar involvement. The youngest, aged 4 years, had artificial respiration for one week because of intercostal and diaphragmatic weakness. The other child had gross intercostal involvement, but the diaphragm was intact and artificial respiration was required for only nine days. The adult, however, had almost complete paralysis of intercostals and diaphragm. His respiratory embarrassment was further complicated in the first few days by abdominal distension which resisted all treatment. Continuous artificial respiration was required for six weeks. He was then gradually weaned from the mechanical lung until at the end of eight months he could do without artificial aid.

Involvement of the cranial nerve nuclei is relatively common in acute poliomyelitis, that of the seventh nerve being most frequently affected. In this series isolated facial nerve palsies were seen in seven cases. Three patients showed complete recovery and the remainder were improved. When the upper cranial nerves are involved there is no threat to life, although residual paralysis may be a permanent handicap. With bulbar involvement the outlook is much more serious and interference with swallowing may result in asphyxia or aspiration bronchopneumonia. Patients may present with hoarseness, nasal speech, inability to swallow and regurgitation of fluids. One of our patients, a boy aged 4 years, had paralysis affecting the fifth, seventh, tenth, eleventh, and twelfth cranial nerves. The fifth nerve palsy was bilateral, affecting both masseters, though internal pterygoid movement was normal. Recovery was complete except for a slight left facial weakness. Another patient, aged 33 years, with an extensive spinal paralysis had an associated bilateral masseter palsy. She was unable to eat and the mouth remained open, drooling saliva. Recovery was almost complete after eight weeks.

Five cases were diagnosed as polio-encephalitis. Two were children under six years and three were adults. Four patients presented with general encephalitic manifestations and complained of constant headache which was associated with restlessness, drowsiness, and disorientation. Focal lesions were present in two

cases. One was a boy of 18 years who developed an immobile palate; the other, a child of 2½ years, deserves more detailed mention. She was admitted in a stuperose condition with twitchings of the right face and arm, but no obvious muscular weakness. Her condition remained unchanged for five days, and it was not until the level of consciousness had improved that a right facial palsy was noted. She appeared to see and hear but did not, or could not, speak, and was reluctant to use the right arm. Final evaluation revealed hyperactivity, emotional instability, aphasia, and athetosis of the right hand. E.E.G. revealed a generally abnormal pattern. One of the adults mentioned experienced a slow recovery, passing from the stuperose state to one of mental instability and irrationality which lasted for the most of six weeks.

Cause of Death.

Of the one hundred and twelve patients admitted three died, and in all death was due to bulbar involvement following extensive and progressive paralysis.

Their case histories are as follows:—

Case 1.—A male aged 27 years who was admitted on the fourth day of an illness in which severe headache was the predominant feature. He was restless, dyspnœic, and cyanosed. Respiratory movements were minimal and there was complete paralysis of all limbs. The upper respiratory passages were cleared of mucus by suction, and artificial respiration instituted immediately while oxygen was administered by nasal catheter. The paralysis continued to spread, involving the muscles of deglutition and probably the medullary centres. Death occurred fifteen hours after admission.

Case 2.—A female aged 7 years who was said to have had an attack of scarlatina fever three days prior to admission. She exhibited meningism but had no muscle weakness until her third day in hospital when paralysis involving both lower limbs, intercostals and deglutition became evident. Artificial respiration was begun and aureomycin given prophylactically. Oxygenation appeared satisfactory but she suddenly collapsed, and died on the fourth day in hospital. Death was probably due to respiratory failure and severe circulatory collapse.

Case 3.—A male aged 4 years, who was admitted on the second day of illness. He had an extensive paralysis affecting arms, legs, diaphragm, and abdominal musculature. Artificial respiration, postural drainage and suction were begun immediately, but the oxygenation remained poor. Finally, as the medullary centres became affected, respirations became shallow, irregular, and gasping. Death occurred forty-six hours after admission.

Diagnosis.

The diagnosis was established by clinical examination and lumbar puncture. When there was obvious flaccid paralysis no difficulty was encountered, but when only meningism was exhibited, several diagnoses had to be considered.

On admission to this hospital each patient is subjected to a routine lumbar puncture. At the same time a sample of blood is taken for blood sugar estimation, and a Mantoux 1/1000 skin test inserted. Normal readings for the cerebro-spinal fluid are taken as protein under 40 milligrams; white cells under 10; and sugar of more than 40 milligrams. In most cases of poliomyelitis the cerebro-spinal fluid is clear, under increased pressure, with a white cell count of between 20 and 250 per millilitre, and an accompanying rise in protein. The cells are mainly lymphocytes, and when these exceed 200 per millilitre the fluid becomes steamy.

Occasionally the cell count may reach a very high level. The cerebro-spinal fluid in tuberculous meningitis reveals a low sugar, with a marked increase in white cells and protein, the cells being predominantly lymphocytic. The blood sugar is valuable for comparison with that of the cerebro-spinal fluid. A positive Mantoux reaction, especially in a child, aids the diagnosis of tuberculous meningitis.

It is widely accepted that a polymorphonuclear leucocytosis occurs in the cerebro-spinal fluid in the early stages of acute poliomyelitis. The findings in this series are noteworthy. Sixty-seven cases were admitted on and before the fourth day of illness, and of these, only six presented this feature with polymorphonuclears varying between 10 and 90 per cent. Seven other cases admitted between the sixth and fifteenth day of illness showed a similar polymorphonuclear count varying between 20 and 60 per cent. Only ten of the one hundred and twelve cases admitted had normal cerebro-spinal fluids.

An abnormal cerebro-spinal fluid may be found in various other virus infections. A history of contact or recent infection with measles, varicella, pertussis, or mumps may help. This was so in four of our cases where the infecting agent was the mumps virus. All had clear cerebro-spinal fluids, with a lymphocytic pleocytosis, raised protein and a normal sugar. Another child, aged five years, gave no such history but complement fixation tests for mumps virus were positive to high titre in all five.

In most of those cases where there was an altered cerebro-spinal fluid and no paralysis, two specimens of blood were taken for serological examination. The first sample was taken during the first week of illness, and the second, after the twenty-first day. Leptospiral agglutination tests and complement fixation tests for the viruses of lymphocytic chorio-meningitis and mumps were carried out by the Virus Reference Laboratory, Colindale. Paul-Bunnell tests were done on 23 patients—none was positive. Six other patients returned a titre for mumps which suggested a recent infection with the virus. No history of contact or infection could be obtained, and these are still included in the list as non-paralytic poliomyelitis.

In the differential diagnosis interesting cases rejected were :—

Case 1.—A Guillain-Barré syndrome. The patient was a boy aged 7 years who developed a symmetrical flaccid paralysis of all limbs and weakness of the trunk musculature without any initial meningeal signs. The deep reflexes were absent. Examination of the cerebro-spinal fluid showed a cell-protein dissociation. Recovery was progressing satisfactorily when he was removed from hospital six weeks after admission.

Case 2.—A female child of six months who was admitted as a case of poliomyelitis and subsequently diagnosed as suffering from scurvy. On examination no obvious scorbutic lesions were present. The right leg was abducted and exhibited pseudo-paralysis. The only positive finding was an acutely tender area over the medial tibial condyle. Diagnosis was established by X-ray, which showed a zone of rarefaction and destruction in the metaphyseal area with elevated periosteum. A sample of blood taken at this time revealed a low vitamin C level. Recovery was complete on an adequate diet.

Treatment.

Treatment of our patients has been along well recognised lines, the object being to produce mental and physical rest. This is achieved by adequate sedation,

and, when there is paralysis, the affected parts are splinted to prevent deformity. Physiotherapy is commenced when muscle tenderness has abated.

Non-paralytics are detained in hospital for three to four weeks or until the cerebro-spinal fluid has returned to normal.

Six cases requiring artificial respiration were nursed in Both respirators. In addition, four of these required oxygen, and this was given by nasal catheter. Nutrition is maintained in the acute stage by small fluid feeds. If the patient can swallow comfortably these are given by mouth, if not, the nasal route is used.

Antibiotics are not prescribed routinely but are only given in those cases where there is clinical evidence of respiratory infection or as prophylaxis in special cases. With recovery of respiratory musculature, the patient may be removed from the respirator for a longer period each day. Where there is bulbar involvement the major problems are :—

1. Difficulty in maintaining an airway, and
2. Difficulty in feeding.

Here the patient is unable to handle his secretions. Saliva and mucus accumulate in the pharynx, and an adequate airway is only maintained by postural drainage and continuous suction. Again, oxygen is often necessary. Fluids may have to be given by intravenous sub-cutaneous or nasal routes, because of inability to swallow.

The place of tracheotomy in the treatment of respiratory and bulbar paralysis has not yet been decided. In the past three years, using the Both respirator with suction apparatus and postural drainage, our mortality rate has been 39 per cent. This is comparable with the recent figure of 40 per cent. issued from Copenhagen in the 1952 epidemic, where tracheotomy was combined with artificial respiration carried out by manual bag compression.

Retention of urine is not uncommon, but being only a temporary embarrassment, is treated with intramuscular carbachol in preference to repeated catheterisation. Prostigmine and pituitrin are given when abdominal distension is troublesome.

Complications.

Patients who have had intercostal and diaphragmatic paralysis are unable to combat any respiratory infection. Bronchitis and broncho-pneumonia occur frequently and may terminate fatally, despite the administration of antibiotics and renewed artificial respiration. Visitors to these wards are not encouraged during the season of respiratory infections. Abdominal distension was present in only one patient who was under treatment in the Both respirator.

