THE

ST. LUKE'S HOSPITAL GAZETTE

MALTA JUNE 1970 Vol. V No. 1

Published for the Consultant Staff Committee, St. Luke's Hospital, Malta, and the Medical and Dental Surgery Faculties of the Royal University of Malta.

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THE PURSUIT OF LEARNING

Man is driven by many urges to which he responds often consciously, sometimes, more dangerously, subconsciously and the motives and mechanisms of the mind have been for long and quite properly the objects of study of the philosopher. This is quite right since while some motives are admirable and socially beneficial, others have to be kept in check and for this to be possible they have firstly to be known. Knowledge is science and science and learing can themselves be worthy of study The extrovert will act and carry out his desires; the introvert tends to let "the native hue" of his resolution get "sicklied o'er with the pale cast of thought" so that "enterprises of great pitch and moment with this regard their current turn awry and lose the name of action". A more modern poet bade us "think and not make thought our aim", which comes to the same thing. Our present day society appears, rightly or wrongly, to have adopted science at its ultimate objective not fearing in the least, or, perhaps, realising the danger but thinking it to be one well worth incurring.

In a subject like medicine, which is primarily and almost exclusively a materialistic one, we do not need to have any qualms. After all the doctor is but a veterinarian who has specialised in treating *Homo sapiens. Homo* is certainly a beast;

the *sapiens* aspect raises difficulties with which the vet is not commonly troubled. Still on the whole in some nine tenths of the cases we deal with an animal and to do this effectively the more we know of the working of the body machine the more likely are we to be able to do this effectively. Hence medical research which extends ever more widely and probes deeper. There are moments, indeed, when one wonders whether research is not letting itself be deviated into academic channels which could be leading it too far away from any practical objective. This is probably heretical. We agree very readily that one should not insist on immediate practical results, but one does tend to wonder whether it would not be more beneficial to relieve chronic Asiatic starvation by improving agriculture rather than by pursuing the study of the physiology of digestion into enzymatic labyrinths. After all, Jenner and Pasteur stopped smallpox and rabies before they knew what a virus really was.

Bearing this in mind we can safely go on to pursue learning, to discover it and to make it better known. It is reassuring to know that thousands throughout the world are engaged in pure research; it has been truly said that there are more scientists alive now than there have been in all past ages put together. Indeed the pure scientist as we now know him is a product of our own times, though it is also true that so many of the great discoveries (the basis of physics and chemistry, for instance) were made by amateurs, gentlemen who played about with flasks and retorts just as others of the time chose to spend their days writing verses. On the whole we probably do not have to fear the medical research worker much. Actually, of course, he is supposed to be purely beneficial: his objective is the prevention of disease and the positive improvement of life. What creates a puzzled dread in mankind is the possibility that Frankenstein might once again create some monster which could get out of hand.

In our own country, with our own very limited resources, we are not absolved from the necessity of contributing to the advance of science. Naturally this contribution will probably be limited but such as it is we must make it; if the opportunity arises we have to use it as best we can. We note with some satisfaction that in this Gazette we have published a fair amount of original observations which others have found of interest, even if we must emphasise that present day research is not something which one does in a spare moment, things having become too complex for that to be possible.

The other aspect of research — the reverse of doing it oneself — is knowing of it. From so many laboratories and institutions the findings are pouring out in reports and papers without number. It is the duty of every member of the learned profession of medicine to know what is happening, since it is he who will have to put it to use. This is not as easy as it sounds but, difficult as it is, the physician has the obligation of keeping abreast. To subscribe at least to one medical periodical and to read in it what can have a bearing on one's own practice is a duty. Most papers are helpfully provided with a summary and there are, in fact, periodicals which summarise the papers in a vast number of other publications. It is pleasant to note that most members of the medical profession in Malta belong to the Malta Branch of the B.M.A. which means that they subscribe to the "British Medical Journal". The library of our medical school is not only reasonably well supplied with periodicals and books but it is put to considerable use.

We would like to see every doctor reading more and present conditions do not provide grounds for complete satisfaction but in this as in so many other things we are improving. Let us hope this will ever continue to be so.