Less serious complications are those due to over-activity of the sympathetic nervous system. Retention of urine and abdominal distension occur in the early phase of the disease and are temporary. In this series retention of urine was not confined to those cases with extensive spinal paralysis, but occurred also in an adult male suffering from polio-encephalitis.

Skeletal deformities are prone to occur but are minimised by adequate physiotherapy. Poor circulation is a common finding in paralysed limbs.

Prognosis.

The prodromal illness seems to bear no relationship to the severity of the ensuing paralysis. When the latter does occur it is impossible to forecast with accuracy the extent of muscle recovery.

A combination of bulbar and spinal paralysis constitutes the major cause of death. It has been noticed that when bulbar paralysis occurs alone without involvement of the autonomic centres, prognosis is good if a clear airway can be maintained. All patients with palatal and pharyngeal paralysis made a good recovery.

When there is primary involvement of the respiratory and vasomotor centres death usually occurs in the first few days of illness. With respiratory paralysis of spinal origin the immediate outlook is rather better but remote prognosis is poor because of inadequate recovery of the respiratory musculature. Ventilation may be sufficient for basal requirements but repeated respiratory infections may cause death or confine the patient to the precincts of a hospital for the remainder of his days.

Summary.

In the year ending on the 31st December, 1952, one hundred and twelve cases of poliomyelitis were admitted to the Northern Ireland Fever Hospital. Of these, sixty-two were non-paralytic, forty-five were paralytic, and five had polio-encephalitis. The symptomatology, age incidence, and seasonal incidence of this series are similar to those reported elsewhere.

Ten cases had normal cerebro-spinal fluids. Those who had abnormal cerebro-spinal fluids and were without paralysis were subjected to further agglutination and complement-fixation tests before being listed under the heading of non-paralytic poliomyelitis.

The value of tracheotomy in the treatment of bulbar poliomyelitis has not yet been decided.

There were three deaths due to bulbar involvement following progressive and widespread paralysis. Eighteen cases remained in hospital at the end of the year.

I am indebted to Dr. F. F. Kane, Medical Superintendent of the Northern Ireland Fever Hospital, for permission to publish these cases; and to Dr. G. F. W. Tinsdale and Dr. A. R. Crawford for the cerebro-spinal fluid reports.

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A Report on the Cases of Purulent Meningitis admitted to the Northern Ireland Fever Hospital in 1952

By SARAH L. CAMPBELL, M.D., B.CH., M.R.C.P.I.

Senior House Officer, Northern Ireland Fever Hospital, Purdysburn, Belfast

THE Northern Ireland Fever Hospital serves a population of one and a quarter million. Between the 1st January and the 31st December, 1952, 276 cases of suspected meningitis were admitted to the hospital. Intracranial disease was confirmed in 143. Sixty-six had acute purulent meningitis, and 32 had tuberculous meningitis. The others were suffering from acute poliomyelitis (36), subarachnoid hæmorrhage (4), brain tumours (3), brain abscess (1), and congenital hydrocephalus (1). In 64 of the cases admitted nothing abnormal was found, and in the remaining 69 cases an infection outside the cranial cavity had misled the practitioner. These infections were—pneumonia (17), tonsillitis (16), acute otitis media (10), mumps (6), primary tuberculosis of lung (4), gastro-enteritis (3), two cases each of pertussis, sinusitis, influenza, cervical lymphadenitis, and one case each of miliary tuberculosis, rheumatic fever, acute nephritis, pyelitis, and measles.

The 66 cases of acute purulent meningitis are the subject of this report. Of these, 47 had cerebro-spinal fever, 14 had pneumococcal meningitis, 4 had influenzal meningitis, and in one fatal case no organism was grown from the purulent cerebro-spinal fluid. The cases can be divided into age groups as shown in the table below. The number of deaths in each group is shown in brackets.

TABLE.

	Age in Years.						
Organism.	0-1 yrs.	1-5	5-10	10-20	40-50	Over 70	Total
Meningococcus	24 (0)	17 (1)	2 (0)	4 (0)	—	—	47 (1)
Pneumococcus	7 (1)	1 (1)	2 (0)	2 (0)	1 (1)	1 (1)	14 (4)
H. Influenzæ	3 (1)	1 (1)	—	—	—	—	4 (1)
Unknown	—	—	—	—	—	1 (1)	1 (1)

DIAGNOSIS.

In the adult, the onset of acute meningitis is sudden with fever, intense headache, rigors, vomiting and delirium gradually deepening into coma. These symptoms associated with neck stiffness and a positive Kernig's sign usually make the diagnosis obvious in the adult patient.

In the infant, the symptoms and signs are rarely clear cut. But in the 178 cases in which the diagnosis before admission was in error only 26 of the patients were

under 1 year and 66 under 5 years. The onset may be abrupt or insidious with little pyrexia. Irritability, vomiting, screaming or convulsions may occur. The classical signs of neck stiffness and rigidity of the hamstrings are most unreliable in infants. A much more important sign is the presence of a tense or bulging fontanelle in a quiet infant. The diagnosis of acute meningitis in infancy has been discussed recently by Hapworth (1953). He emphasises that clinical diagnosis may be very difficult and, if suspected, a diagnostic lumbar puncture should not await the development of typical meningeal signs.

In a febrile patient, stiffness of the neck per se does not necessarily mean meningitis. Local conditions such as tonsillitis or mumps are often the cause in the adult. In infancy such conditions as apical pneumonia or otitis media may result in meningismus. In this series of admissions pneumonia was the revised diagnosis in 17 cases, tonsillitis in 16, otitis media in 10, and mumps in 6.

All cases admitted as suspected meningitis have a diagnostic lumbar puncture. The infecting organism was seen on direct examination of the turbid cerebro-spinal fluid in 21 cases of cerebro-spinal fever, 10 cases of pneumococcal meningitis, and 3 of the cases of influenzal meningitis. If the organism is not seen chemotherapy is commenced on clinical assessment of the case and changed if necessary when the organism is grown. A blood culture may be of value in determining the infecting organism, especially if it is the meningococcus. A positive blood culture was obtained in 8 out of 15 of the cases of cerebro-spinal fever in which this investigation was done.

Treatment.

Good nursing, adequate fluid intake, orally or intravenously if necessary, effective sedation and the appropriate chemotherapy given immediately, form the basis of treatment. The amount of sedation required varies with the degree of irritability and restlessness seen in the individual patient. An adult may require morphia for immediate sedation. For prolonged sedation oral phenobarbitone or potassium bromide are the drugs used. The dosage varies from $\frac{1}{8}$ grain phenobarbitone six-hourly in the under one year olds to 1 grain six-hourly in the adult. The comparable dose of potassium bromide is $3\frac{3}{4}$ grains to 30 grains. A mixture of potassium bromide 30 grains in 1 ounce is used.

A routine chemotherapeutic schedule for each of the groups mentioned in the table is employed. In cerebro-spinal fever patients under 2 years are treated with intramuscular penicillin .25 mega units six-hourly for five days. Penicillin is used in this age group in preference to sulphonamides as it is easily given in effective dosage and obviates the risk of additional injury to the kidneys. In the older age group sulphamezathine affects a rapid cure, unless the patient is vomiting or is comatose, when again penicillin is the treatment of choice. Children are given an initial dose of 2 gm. sulphamezathine, intravenously if possible, followed by 1 gm. six-hourly orally to a total of 12 gm. The adult requires double this dosage. Intrathecal treatment is unnecessary. Intravenous plasma is of value when this acute infection is associated with peripheral circulatory failure.

In pneumococcal meningitis intrathecal therapy with penicillin is used. Daily dosage varies from 5,000 units in the infant to a maximum of 20,000 units in the adult. Five consecutive daily doses are given. This is the average duration of intrathecal therapy suggested by most authorities and a longer course does not seem to give a better prognosis. Both penicillin and sulphamezathine are given systemically. Sulphamezathine dosage is used as described for the cerebro-spinal fever group. The intramuscular penicillin is given for ten days.

Until 1952 the schedule of treatment of influenzal meningitis was intrathecal penicillin and streptomycin, with intramuscular penicillin and streptomycin and oral sulphadiazine. The satisfactory results obtained by this treatment in this hospital were published by McConnell (1950). The *H. influenzæ* is sensitive to chloramphenicol and this is now the antibiotic of choice in this infection, as oral medication is simple and effective. However, it must be recognised that relapse may occur with cessation of treatment and this was seen in one of our cases. The child relapsed clinically two weeks after chloramphenicol was discontinued. Lumbar puncture gave a purulent fluid from which *H. influenzæ* was again cultured. Cure was affected by a further course of chloramphenicol. One case did not respond well clinically until oral sulphamezathine was also given. The third case was cured on one course of chloramphenicol only. The fourth case died before therapy could be effective. The dosage of chloramphenicol given is 50 mg. per kilogram body weight daily for ten days.

When the infecting organism is *Staphylococcus aureus,* the hæmolytic streptococcus or *B. coli*, therapy depends entirely on the sensitivity of the organism. It is worth noting that chemotherapy given imperically before admission may be sufficient to make the cerebro-spinal fluid sterile though still purulent. The disadvantage is that the organism cannot be isolated and so the necessary schedule of treatment cannot easily be decided, and delay in adequate medication may result.

Complications.

The only complication seen in this series was polyarthritis occurring in a boy of three years with cerebro-spinal fever. His elbows and knees became swollen five days after admission. The swelling gradually subsided and normal mobility of all the affected joints returned. There were no cases of prolonged fever, repeated convulsions or persistent vomiting to warrant subdural tap for the diagnosis of subdural effusion. This has been discussed recently by Guthkelch (1953) as a sequel of purulent meningitis.

Prognosis.

The majority of cases of purulent meningitis are discharged after a three-week stay in hospital. The cerebro-spinal fluid has usually returned to normal in this time. If this has not occurred the patient is detained in hospital and has a weekly lumbar puncture until a normal fluid is obtained. Normal readings are taken as protein under 40 milligrams, white cells under 10, sugar over 40 milligrams.

At the British Pædiatric Association in 1952, Wolff pointed out that, in the follow-up of 134 cases of cerebro-spinal fever occurring since 1939 in Birmingham

all cases in infants under 6 months showed a retarded intelligence. Deafness was also commoner in infants under 1 year old than in the older child. Clinically it is easy to recognise deafness in a child who could talk prior to contracting meningitis, but it is extremely difficult to detect deafness in infancy. It can be seen that the majority of our cases of cerebro-spinal fever occurred in the under 1 year age group. A long-term follow-up of these cases will be necessary to exclude the grave prognosis with regard to both intelligence and hearing in these infants.

Summary of Fatal Cases.

The one fatal case of cerebro-spinal fever was a boy of 4 years who was transferred from a general hospital. He had been ill for 24 hours with headache and vomiting. On admission he was semi-comatose with a profuse purpuric rash, cold extremities, and a feeble pulse. His blood pressure could not be recorded. He did not respond to intravenous plasma and intramuscular penicillin and died five hours after admission. Permission for a post-mortem examination was not obtained. Transfer of such an ill child is not always advisable, as a long ambulance journey may increase shock and seriously delay treatment. A meningococcal infection kills rapidly and a few hours' delay may be fatal.

In the pneumococcal group there were four deaths. Two cases, a child of 4 months and a man of 76 years died less than 12 hours after admission. A child of 2 years who was progressing satisfactorily collapsed and died suddenly 4 days after admission. The fourth fatal case was a woman of 48 transferred from a surgical unit with pneumococcal meningitis and jaundice. The cerebro-spinal fluid became normal with chemotherapy but she died five weeks after admission. Post-mortem showed necrosis of the liver and pancreas with empyema of the gall bladder. The meninges had returned to normal. Nemir and Israel (1951) pointed out that the addition of penicillin to the therapy of pneumococcal meningitis introduced a new era in the prognosis of the disease. They report an 81 per cent. survival rate in 158 cases described in the literature, treated by combined penicillin and sulphonamide therapy.

The fatal case of influenzal meningitis was a child of 6 months who had been ill for two days prior to admission. She survived admission by only six hours.

One fatal case was probably due to a staphylococcal infection. A man of 76 years was unconscious on admission. He had a three-day history of pain in his left ear followed by otorrhœa, headache, vomiting and a rapid decline into coma. He died seven hours after admission. A penicillin sensitive *S. aureus* was grown from his ear swab. No organism was cultured from his purulent cerebro-spinal fluid.

Summary.

In 1952, 276 cases of suspected meningitis were admitted to the Northern Ireland Fever Hospital. The diagnosis was confirmed in 98 cases only. Acute purulent meningitis was found in 66, and of these 59 survived. Tuberculous meningitis was found in 32 cases.

The chemotherapy used according to the infecting organism is described.

A summary of the seven fatal cases is given.

I am indebted to Dr. F. F. Kane, Medical Superintendent of the Northern Ireland Fever Hospital, for permission to publish these cases and for direction and control of the therapy; to Dr. G. F. W. Tinsdale and Dr. A. R. Crawford, Northern Ireland Fever Hospital, for laboratory reports.

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RESPIRATORY FUNCTION : MANAGEMENT IN DISEASE. By Richard D. Tonkin. (Pp. 64; figures 11. 3s. 6d. (paper), 5s. 6d. (cloth.). London : Actinic Press. 1953.

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The chemotherapy used according to the infecting organism is described.

A summary of the seven fatal cases is given.

I am indebted to Dr. F. F. Kane, Medical Superintendent of the Northern Ireland Fever Hospital, for permission to publish these cases and for direction and control of the therapy; to Dr. G. F. W. Tinsdale and Dr. A. R. Crawford, Northern Ireland Fever Hospital, for laboratory reports.

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Progress in the Prevention of Poliomyelitis

(With a Note on the Legal Control of Contacts)

By A. T. ELDER, M.D., PH.D., B.HY., D.P.H., BARRISTER-AT-LAW

Ministry of Health and Local Government, Stormont, Belfast

INTRODUCTION.

THE recent visit to the United Kingdom of Professor H. C. A. Lassen and Dr. B. Ibsen of Copenhagen recalls to mind the severity and the aftermath of the outbreak in Denmark a year ago. During their visit to Belfast, Lassen and Ibsen kindly answered many questions. Two which were not asked but which must surely have been in the thoughts of many of those present were these: What is the present state of health of those sufferers from severe respiratory paralysis who were saved by modern techniques, and what is the prognosis of the twenty-five to thirty sufferers still, a year later, being kept alive by propulsion respiration?

Lassen (1953) assessed the number of cases occurring in the metropolitan area of Copenhagen (population 1,200,000) between July 24 and December 3, 1952, at 2,722. The writer visited the Ministry of Health in Copenhagen, where it was stated that 390 of the notifications had not been confirmed as poliomyelitis, and that 70 cases admitted on other diagnoses were proved to be poliomyelitis. Still it appears that, even on their own most accurate reassessment, the Danes were faced with 2,400 proven cases, of which one-quarter were paralytic and one-eighth suffered from respiratory failure.

On a population basis, were the attack rate of this particular virus to be the same in a possible outbreak in Northern Ireland, we might expect at least 1,000 cases in Belfast and perhaps 1,200 to 1,500 in the Province as a whole. It is clear that, without advance hospital preparations, such facilities as we possess at present would be rapidly exhausted, and accommodation overrun. It is, however, not merely a matter of beds, but of suitably prepared accommodation with adequate modern equipment. Special poliomyelitis treatment centres are being established both here and in Great Britain, and standard modern equipment issued, based on the lessons of Denmark.

In 1952 rates of incidence in Denmark, Netherlands, Belgium, United States of America, and New Zealand were above the median of the years 1945-51, while in the United States of America the incidence in 1952 was the highest ever recorded for the country as a whole, but particularly high rates were recorded in some of the major geographical divisions (Peters, R. J.; 1953). The case rate per million of population in Northern Ireland in 1952 was approximately one-third of that for the United States of America, which is stated by Peters to have been 360 per million.

During July and August of this year in the City of Londonderry there were 33 cases in a population of 50,000 approximately. The attack rate for Denmark

as a whole in 1952 was 132 per 100,000 of population. It is clear, therefore, that we in Northern Ireland have experienced the full effects neither numerically nor in severity of a comparable epidemic, and we have time to reflect on the adequacy of our present preventive measures.

There is little justification, on the face of things, for our not pursuing a vigorous policy of prevention, if such a policy can be clearly defined. A study of recent papers seems to indicate that the time has already arrived for vigorous action. To this end, the writer has assembled a few points from recent papers, coupled with his experiences of a visit to Denmark in April of this year. The result is here presented as simply and as briefly as possible in relation to the control of the disease.

Pathogenesis.

Rhodes (1953) summarises the evidence neatly, concluding with a reference to Faber's view (1950) that the virus enters through the mucosa of the pharynx or mouth and thence invades through peripheral nerves. "The virus is primarily neurotropic and is 'locked away' inside the nervous system from shortly after penetration of the superficial mucosæ."

Mention is made of an alternative theory which has recently been revised by Bodian (1952), who postulates that virus multiplies first in the alimentary mucosa, then in the organs associated with the blood, and finally in the central nervous system and sensory ganglia. "Viræmia is initiated by the escape of virus from the primary alimentary multiplication sites and is brought to an end by the appearance of antibody. . . ." Several factors may convert inapparent infections into paralytic illnesses. These precipitating factors operate at various stages after deposition of virus on the mucosæ, e.g., trauma from tonsillectomy, various intra-muscular injections, increased physical exertion after the onset of the major illness. Pregnancy is thought by some to serve to increase susceptibility to paralysis probably through hormonal mechanisms (Garlick, 1948; Anderson, Anderson, Skaar and Sandler, 1952). Lassen (1953) quoted six cases amongst his patients who were dealt with by Cæsarean section.

Virus Isolation.

Weaver (1953) points out how essential it is to determine how many different viruses are capable of causing human poliomyelitis. He states that it cost more than 1,337,000 dollars to learn that there are three different types of the virus circulating throughout all parts of the world.

It is believed that all three types exist in the United Kingdom to-day. The active participation of the Colindale Virus Reference Laboratory in the typing of the virus during outbreaks is already a practicable measure but is not one which can yet be carried out speedily. Though the diagnosis in each case in the maternity home outbreak reported recently by Sims-Roberts and Thompson (1953) was confirmed in each, some months elapsed before the findings could be made known. Primary isolations were made in monkeys, and tissue cultures of monkey testicle, and the typing was carried out in the latter.

In the Copenhagen epidemic it was impossible to obtain virus from the spinal cords of patients who died, or from drinking water, or from flies, and only with very great difficulty from the naso-pharynx of cases.