THE LOGIC OF SURGERY

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This is the first P. P. Debono memorial lecture, instituted by the "Association of Surgeons and Physicians of Malta", delivered on the 30th. October 1969 at the Medical School of the University.

We are met here tonight to commemorate professor Peter Paul Debono, who occupied the Chair of Surgery at our Royal University from 1926 to 1951. It is a pleasure to have among us his brother professor J.E., his sister, Sister Debono of the Order of the Sacred Heart, and his two daughters, Mrs. Ellis and Mrs. Micallef Eynaud. We thank them for honouring us with their presence this evening. We are only sorry that Mrs. Debono is unable to be with us; through her family, we send her our best wishes.

Before I set about my task of developing my theme, I wish to thank my colleagues and the Council of the Association of Surgeons and Physicians of Malta for the signal honour of inviting me to deliver this Foundation Commemorative Lecture and thereby giving me a unique opportunity to pay a pious tribute to our beloved Peter Paul, who was my teacher throughout my formative years. However great I count this privilege I cannot help but be overawed by a sense of inadequacy. In choosing to charge me with this responsibility I imagine that my colleagues must have taken regard not so much of my erudition which I know to be scanty, but of my seniority and my long and close association with the man whom we are commemorating. This association started when I was a student and, I gather, his proverbial blue-eyed boy. Later I became one of his chief assistants, his anaesthetist, his confidant, his comforter in disappointments, the patient listener to his grievances, his helpmate in the B.M.A. and the Camera Medica and goodness knows what else. Later we became colleagues and I was fortunate to become his immediate successor in the Chair of Surgery; our friendly association carried on until the 3rd. June 1958 when death did us part.

I happened to be president of this association when the idea was mooted by professor Ganado of founding this commemorative lecture and it was happily acclaimed by all of us. It seemed so fitting that this association which has as one of its objectives the safeguarding of the standards and prestige of our consultant service should honour professor P.P. Debono, who was a supreme teacher and was the pioneer of scientific surgery in these islands. He set for us a standard which with all our zeal we strive to emulate and he founded a school, based primarily on the worth of good doctoring and the wisdom of clinical surgery. In this lies the chief claim of professor Peter Paul Debono to greatness and it is our hope that the institution of this biennial memorial lecture may perpetuate not only his memory but also the standards, the trends, the ideals and the influence of that school.

Most of you will have heard a lot about professor Peter Paul Debono, the surgeon; I shall briefly tell you something about Peter Paul the man. Short in physical stature, rather overweight by present day standards: he used to say that unless he had a substantial mid-day meal he was apt to make silly mistakes at his work in the afternoon — as good an excuse as any other, I thought, for satisfying one of the major pleasures of life. He was himself an excellent cook and was a master at boning a chicken and he always liked to cook the meal himself whenever he had guests to

dinner. A dreadful driver, (though he never admitted it and felt insulted if ever this was hinted at) he was good at everything else that needed the cooperation of mind with hands. He had a sense of humour and a charm of his own once you got to know him, being kind hearted and deeply religious. An exemplary family man, he led a simply kind of life; his hobbies were unsophisticated — the occasional game of bridge. so often interrupted by an emergency call, stamp collecting, gardening at five o'clock in the morning and tending his aviaary. He once had me hunting all over London at stores and chemist's shops for Robinson's food for babies — an obsolete brand — because one of his parrots thrived on it; I managed to get two tins for him and he was delighted. During the season he went to the opera one a week and loved it; only, when he was tired, I used to watch him being roused to consciousness by the applause. I end this epitome by quoting from one of the testimonials given him by professor C. Sammut: "I have known Dr. Debono from childhood and have had an opportunity of seeing him grow and wax into that character of a true Christian gentleman for which, apart from his high professional qualifications, he is justly esteemed by all who know him." What greater tribute could one give?

The topic I have chosen to argue today is an ambitious one. I only felt the full impact of it as I came to write it. I chose it from among the alternatives because I thought it would be one that might have appealed to P.P. One of his most impressive characteristics was that he constantly sought a reason behind phenomena and in matters of symptom, diagnosis and therapy he looked for a "rationale". One of the meanings of this favourite word of his is given by the "Concise Oxford Dictionary" as "logical basis" and in this lecture I propose to deal with surgery considered as a rational activity.