At the Symposium of Copenhagen, early this year, the writer learned from Dr. Von Magnus of Denmark that virus was best grown on Parker 199 (Morgan, Morgan and Parker, 1950; Franklin, et al., 1952; Wood, et al., 1952), an artificial medium of some fifty-five ingredients, but amnion of cow and human embryo living tissue was used in other instances. Beef amniotic fluid from slaughter-houses and even human tonsils have been used. The difficulties of tissue culture, involving also the training of technicians, are well known, and special laboratory facilities are essential.

Material from cases occurring during the present outbreak in Northern Ireland has been sent from time to time to Colindale but results will not be to hand for some time.

The Origin of Outbreaks and Epidemiology Generally.

The evidence, reviewed by Sabin (1951), indicates that human fæces are the most significant source of virus; the period of communicability may extend for longer than a few days after onset; the mouth is the usual portal of entry; fæcal-feeding flies may act as carriers of virus; and it is likely that several methods of transmission are involved.

Weaver (1953) points out that fly abatement programmes in the United States of America did not modify epidemics of the disease.

According to Weaver human beings constitute the principal reservoir of the virus in nature. The order of frequency with which individuals may be found to be excreting the virus may be listed as: (a) the individual with acute poliomyelitis; (b) household associates of the case, and (c) close personal, extra household associates of the family.

According to Peters (1953) "it is not possible to predict the occurrence of an epidemic from the behaviour of the disease in the early months of the year." This is borne out by our experience of poliomyelitis notifications in Ulster in the spring and summer months of 1952 and 1953. The table overleaf shows the remarkable divergences in June, July, and August, which could not have been foreseen by any present methods of assessment.

It is thought that in temperate zones virus survives between epidemics in the human population of urban areas. "As paralytic cases are very rare during the winter, it is suggested by many that virus passes sporadically from person to person, causing a chain of abortive illnesses or carrier states. Then with the onset of warmer weather, for some reason there is increased transfer of virus and thus an increased incidence of infection.

It is doubtful whether it is possible to forecast the outcome of such passage of virus by the number of cases pre-existing in December. It has, however, been suggested that a relatively high infection rate in December may be a basis for such a forecast. Invasiveness of the virus cannot be measured in the laboratory,

and much depends on the state of immunity of the population. All three strains of virus may, theoretically, be introduced and the epidemiological pattern of one superimposed on another.

MONTHLY INCIDENCE OF POLIOMYELITIS IN NORTHERN IRELAND, 1947-1953.

	1947	1948	1949	1950	1951	1952	1953
January	—	1	1	1	1	3	6
February	1	3	—	3	—	6	3
March	2	—	—	3	1	5	1
April	—	—	2	6	—	3	—
May	—	—	2	19	3	2	2
June	3	—	—	34	8	12	14
July	14	2	2	63	7	16	45
August	84	7	5	52	14	36	59
September	38	1	9	61	21	33	63
October	38	2	11	14	17	17	6
November	16	1	4	12	5	5	—
December	12	—	4	4	3	4	—
Totals	208	17	40	272	80	142	199

Graphs drawn of notifications from a localized outbreak usually show a slight, rising, pre-epidemic phase, an explosive outburst, a gradual decline interrupted towards the mid-point by a secondary peak from which the graph tapers away gradually to zero.

If notifications from an entire region are so planned on a graph this true epidemic curve is not usually shown because of the fact that spread of the virus by contact from area to area leads to secondary outbreaks and the over-all picture may be rather one of a series of peaks occurring at fortnightly or monthly periods, before there is a final and permanent diminution for the entire region towards the end of October.

Miss Margaret Agerholm (1953), in a paper which well repays careful study, attempts to bring down to practical detail the part played by symptomless and abortive cases. Epidemics of poliomyelitis, she states, could be, if not entirely prevented, at least reduced by control of the movements of the contact carrier. Usually "the chain of notification remains hidden and is never published." But in her exposition she is able to make use of an epidemic in the Isle of Wight (1950), which has been reported in sufficient detail for the purpose (Ministry of Health, 1951). The Isle of Wight epidemic, 1950, showed forty-nine cases, of which forty-one were paralytic and two died. The analysed chain of infection shows clinical cases, symptomless cases, those preventable by quarantine, those preventable or modifiable by passive immunization, those in which there are insufficient data. Case 16 represents a "nurse" not observing full fever nursing precautions. Though symptomless herself, she transmitted the disease to her sister, to a social contact

and directly or indirectly to four other cases. Those patients who would have been likely to gain some benefit from effective passive immunization of contacts have also been picked out. It is estimated that seven of the forty-nine cases could have been so prevented, but twelve cases could have been prevented by quarantine measures, and strict nursing technique on the part of a contact might have prevented six others. Thus it appears twenty-five, or approximately half, of the cases in this epidemic need not have occurred.

Passive Immunisation.

Poliomyelitis-neutralising antibody is present in gamma globulin (Enders, 1944); this fraction, prepared from pooled human plasma collected during the Second World War by the American National Red Cross, contains antibody to the three types (Bodian, 1949).

Encouraged by results in the prevention of measles and infectious hepatitis, Hammon, et al. (1952), conducted field trials in 1951 and 1952. (Bulletin of Hygiene, 1953.) The attack rate amongst children aged two to eight years so protected was 34.8 per 100,000 as against 175.0 in the contact group in County Utah (population 72,000). The total number of children inoculated in three trials was 54,772.

Criticisms of the reports from Hammon and his co-workers made by the Danes lay in the lack of information as to the actual dose of gamma globulin and as to the titration of blood for antibody content.

According to the Danish workers, one gm. of dry substance can be given in each of four or five injections between August and December. This total of five gms. is equal to $2\frac{1}{2}$ litres of whole blood, and produces an antibody response (one in ten). Clearly what is required is a high potency gamma globulin blood factor, and careful selection of donors. If even convalescent donors are not taken at random but selected, the titre will be greatly raised, for example, using only 5 per cent., approximately, of convalescents. The Icelandic representatives at Copenhagen stated that the titre of the antibodies in their cases was too low for them even to produce their own gamma globulin successfully.

Questions which next arise are whether the antibody level of the population can be readily assessed from, say, random samples from the Blood Transfusion Service, and whether it is reasonable and practicable to fractionalise blood from convalescents in hospital.

Again, much has been said about the cost of gamma globulin. This is, however, reasoning based on the giving of the material in the dose above-mentioned, to all children within the age group at risk in an area affected. In the recent outbreak at Londonderry, however, this policy was not followed. One dose only of 250 mgms., as used against measles, was given, on the assumption that after an initial period of about a week, protection would develop to last over a subsequent four or five weeks. Only children in the age group affected at the time, that is up to six years of age, were so treated with one intramuscular injection. Again, contacts

were carefully selected from (a) members of the same family as the patient; (b) close household contacts. At the same time quarantine measures were introduced, according to the Medical Officer of Health. Unfortunately for research purposes, whether for climatic or quarantine reasons, the epidemic came to a somewhat abrupt end before more than a handful of cases had been inoculated. The expense involved up to that point, however, was negligible. Such field trials of the use of gamma globulin in a selective sense have yet to be reported upon.

Experts now await an authoritative report on the use of gamma globulin by seven workers under the chairmanship of Dr. Alexander D. Langmuir of the U.S. Public Health Service. Whether the use of gamma globulin during the pre-epidemic phase would be successful in modifying an outbreak is yet problematical.

Active Immunisation.

There appears to be something of a race between major laboratories in Denmark, Germany, France, and America to produce a potent vaccine. The American work is excellently summarised in the leader article of the "Lancet" of April 18, 1953.

At the Symposium of Copenhagen three types of vaccine were mentioned: (a) Inactivated Virus Adjuvant Vaccine of Salk ("Lancet," 1953); (b) Virus Attenue —non-paralytic for monkeys giving a 90 per cent. protection rate in monkeys, and (c) virus mutation vaccine—virus from man is given intravenously to monkeys and an irreversible mutation of virus occurs. The Salk vaccine was inactivated with formaldehyde and preliminary reports are encouraging. Tests in America, costing £2,500,000, are stated to be going to be completed before the next poliomyelitis "season" starts. ("Belfast News-Letter," October, 1953.)

Administrative Action by Medical Officers of Health.

Miss Agerholm states that "those requiring quarantine include all infants who have been in contact with the patient up to four days before the onset of the illness, that is, the household, contacts outside the family and contacts at the place of work or education. The period of quarantine should be fifteen days for an individual and thirty days for a group (to safeguard against the symptomless intermediate) from the last time of contact with the case." She goes on to state that quarantine is bound to cause hardship. The point, however, goes much further than that, in that in many instances it is quite frankly legally impossible. This point is dealt with below. However, much can be done by way of advice to family and close household contacts. Notification could be made by telephone to the Medical Officer of Health, and either medical or public health nursing visitors could call and give advice as a follow-up measure.

In view of the evidence as to the probable method of spread of the virus (Weaver, Rhodes, Agerholm, Sims-Roberts and Thompson and many others), advice similar to that given to contacts of other enteric diseases would appear to be appropriate. Advice to intimate contacts of contacts forms part of the follow-up measures (Agerholm), and it is important to reduce the numbers of those requiring quarantine or restriction of movement to the smallest necessary fraction.

Administrative Action by Central Authorities.

In a "Plan for the Allocation of Gamma Globulin" issued April 15, 1953, by the Office of Defence Mobilisation in the Executive Office of the President (United States of America) full details are given as to a planned allocation throughout the various territories, a reserve of 10 per cent. being retained by the national allocating authority

The State Health Officer is given full authority for the distribution of the gamma globulin allocated to him. When used for the prophylaxis of contacts of clinically diagnosed cases the following criteria are recommended:

(*a*) Household contacts thirty years of age or under.

(*b*) Pregnant women of any age.

Mass Community Prophylaxis is mentioned but importance is laid on household and other intimate contacts.

As suggested above, issues might be placed on an even more selective basis, thus reducing the cost, and the amounts of prophylactic given could, it is argued, be usefully restricted also. Much field work is, however, required before final conclusions can be drawn.

A Note on the Legal Position in Regard to Poliomyelitis Control.

In England, by order of the Ministry of Health (1912), acute poliomyelitis was made notifiable to the Medical Officer of Health. Under the National Health Service Act, 1946, the Medical Officer of Health of a county district council must send a copy of any notification of infectious disease within twelve hours after its receipt to the county council.

In Northern Ireland, under the Infectious Diseases (Notification) Act, 1889, Section 7, power is given to a local authority to extend the definition of infectious disease. By such resolution of councils poliomyelitis was made notifiable, and approved by the Ministry of Health and Local Government. Poliomyelitis would appear to be the only remaining infectious disease made so notifiable by resolutions of all the sanitary authorities. The duty to notify is a dual responsibility laid also on the head of the household, whereas in the case of diseases made notifiable by regulation of the Ministry under the Public Health (Ireland) Acts of 1878 and 1896, notification thereof to the Medical Officer of Health is the responsibility of the medical practitioner only (Statutory Rules and Orders, 1948, No. 324, Paragraph 5). The duties of the Medical Officer of Health are laid down in paragraphs 9 and 10 of the latter Order, but poliomyelitis does not figure amongst the diseases listed in the first schedule.

Suspected cases are not legally notifiable. Hospital medical staffs would normally only notify if they had reason to suspect that the case had not already been so notified.

As to contacts, it would appear to be unlawful, under paragraph 9 of the Dairies, Cowsheds, and Milk-Shops Order (Northern Ireland), 1935, for recent contacts of any infectious disorder to milk cows, handle vessels used for containing milk for sale, or . . . take part in the production, distribution or storage of milk.

Though known to be spread by means similar to other enteric disorders, poliomyelitis would hardly come within the definition of disease as far as control of contacts mentioned in Part III of Statutory Rules and Orders, 1953, No. 299 (England and Wales) or Statutory Rules and Orders (Northern Ireland), 1948, No. 324, Second Schedule, so far as they relate to control of food poisoning.

Thus the legal powers of the Medical Officer of Health or Health Authorities are limited so far as control of contacts is concerned. Much can be done, however, by educational methods, and the co-operation of employers during an epidemic.

Closure of schools is not a practical method of control but restriction of movements of child contacts individually would appear to be advantageous.

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REVIEWS

ROYAL VICTORIA HOSPITAL, BELFAST: 1903-1953. By Robert Marshall, M.D, F.R.C.P.(Lond.), F.R.C.P.I., D.P.H. (Pp. 139 + xv; plates 12. 7s. 6d.). Belfast: W. and G. Baird. 1953.

GRADUATES of the Belfast medical school the world over will welcome this fine and fitting tribute to the work of the Royal Victoria Hospital. The Board of Management have been fortunate in that the one person pre-eminently qualified to undertake the work has done so, and in doing so has given so generously and so tirelessly of his time and energy. Dr. Marshall has produced a record at once scholarly and of absorbing interest to both medical and lay readers. The record is replete with detail which is yet so cleverly woven into the narrative that this never becomes a catalogue of facts. Dr. Marshall has devised the novel plan of arranging the narrative in five-year periods. He gives in each of these first a brief record of the events in the world and in the city of Belfast, and he then describes changes within the hospital. The reader is thus orientated in time and can appreciate the external conditions in which events affecting the hospital took place. The record at all times has that quality of lucidity and simplicity of style which shows true mastery of the English tongue and which we expect from the author.

The printing, arrangement, and binding of the book will challenge comparison with that of any press in the world, and Messrs. W. and G. Baird, Ltd., of Belfast, are to be congratulated on this.

We are sure that those of our readers who have not already obtained this book will wish to possess it, and that they will treasure it as a worthy link with a great teaching hospital.

SOME ASPECTS OF ENZYME RESEARCH, being No. 2 of Volume 9 of the *British Medical Bulletin*. (Price 15s.). London: British Council. 1953.

THIS volume is described as a sequel to the Gowland Hopkins memorial volume, "New Currents in Biochemistry," published five years ago. The earlier volume included articles by Peters and his colleagues in Oxford describing how peace-time academic researches on carbohydrate metabolism had led, in war-time, to the development of British Anti-Lewisite (dimercaprol). Conversely, the war-time developments in biochemistry are now leading to peace-time applications and to further advances in fundamental research. For example, dimercaprol has been found useful in medicine in the treatment of acute poisoning by arsenic, mercury and gold; and the intensive study of organic fluorine compounds as potential war gases has stimulated fundamental studies on these substances and their biological actions. One such instance in the present volume, again from Peters, is the study of fluoroacetic acid as a inhibitor of enzyme processes. This compound, which curiously turns up in nature as the poisonous principle of a South African plant, is shown to exert its toxic action by being taken up by the animal cell along with acetic acid and then being built up into fluorocitric acid instead of the normal citric acid. The fluorocitric acid then acts as a biochemical "spanner in the works" and stops the machinery of biological oxidation by blocking a particular enzyme.

Fifteen different aspects of enzyme research are covered in this volume in the form of short reviews, all of them written by experts in their respective fields. Some of them will make rather difficult reading for those who tend to fight shy of chemical formulæ, but it is becoming more and more difficult to give worth-while summaries of modern biochemical research without describing in some detail the chemical changes involved.

The following articles may be mentioned as being of special interest to medical practitioners:—Cholinesterases (by R. H. S. Thompson), Plasma Alkaline Phosphatases (by E. J. King), and The Action of Drugs on Enzymes (by J. H. Quastel).

The volume as a whole presents a valuable up-to-date survey of current work in this major branch of biochemistry, a field of research which will continue to play a fundamental part in the understanding of what goes on in the body in health and disease. D. C. H.

REVIEWS

ROYAL VICTORIA HOSPITAL, BELFAST: 1903-1953. By Robert Marshall, M.D, F.R.C.P.(Lond.), F.R.C.P.I., D.P.H. (Pp. 139 + xv; plates 12. 7s. 6d.). Belfast: W. and G. Baird. 1953.

GRADUATES of the Belfast medical school the world over will welcome this fine and fitting tribute to the work of the Royal Victoria Hospital. The Board of Management have been fortunate in that the one person pre-eminently qualified to undertake the work has done so, and in doing so has given so generously and so tirelessly of his time and energy. Dr. Marshall has produced a record at once scholarly and of absorbing interest to both medical and lay readers. The record is replete with detail which is yet so cleverly woven into the narrative that this never becomes a catalogue of facts. Dr. Marshall has devised the novel plan of arranging the narrative in five-year periods. He gives in each of these first a brief record of the events in the world and in the city of Belfast, and he then describes changes within the hospital. The reader is thus orientated in time and can appreciate the external conditions in which events affecting the hospital took place. The record at all times has that quality of lucidity and simplicity of style which shows true mastery of the English tongue and which we expect from the author.

The printing, arrangement, and binding of the book will challenge comparison with that of any press in the world, and Messrs. W. and G. Baird, Ltd., of Belfast, are to be congratulated on this.

We are sure that those of our readers who have not already obtained this book will wish to possess it, and that they will treasure it as a worthy link with a great teaching hospital.

SOME ASPECTS OF ENZYME RESEARCH, being No. 2 of Volume 9 of the *British Medical Bulletin*. (Price 15s.). London: British Council. 1953.

THIS volume is described as a sequel to the Gowland Hopkins memorial volume, "New Currents in Biochemistry," published five years ago. The earlier volume included articles by Peters and his colleagues in Oxford describing how peace-time academic researches on carbohydrate metabolism had led, in war-time, to the development of British Anti-Lewisite (dimercaprol). Conversely, the war-time developments in biochemistry are now leading to peace-time applications and to further advances in fundamental research. For example, dimercaprol has been found useful in medicine in the treatment of acute poisoning by arsenic, mercury and gold; and the intensive study of organic fluorine compounds as potential war gases has stimulated fundamental studies on these substances and their biological actions. One such instance in the present volume, again from Peters, is the study of fluoroacetic acid as a inhibitor of enzyme processes. This compound, which curiously turns up in nature as the poisonous principle of a South African plant, is shown to exert its toxic action by being taken up by the animal cell along with acetic acid and then being built up into fluorocitric acid instead of the normal citric acid. The fluorocitric acid then acts as a biochemical "spanner in the works" and stops the machinery of biological oxidation by blocking a particular enzyme.

Fifteen different aspects of enzyme research are covered in this volume in the form of short reviews, all of them written by experts in their respective fields. Some of them will make rather difficult reading for those who tend to fight shy of chemical formulæ, but it is becoming more and more difficult to give worth-while summaries of modern biochemical research without describing in some detail the chemical changes involved.

The following articles may be mentioned as being of special interest to medical practitioners:—Cholinesterases (by R. H. S. Thompson), Plasma Alkaline Phosphatases (by E. J. King), and The Action of Drugs on Enzymes (by J. H. Quastel).

The volume as a whole presents a valuable up-to-date survey of current work in this major branch of biochemistry, a field of research which will continue to play a fundamental part in the understanding of what goes on in the body in health and disease. D. C. H.

BASIC PRINCIPLES OF CANCER PRACTICE. By Anderson Nettleship, M.D., F.C.A.P. (Pp. 398 + xii; figures 196. 54s.). London: Ballière, Tindall & Cox. 1952.