What, then, is Surgery? It is a matter of common experience that quite often we know and understand perfectly well what a word means until we look for a definition. Medicine and Surgery seem to be such different disciplines that it looks as though there should be no difficulty in defining either of them in terms of their different activities. And yet they have so much common ground — a common ground that keeps varying from time to time. Billroth in the 1890s said with some pride that "internal medicine had become more and more surgical." We now think that we are adopting so much medicine in our surgery, in matters of diagnosis, in anaesthesia, in pre- and post-operative care and in those diseases where treatment is both medical and surgical. Is the differential diagnosis of jaundice a matter for the physician or for the surgeon? When did pulmonary tuberculosis change over from medicine to surgery and back again to medicine? Are duodenal ulcer, ulcerative colitis and thyrotoxicosis medical or surgical? The "Shorter Oxford Dictionary" defines surgery as "the art of treating injuries, deformities and diseases by manual operation or instrumental appliances". Perhaps this may have been true of pre-Hunterian surgery. As a definition of modern surgery it is grossly out of date. In the first instance it takes no account of the intellectual element in surgery nor of its constant pursuit of truth; and what about those crucial situations in a surgeon's work when he rightly decides on masterly inactivity? I trust it should become clear by the end of this lecture that there is much more to surgery than mere handicraft.

By its emphasis on the manual exercises of a surgeon's work that definition takes us back to the origins of surgery in prehistoric ages. The art of healing in those times was a magico-religious practice based on the concept of illness as a visitation by evil spirits which had to be driven out by magical rites and incantations. It is possible that the operation of trephining of the skull as carried out in prehistoric times — the first surgical operation we know of after the one of rib resection — may have been one of such rites meant to allow the departure of the evil visitors. In later times it certainly became an empirical therapeutic operation. It only became rational relatively recently when we became acquainted with the cause and effect of increased intra-cranial pressure. It was bound to be obvious even to pri-

mitive man that a deformity, a wound or a broken bone could not be put right by any magic spell. Instinctively he must have felt that some of these disorders needed rest and immobilisation while others manual or instrumental correction. In early historical times this is borne out by documents either in writing or engraved in stone. Surgery, therefore, is something that arose out of sheer human necessity as an art based on a purely empirical foundation. Undoubtedly, it still retains a lot of practical empiricism and necessarily, it still remains an art in the sense that the surgeon has to apply his knowledge to certain variable situations at some particular definite time on an individual patient.

However, since John Hunter (in the eighteenth century) surgery has grown into a scientific discipline. Not only has it drawn on the findings and conclusions of the other sciences but it has itself materially contributed to the understanding of the working of the living organism both in health and disease. It has thus come to form part of the biology of man.

The number of the sciences and technologies the modern surgeon applies to his work is too large to enumerate. Just consider, for instance, how impossible it would be for a surgeon to place an electronic pacemaker inside the body, employ an artificial kidney or institute an extracorporeal circulation, put in an intramedullary nail, perform a total hip replacement or even give a safe blood transfusion were it not for the recent advances in physics, chemistry, biology, pharmacology, metallurgy and plastics technology. Even the results of our various forms of treatment are assessed on statistical analysis which, in its turn, is an application of the calculus of probablity.

The scientific foundation of the surgery of today is mainly based on what have come to be known as the basic sciences: Anatomy, Pathology, Physiology and experimental surgery.