THIS book has been written by the Professor of Pathology in the University of Arkansas and is intended for the general practitioner and for the medical student. It will be of greater interest to many general surgeons and physicians, and, indeed, the author's desire for completeness has resulted in a presentation too detailed for many busy practitioners.

The more practical aspects of cancer are well presented. The details of histological diagnosis and of operative therapy are avoided, but, despite this, the whole armanterium of diagnostic methods and the more acceptable methods of treatment are indicated.

After discussing methods of cancer diagnosis, which are shown to require primarily a thorough physical examination and a knowledge of the clinical behaviour of neoplasms, the author pleads for proper and accurate confirmation of the nature of the growth by microscopy and for its early treatment. Most pathologists here will agree with his conservative attitude to attempts at diagnosis by the study of individual cells. By prompt treatment is meant therapy instituted within one week of the discovery of the neoplasm. Twenty-four to forty-eight hours is regarded as ideal. The author insists that the physician should not deceive himself as to whether he is effecting radical or palliative therapy. He is probably too much inclined to regard radiation therapy as simply palliative, and he is probably over-optimistic about surgical excision in gastric carcinoma. However, there is little departure from accepted practice in this country.

The seventh chapter is devoted to neoplasms in children, and in the ten succeeding chapters the neoplasms of the various organs and tissues of the adult are reviewed.

Each of the nineteen chapters is accompanied by a bibliography. The titles of the papers are given, but they are not assessed or referred to in the text. These references are almost all recent and are often to mediocre work. Many chapters give no reference to British or Continental work, and of the total of 342 references only 16 are by British workers or to British publications while only two are to Continental sources. This preference is probably dictated by the author's awareness of the contents of the libraries to which his American reader will have access. Too many present-day publications from the United States show a similar disregard of the world literature and this must suggest that their authors are inadequately informed or have presumed that the rest of the world has nothing to contribute. Unless such publications themselves present significant advances they can scarcely expect to excite interest outside their home province. J. E. M.

PULMONARY TUBERCULOSIS: A Handbook for Students and Practitioners. By R. Y. Keers and B. G. Rigden. Third Edition. (Pp. 324 + xvi; plates and figures 150. £1. 4s.). Edinburgh: E. and S. Livingstone. 1953.

MUCH has been discovered in the field of tuberculosis since 1945 and the latest edition has been carefully revised by the authors to embody all important advances. This has been achieved without adding to the length of the book by the judicious pruning of obsolete material, a practice which might well be imitated by other authors. The book begins with a résumé of clinical pathology, epidemiology and symptomatology. There is an excellent section on the examination of the patient, in which history-taking is rightly stressed. The value of the examination of the gastric contents in diagnosis is recognised, but the authors consider the laryngeal swab technique more suitable for home and clinic use. Tuberculin testing is possibly under-valued, being listed under the heading of procedures occasionally required. The section on radiology is illustrated by a large series of well-chosen diagrams and illustrations.

The chapters on treatment form the most valuable part of the book. There is a well-balanced account of chemotherapy and the various collapse and operative procedures, including resection surgery, are clearly explained. The book is astonishingly well produced for the price and the reproductions of radiograms are of high quality.

The appearance of a third edition is an indication of the popularity of a work which presents a clear, well-balanced and thoroughly sound account of pulmonary tuberculosis. It is an excellent guide for under-graduate and post-graduate students alike. B. R. C.

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THE NEW WAY TO BETTER HEARING. By Victor L. Browd, M.D. (Pp. 252 + xii; figures 8. 12s. 6d.). London: Faber and Faber. 1953.

DR. VICTOR L. BROWD is well known in the United States of America. "The message in this book is designed for those with impaired hearing, parents and relatives of these and teachers, social workers and special therapists. The key to hearing re-education and the secret of its method lie in the considerable accumulation of unused hearing power, which every partially deaf person has locked away."

The book is divided into three parts.

Part one "expresses simply, but in detail, the nature of sound and the structure of the ear, the effects of damage on the hearing and the way in which it causes deterioration of hearing." It is stressed that poor hearing results more from the inability to understand than the inability to hear. "Sounds whose meaning is not clear actually appear fainter or more distant than sounds which can be recognised readily." . . . "The vicious interaction of poor understanding and poor response is the basic cause of the progressive hearing deterioration observed in all deaf patients." A hearing disability questionnaire enables the patient to record the amount of difficulty he experiences under a variety of conditions.

Part two sets out the basic principle of hearing re-education and describes in simple terms the method used. An assistant is selected, usually a relative or friend. The hearing disability questionnaire is next filled in. Several demonstrations are carried out to reveal the hidden hearing power possessed by the patient. The question of whether a hearing aid should be used during the re-education is discussed. Instructions to the patient on how to listen to conversation and how to conduct, enjoy and gain most from it are simply and minutely set forth. Those who use a hearing aid are advised to read aloud to themselves into the hearing aid for five minutes every day. "Ignore tinnitus; as you hear better, noises will get less." Great stress is laid on the keeping of progress notes by the patient.

Instructions for listening to the radio, television and cinema are given, also how to use them as exercises. The two duties of the assistant are to conduct the ten-minute practice sessions five days per week, and to carry out certain instructions during the course of the day, i.e., create as many normal hearing experiences as possible during the day, call attention to every commendable performance, call attention to household and other ordinary sounds. Poor hearing performances should be ignored. "The purpose of the practice sessions is to present sounds to the patient in a systematic way and conversation is an excellent source of sounds." Then follows minute instructions for the assistant on how to present the various sounds during the sessions. "The purpose of the speech sounds lists is to present the small differences for the patient to examine, weigh, and compare. The lists are not simply word lists but sounds lists."

Conversation, sound other than speech and reading matter face to face, behind the patient's back and from room to room, confidential type of conversation, whispered conversation, etc., are all used during the sessions.

A definite programme for each of the 69 practice sessions is given. Modification of the hearing re-education programme is given for re-education of the poorer ear, patients with slight hearing loss, elderly patients, children, severely deafened persons and those with one normal ear and one poor ear. Refresher courses may be required. The whole course takes ten weeks.

Part three consists of—

Appendix A—Speech sounds and interpretation test for detecting hearing difficulty.

Appendix B—The hearing disability questionnaire with models and instructions.

Appendix C—The demonstrations to show that the patient has hidden hearing power.

Appendix D—Progress notes.

This is a most comprehensive book on the subject of hearing re-education, and should have a wide appeal in the British Isles, where this subject is comparatively new. K. H.

PROBLEMS OF FERTILITY IN GENERAL PRACTICE. By J. Stallworthy, M.A., F.R.C.S., F.R.C.O.G.; K. Walker, M.B., F.R.C.S.; J. Malleson, M.B., B.S., and M. H. Jackson, M.B., B.S., D.R.C.O.G. Second edition. (Pp. xiv + 259; figs. 32. 18s. 6d.). London: Cassell. 1953.

THIS book, with a foreword by Sir Eardley Holland, and published under the auspices of the Family Planning Association (F.P.A.), represents the considered advice of that Association on some of the physical problems associated with family life under present-day conditions in an industrial society. There are essentially two aspects of fertility dealt with in the book, namely, the ability to regulate normal procreative activities so that the successive births in a family may be suitably spaced out to give the optimum conditions of nurture for the infants, and relief from the strain to the mother of too frequent pregnancies; and, secondly, the inability of some married couples to produce the desired children. Information on these social problems has been gathered by the F.P.A. over a considerable number of years, and the authors have been able to draw freely on this valuable material as well as on their own records.

The main emphasis in the book is on the problem of sub-fertility and its investigation and treatment. Useful practical advice is given on the difficult enquiries and investigations necessary if suitable help and treatment are to be given to the infertile or sub-fertile couple. The details of treatment of mental difficulties are omitted, as they are outside the scope of this small and essentially factual book. That sub-fertility is a matter calling for an investigation of the "couple," and not of the female partner only, is rightly stressed. All too often the investigation of the male is confined to the determination of the presence of spermatozooa in the seminal fluid, a fact in itself of importance, but virtually useless as the sole test of the ability of the male to fertilise an ovum. Elaborate and potentially dangerous tests of a perfectly normal female may be avoided if the advice given here on investigation of the couple is carried out. The most important single test is the post-coital test (Simms or Huhner test) for the presence in considerable numbers of actively motile and normally formed sperms in the upper vaginal or cervical canal. Details are given of how this, and the various other tests required for the full investigation of both male and female, may be carried out. Not all the procedures advocated will necessarily be accepted uncritically by specialists in the various types of investigation. Such investigations and the correct assessment of the various factors involved are usually beyond the scope of general practice. An appendix lists seven centres—all in England—where teams of experienced workers have been established. At many of the other centres noted in Great Britain some advice and treatment may be obtained.

The second part of the book is devoted to illustrating and describing methods of preventing conception. Some of the drawings are not particularly helpful, and anyone attempting the fitting of preventive appliances to the female should have suitable instruction at one of the numerous clinics mentioned. Useful appendices describe suitable proprietary contraceptive appliances and chemicals, the keeping of temperature records for the determination of ovulation times, and the details of the laboratory investigations mentioned in the main text.

It can be said that general practitioner, specialist, and also medical student will gain much from a perusal of this book, which deals in an admirable and restrained way with the investigation and treatment of a subject practically untouched in an ordinary text-book. W. R. M. M.

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Volume II is confined to a straightforward presentation of disease as it affects the major systems, central nervous system, heart, alimentary tract, etc.

As a whole, the production is of a very high order and the general standard of articles by the various authors is excellent. Naturally, in a text-book of this size and comprehensiveness, there is a little unevenness, but, judged as a whole, the book reaches and maintains a high standard.

In brief, this new text-book is a major contribution to medical literature, and contributors, editors and publishers are to be congratulated on a splendid achievement. D. A. D. M.

TEXT-BOOK OF PHYSIOLOGY AND BIOCHEMISTRY. By G. H. Bell, B.Sc., M.D., J. N. Davidson, M.D., D.Sc., and Harold Scarborough, M.D., Ph.D., F.R.C.P.E. Second Edition. (Pp. 1,002 + xii; figures 55; tables 55. 50s.). Edinburgh: E. and S. Livingstone Ltd. 1953.

THE publication, just before the start of Michaelmas Term, of the second edition of Bell, Davidson, and Scarborough's text-book is an example of the efficient planning and co-operation of authors and publishers which is to be found all through the book. This book steers a middle course—it is intermediate in size between the books that many medical and dental students find overwhelming and those that are barely sufficient in their content and explanations. It is intermediate in price. Its authors have, in selecting their material, consciously remembered Alexander Pope's advice—"Be not the first by whom the new are tried, nor yet the last to lay the old aside." The term "B.D.S. Textbook" on the dust cover is unfortunate. Most people would expect this to mean a text-book for B.D.S. students, and not one written by Bell, Davidson, and Scarborough.

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The book received a warm welcome when it first appeared in 1950, and in the second edition the minor errors of the first have been corrected, and the text has been revised. The presentation is clear. The illustration is exceptionally good; in many respects it is lavish. The matt-surfaced pale cream paper is pleasant to read from, and totally avoids glare and reflexions. The publishers are to be congratulated on producing the volume at a price of fifty shillings. The book is one that may confidently be recommended to medical and dental students, but it will also continue to appeal to clinicians and to those working for higher degrees and diplomas. A. D. M. G.

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VIRUSES IN MEDICINE; being No. 3 of Volume 9 of British Medical Bulletin. (Pp. 169-244; plates 4. 15s.). London: Medical Department, British Council, 65 Davies Street. 1953.

THE British Medical Bulletin is perhaps better known abroad than to medical men in this country. It is one of the more valuable influences by which the British Council is making known to the world the contribution of British medicine. This it does by taking some subject for discussion in each issue and obtaining contributions from the leading workers in that field in this country. These almost always present balanced and up-to-the-minute reviews in which British contributions to progress are made clear without minimising the work done elsewhere.

The present number can only be described as a monograph and is on viruses in medicine. It has been edited by Dr. Forrest Fulton, who contributes the chapter on techniques for the study of virus diseases. Dr. C. H. Andrewes has assisted with planning and writes the introduction. In a short chapter he manages to convey most of what has yet been learned about the common cold by his research team and by other workers. Articles on the ecology of virus diseases by Sir Macfarlane Burnet, progress in viral immunity by Wilson Smith, chemotherapy by Weston Hurst, poliomyelitis by A. J. Rhodes and hepatitis by F. O. MacCallum may be mentioned, but the other articles on smallpox, coxsackie viruses, influenza, mumps, yellow fever, the psittacosis-lymphogranuloma group, Q fever, the post-infective encephalitides and on some veterinary diseases are all of a high standard. In general, these reviewers are critical and selective rather than encyclopædic, and they presume a working knowledge of modern bacteriology. J. E. M.

THE NATIONAL HEALTH SERVICE: A Guide for Practitioners. Edited by Max Sorsby, L.M.S.S.A. (Pp. xii + 267. 12s. 6d.). Edinburgh: E. and S. Livingstone, Ltd. 1953.

IN his foreword Sir Allen Daley, who was formerly medical officer of health for the County of London, points out that the best can only be obtained from the Health Service if the individuals working in it realise what resources are available from other sections, how they can be brought into action, and what are the relationships of the parts to the whole. This book briefly and clearly outlines the scope of the National Health Service itself, and has also chapters on the National Insurance Act and Pensions in relation to the Health Service and on the work of a coroner.

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Though no mention is made of the minor differences which exist in Northern Ireland practitioners here will find this book stimulating in its outlook and informative on many problems.

AIDS TO MALE GENITO-URINARY NURSING. By John Sayer, M.B.E., S.R.N., D.N. Second Edition. (Pp. 146 + xii; illustrations 46. 5s.). London: Baillière, Tindall & Cox. 1953.

THE second edition of this book is an excellent production. It is small in size, clearly and simply written, and provides all the information the nurse needs to possess. The illustrations are well produced and greatly enhance the value of the text. It is recommended to all nurses. E. M.

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The present number can only be described as a monograph and is on viruses in medicine. It has been edited by Dr. Forrest Fulton, who contributes the chapter on techniques for the study of virus diseases. Dr. C. H. Andrewes has assisted with planning and writes the introduction. In a short chapter he manages to convey most of what has yet been learned about the common cold by his research team and by other workers. Articles on the ecology of virus diseases by Sir Macfarlane Burnet, progress in viral immunity by Wilson Smith, chemotherapy by Weston Hurst, poliomyelitis by A. J. Rhodes and hepatitis by F. O. MacCallum may be mentioned, but the other articles on smallpox, coxsackie viruses, influenza, mumps, yellow fever, the psittacosis-lymphogranuloma group, Q fever, the post-infective encephalitides and on some veterinary diseases are all of a high standard. In general, these reviewers are critical and selective rather than encyclopædic, and they presume a working knowledge of modern bacteriology. J. E. M.

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TO DEFINE TRUE MADNESS. By Henry Yellowlees, O.B.E., M.D., F.R.C.P., D.P.M. (Pp. 215. 12s. 6d.). London: Sedgwick & Jackson.

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I CAN heartily recommend this book to all interested in the human mind, disordered or otherwise. Dr. Yellowlees writes with a great background of good literature ranging from the Scriptures through the classics, Shakespeare to "Alice in Wonderland." His style is very lucid, simple, and annotated with quotations, wisecracks, etc., making it a book eminently easy to read. He uses as few scientific or pseudo-scientific terms as is compatible with clarity and confines himself mainly to the homely speech readily understood by all. He has a broad, sympathetic approach to life in general and perhaps most particularly to life's mental misfits. Although the book is referred to as "Commonsense Psychiatry for Lay People," there must be few if any doctors who will not profit by it. It is reasonably priced and is not beyond the capacity or the purse of the average medical student. In addition to being full of interest and highly entertaining as well as highly informative it will well repay a perusal even by the balder and greyer sections of our medicals.

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SURGERY OF REPAIR AS APPLIED TO HAND INJURIES. By B. K. Rank, M.S., F.R.C.S., F.R.A.C.S., and A. S. Wakefield, M.S., F.R.C.S., F.R.A.C.S. (Pp. 256 + xiv; figures 188. 40s.). Edinburgh: E. and S. Livingstone. 1953.

In most books of general or operative surgery mention of the hand is mainly confined to the treatment of sepsis, with little or no reference to the special application of surgery to hand injuries. The present era of antibiotics has not only changed the whole picture of sepsis but has vastly improved the results of repair. In these days of increasing mechanisation the hand is increasingly liable to varied and severe damage, and a book dealing exclusively with this problem is both important and welcome.

This book is little concerned with the works or results of others—some may think too little—but with the first-hand experience of the authors. This makes for a refreshingly readable book, which, while freely acknowledging the inspiration of pioneers such as Gillies, Bunnell, and Seddon, in no way undertakes to agree with them in all their opinions.

The social and economic aspects of hand injuries are reviewed, the anatomy is covered in very considerable detail, but always from the point of view of movement and function, which gives it a life and interest which is so lacking in the dissecting-room outlook of the usual text-book.

The importance of organisation, team work, and continuity throughout all phases of reconstruction and repair is emphasised. Correct primary treatment is described and is essential if secondary repairs are to have the best chance of success. The authors have some sharp, but in many cases deserved, criticisms to make of the outlook which has prevailed all too long in some hospitals on this matter, and there is a very clear and practical section on the examination and assessment of injuries.

Indications for repair of deep structures at the time of injury are discussed in the same clear style. This is a typical sample—"Fractures and dislocations must be reduced and maintained, but whether or not tendons and nerves are repaired is a different matter. Physical continuity in these structures is insufficient—they must function. They cannot function in a mass of scar tissue, so that if the highest standard of primary healing cannot be anticipated with absolute confidence the repair of tendon or nerve is generally ill-considered at the primary procedure."

General principles of operative technique are given, including the use of a tourniquet, so essential especially in the intricate and tedious procedures of nerve and tendon repair. Not all will favour the authors' recommendation to use a light Esmarch bandage both for the exsanguination and as a tourniquet. In their experienced hands accurate judgment of the exact tension to overcome arterial pressure and no more may come easily, but the inflatable cuff which they do not favour, if applied evenly and used with a pressure gauge, is in our opinion more suitable for general use.

After-treatment is well described, and the old mistaken idea of early movement after repair is suitably condemned and the fact emphasised that "Early healing rather than early movement" will lead to the fullest range, especially in tendon repairs. In the cases where primary repair is not actually contra-indicated—such as flexor tendons in the finger tunnels—they favour primary repair in many areas usually regarded as optional. Primary nerve suture is also contrary to generally accepted practice.

Much useful material is given on the technique of delayed repair of deep structures. One will not necessarily agree with all the details, but they only claim to set down what they themselves have found most useful, as this in no way detracts from the value of this excellent book.