Those of us who studied Anatomy before the war will remember the inscription written in bold letters across the wall of the old dissection room: "He who does not dissect the dead will mangle the living". This was said by John Abernethy, a surgeon. The relevance of anatomy to surgery is immediately obvious; the pathological process which calls for surgical treatment is situated in a specific anatomical site and the access to it at operation calls for a detailed knowledge of anatomical planes. The work of A. K. Henry demonstrates very cogently the logic underlying the anatomical exposure of the deep structures of the extremities. The contribution to the science of anatomy made by the older surgeon-anatomists is perpetuated in the various eponyms in common use up to this day — Hunter's canal, Camper's fascia, Scarpa's triangle, Cooper's ligament, the nerve of Bell, the triangle of Petit, the glands of Littrè and so on ad infinitum. Our Peter Paul was an anatomist. The sheaf of veins unnamed in text books running parallel to Poupart's ligament which he was fond of describing does not carry his eponym; he rather good-humouredly christened it by somebody else's name. In our own time substantial contributions from surgery to anatomy came from John Morley, a contemporary of P.P. in Manchester who elucidated the anatomy of abdominal pain and enabled us to correlate rationally the site of pain, tenderness and rigidity with the site and nature of the underlying lisease. Sir James Patterson Ross, another contemporary of P.P. at Bart's together with Sir James Learmonth perfected our knowledge of the anatomy of the sympathetic system; Sir Clifford Naunton Morgan, one of our external examiners in surgery worked out the anatomy of the anal canal and its sphincters; Sir Charles Ballance, with whom P.P. was in frequent contact during the 1914-1918 war, contributed very largely towards the knowledge of the finer anatomy of the temporal bone and that knowledge is being extended by one of our own surgeons working in the Department of Anatomy of our Royal University.

John Hunter that indefatigable 18th century worker emphasised the relevance of Pathology to Surgery and started the

era of morbid anatomy. From thenceforth surgical treatment was to be modelled on the pathology of the disease. Hunter's extensive collection of specimens illustrating the Morbid Anatomy of so many surgical diseases laid the foundation of the museum of the Royal College of Surgeons of England and provided rich material for study by generation after generation of young surgeons until a large part of it was destroyed by enemy action. The science of Surgery owes a great debt to the large band of pathologists and morbid anatomists who have painstakingly enlightened us on the pathological processes accompanying surgical disease. The work of Rokitansky and of Virchow for instance, was an important factor in promoting the progress of German surgery in the late 19th and early 20th century. I would like to illustrate the bearing of pathological concepts on surgical treatment by relating the history of Hirschsprung's Disease. It was at first thought that the disease lay in the dilated part of the colon — therefore, in those infants who survived the early years, attempts were made to cure the disease by excising the dilated colon. These met with failure. When later it was thought that the underlying pathology was a spasm of the rectosigmoid from sympathetic overactivity, treatment was directed at sympathetic denervation again with out success. Success came when the pathologists demonstrated absence of ganglion cells in the contracted rectosigmoid and various types of resection of this part were devised. In its turn the science of pathology has gained from the observations of the followers of John Hunter. In recent times one can recall the work of Bland Sutton on tumours, that of Fairbank on diseases of the skeleton and the tidy work of Cushing and Bailey on tumours and other intracranial lesions. The morbid anatomy as studied by the pathologist is that of the end result of disease as demonstrated in the postmortem room; the surgeon is given the opportunity of studying what Lord Moynihan used to call the pathology of the living and this has been made possible by the rapid and extraordinary growth of surgery following the introduction of antisepsis by Lister and the discovery of anaesthesia by Wells and Morton.

Peter Paul used to say that he found his experience in Bacteriology and Pathology of invaluable help in his surgical work. It may not be known to the younger generation of doctors that he had published important original work on the anaerobic and on the typhoid group of bacteria, on agglutination in Bacillary dysentery and on amoebic dysentery in Malta. Among his qualifications he held the Cambridge D.P.H. and during the first world war, after being in charge of a surgical ward at the R.N.Hospital at Bighi for the first half of the war, he held appointments as Specialist in Pathology and Bacteriology attached to the R.A.M.C. and throughout the whole war he was Acting Pathologist to the Central Hospital as a substitute for Professor C. Sammut. After the war he demonstrated Surgical Pathology at Barts. He often told me how he enriched his clinical experience by constantly visiting in the wards those patients who required laboratory investigation. His ideal, which is in fact the ideal of scientific surgery, was a perfect integration between Surgery and Pathology. He inculcated this in those who worked with him and I in my turn tried to stimulate those who worked with me to visit the laboratories of Pathology and Bacteriology rather than be satisfied with the mere reading of written reports. Working with P.P. one did not hold formal clinico-pathological conferences as the pressure of work and the organisation of those days did not allow of such exercises but believe me, we kept ourselves well informed of all the aspects of our cases. His knowledge of bacteriology and pathology would come out in various ways: he would, for instance, on incising an abscess or aspirating an empyema tell us immediately what the probable responsible organism would turn out to be and as a rule he was right: as we opened an abdomen with a perforated appendix or incised an ischiorectal abscess he would say: "The books invariably call this B. coli pus but actually the smell of it is due to the intestinal anaerobes". One incident he related with pride concerned a

patient at Barts. Whilst watching a senior colleague incise an abscess in the neck and on looking at the pus he surprised his colleague by saying: "That patient has actinomycosis". His colleague received this with scepticism as this was a rare disease at Barts but P.P. was right.