No review of this work could be complete without mention of the very large collection of beautifully reproduced photographs and drawings, which, combined with very clear lay-out, make it typical of the publishers' best work. W. S. B.

MANUAL OF SURGERY (Rose and Carless). Edited by Sir Cecil Wakeley. Eighteenth Edition. (Two vols. Pp. xviii + 1,471; figs. 1,007; plates in colour, 18. 63s.). London: Ballière, Tindall & Cox. 1952.

Rose and Carless has now reached its eighteenth edition, and it has also now joined the growing ranks of those text-books of medical science which are no longer written by a single author. Eighteen contributors have joined together to produce an attractively written and well-produced book. The paper is good and the print is clear, and the diagrams, in the main, show what they are intended to show. Some of the black and white sketches which are intended to show pathological appearances fail, as they nearly always do, to demonstrate the real life aspect of the lesions which they set out to portray. While the black and white diagrams are, on the whole, excellent, it is a pity that space was taken up in reproducing such diagrams as Fig. 45, which fails to show a double aneurysm of the arm, and scrutiny of Fig. 47 would help no one to recognise a syphilitic erosion of the spine. Numerous other black and white reproductions would have been better put in clear line drawings, and not into photograve.

There is still a tendency to show the extreme forms of disease, which the doctor rarely sees, and should never wait for before making a diagnosis. The elephantiasis demonstrated in Fig. 65 is an example.

The various sections have been well done. The second chapter, "Disorders of the blood of surgical importance," is a good survey of a subject which it is very satisfactory to see included in a text-book of surgery. The discussion of the Rhesus factors is interestingly presented, and a discussion on hæmorrhage and shock is dealt with in a modern quantitative way with very little of the loose statements that used to be found in the earlier editions.

The section on chemotherapy is clear and concise, but in subject moving so rapidly it is not surprisingly already a little out of date. No discussion, for instance, on terramycin is given.

The article on infections of the veins is clear and well written, but does not go deeply enough into the subject which has for so long suffered from imperfections of over-simplification.

The section of affection of nerves does not, I think, do justice to the very careful work done during the war by the various nerve centres, and I think suffers on that account.

The subject of fractures is extensively covered, and is well done, but would have benefited by the greater use of line drawings to illustrate deformities and X-ray appearances. The line drawings that are given are good, even if some are printed upside-down.

In the section of cranial surgery the skull X-rays, and some of the naked-eye appearances reproduced, in photograve, are so indistinct as to make them hardly worthwhile producing.

The ear, nose and throat section has been dealt with very clearly and well, although I think the word "bipped" would need explanation to the modern student, who is not in touch with a practice that was current in the First World War. It is only the older members of us who can remember the familiar sight and smell, and know what "bipped" means.

The sections on abdominal surgery are, on the whole, good and wisely done.

Some of the teaching of these chapters has been superseded, but perhaps it is a good thing to bring the student up with a good historical sense and not too much in the tempests of modern controversy.

In general, the book is a valuable one, and regains a place in the forefront of students' text-books, which it was beginning to lose. The publishers are to be congratulated on the production, and it is pleasant to see so many of the beautiful drawings by Maxwell and Sewell in it. The authors are to be congratulated on the clearness of the exposition, but chiefly the editor on the wisdom of his work—now one of the two best text-books for senior students. H. W. R.

FOOL'S HAVEN. By C. C. Cawley. (Pp. 210. $2.75.). Boston, Mass. : House of Edinboro. 1953.

THIS is a crusading novel by a former U.S. Army engineer and is concerned with a problem perhaps not so important here as in the United States, but one which the reviewer has encountered once. Laid in a technical college in Pasadena in 1930, it is concerned with a description of what happens when a self-appointed minister counsels against medical attention for the daughter of one of his followers, practises faith-healing and the girl dies from appendicitis. The legal anomaly against which the author protests is that the parent who denies the child medical aid can be punished, yet the pastor who counsels that denial goes free.

In general, when an author writes a crusading novel, it is poorer literature than when he is less concerned to right the wrongs of mankind. Mr. Cawley's novel is not great literature, the characters do not come to life and the book, apart from a rapidly developing love affair between the narrator and the victim, a girl of 17 years, is concerned mainly with the illness of the girl and her brother, the stubborn faith of the widowed mother and the advice of her pastor.

There can be no doubt that the book poses a problem. When those legally responsible for their own actions refuse medical treatment their conduct is sometimes most vexatious and that of their spiritual advisers may seem to be even more so. The children of persons so misguided excite our sympathy and sometimes our passions. Much discussion on this subject might, however, broaden the ethical problems concerned very considerably and emphasise the conflict between much accepted medical practice and the faith of millions. It is perhaps fortunate that here faith-healers are numerically few, and that, in serious illness, the resolution of their adherents is more liable to be shaken by the common sense and prejudice of their friends and neighbours than sustained by the ministrations of their pastors.

BERKLEY'S HANDBOOK OF MIDWIFERY. By Arnold Walker, F.R.C.S., F.R.C.O.G. Fourteenth Edition. (Pp. 9 + 411; figures 78; plates 3. 15s.). London : Cassell. 1953.

THIS book is written for pupil midwives and midwives, and the author, as chairman of the Central Midwives' Board and for many years as associate of the late Sir Comyns Berkeley, is the logical successor to carry on this popular handbook.

Like most obstetric books for midwives, it errs in being too long and too detailed, and a valuable opportunity to prune the text and to bring into prominence the essentials of the subject has been lost.

The midwife has a very responsible part to play in any maternity service, and, accordingly, any line of treatment advocated must be essentially explicit and safe. In this respect the advice given to her when left to deal with severe antepartum hæmorrhage, in the absence of medical aid, is, in the reviewer's opinion, dangerous.

Much of the text has been brought well up to date, but an obsolete method of treatment of eclampsia is still detailed, and the most modern lines of treatment are not mentioned.

Despite this, the book reads easily and is well illustrated, and should prove a valuable guide to the midwife. The rules of the Midwives' Board and the Code of Practice are well applied, and the section on the new-born infant by Dr. C. T. Potter has much to commend it.

There is a definite future for this handbook, but its reputation will be further enhanced if future editions are more positive and concise. M. R.

AIDS TO GYNÆCOLOGY. By W. R. Winterton, M.A., M.B., B.Ch., F.R.C.S., F.R.C.O.G. Eleventh Edition. (Pp. 196 + viii; figures 15. 6s.). London : Baillière, Tindall & Cox. 1953.

THIS is an excellent book for the purpose for which it is written. While one cannot recommend it as a text-book, there is no doubt that it can be most valuable from the point of view of revision. The text covers the subject as fully as it is possible in a book of this series and all padding has been left out.

One could certainly recommend this book to students to use for revision before an examination. C. H. G. M.

FOOL'S HAVEN. By C. C. Cawley. (Pp. 210. $2.75.). Boston, Mass. : House of Edinboro. 1953.

THIS is a crusading novel by a former U.S. Army engineer and is concerned with a problem perhaps not so important here as in the United States, but one which the reviewer has encountered once. Laid in a technical college in Pasadena in 1930, it is concerned with a description of what happens when a self-appointed minister counsels against medical attention for the daughter of one of his followers, practises faith-healing and the girl dies from appendicitis. The legal anomaly against which the author protests is that the parent who denies the child medical aid can be punished, yet the pastor who counsels that denial goes free.

In general, when an author writes a crusading novel, it is poorer literature than when he is less concerned to right the wrongs of mankind. Mr. Cawley's novel is not great literature, the characters do not come to life and the book, apart from a rapidly developing love affair between the narrator and the victim, a girl of 17 years, is concerned mainly with the illness of the girl and her brother, the stubborn faith of the widowed mother and the advice of her pastor.

There can be no doubt that the book poses a problem. When those legally responsible for their own actions refuse medical treatment their conduct is sometimes most vexatious and that of their spiritual advisers may seem to be even more so. The children of persons so misguided excite our sympathy and sometimes our passions. Much discussion on this subject might, however, broaden the ethical problems concerned very considerably and emphasise the conflict between much accepted medical practice and the faith of millions. It is perhaps fortunate that here faith-healers are numerically few, and that, in serious illness, the resolution of their adherents is more liable to be shaken by the common sense and prejudice of their friends and neighbours than sustained by the ministrations of their pastors.

BERKLEY'S HANDBOOK OF MIDWIFERY. By Arnold Walker, F.R.C.S., F.R.C.O.G. Fourteenth Edition. (Pp. 9 + 411; figures 78; plates 3. 15s.). London : Cassell. 1953.

THIS book is written for pupil midwives and midwives, and the author, as chairman of the Central Midwives' Board and for many years as associate of the late Sir Comyns Berkeley, is the logical successor to carry on this popular handbook.

Like most obstetric books for midwives, it errs in being too long and too detailed, and a valuable opportunity to prune the text and to bring into prominence the essentials of the subject has been lost.

The midwife has a very responsible part to play in any maternity service, and, accordingly, any line of treatment advocated must be essentially explicit and safe. In this respect the advice given to her when left to deal with severe antepartum hæmorrhage, in the absence of medical aid, is, in the reviewer's opinion, dangerous.

Much of the text has been brought well up to date, but an obsolete method of treatment of eclampsia is still detailed, and the most modern lines of treatment are not mentioned.

Despite this, the book reads easily and is well illustrated, and should prove a valuable guide to the midwife. The rules of the Midwives' Board and the Code of Practice are well applied, and the section on the new-born infant by Dr. C. T. Potter has much to commend it.

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