The 20th century is characterised in the history of surgery by an increasing emphasis on Physiology mainly as a result of the concept of the preservation of the "milieu interieur" introduced by Claude Bernard. I would like to give one out of the many possible illustrations of the change that has occurred within recent years. To the surgeon of the 19th and the first quarter of the present century the only means available for curing a patient suffering from intestinal obstruction was the correction of any mechanical cause of obstruction, combined, in some instances, with the resection of any portion of gut that was not viable. It is a credit to their skill and resourcefulness that a not inconsiderable number of their patients survived; yet the mortality was very high. The ultimate cause of death in this condition is still not fully understood but one factor is certain and that is the profound disturbance of the "milieu interieur" of the body. The introduction of gastrointestinal decompression and the restoration of water and electrolyte balance have been the main factor in lowering the mortality and saving countless lives. Here is another instance. We do not know the ultimate cause of duodenal ulcer and possibly when we do get to know it one day surgical treatment may no longer be necessary. This was Moynihan's forecast of surgery to end surgery. Up to now there is a large number of patients who cannot get relief unless they are operated on. There is one common factor in these patients and that is the presence in excess of hydrochloric acid in the gastric juice and our surgical efforts are directed towards finding the best way of reducing it while interfering as little as possible with the normal digestive functions. This is pure applied physiology. It may be salutary to reflect on the many fallacies that we may fall into while we think we are applying physiological principles. It was at first thought that the primary lesion was a spasm of the pylorus which allowed the acid to accumulate and gain concentration and it seemed logical to relieve the spasm by various kinds of pyloroplasty. The fallacy lay in mistaking the effect for the cause as it was the ulcer that caused the spasm. Then it appeared reasonable to divert the stomach into the jejunum thereby killing two birds with one stone — affording rest to the ulcerated duodenum and neutralising the acid of the stomach. How P.P. used to relish explaining all this — it seemed so rational if only we could see at that time the fallacy on which it was based — the acid was just being diverted into the jejunum. The extensive resections that followed the failure of gastro-jejunostomy did effectively reduce the acid — the more extensive the resection the more effectively they achieved this but at the same time they disturbed more profoundly the normal function of the stomach and the normal metabolic processes of the body. In 1936 Ogilvie propounded an operation to which he even gave the name of "Physiological Gastrectomy" — it was intended to preserve the pylorus and its alkaline secretion. He soon realised that the operation did not give the good results that were expected of it and two years later he himself with characteristic honesty exposed the physiological fallacy which this operation was based upon and said categorically that it should be abandoned. The ideal operation has not yet been devised but in vagotomy combined with a drainage procedure we have found the least mutilating operation that gives acceptably good results. This problem of the surgicaal treatment of peptic ulceration has provided so much information on the function of the stomach and stimulated so much research that it may be regarded as a major contri bution of surgery to the science of physiology comparable to the enormous increase in our understanding of the function of the glands of internal secretion as the thyroid, the pituitary, the parathyroids, the adrenal, the thymus and the pancreas came within the scope of surgical intervention.

In his teaching P.P. constantly introduced physiological considerations to elucidate methods of treatment. He received

with enthusiasm the notion introduced by Böhler that while you rigidly immobilised a limit in the treatment of a fracture you preserved the function of the muscles and the activity of the circulation by active muscle contraction within the plaster cast, exercise and early restoration of function. The posture in which he placed his patients on the operating table which was intended to minimise the lowering of blood pressure from spinal anaesthesia was a simple application of Starling's law of the heart.

There is no doubt about the value of experimental surgery as a tool of research. John Hunter was the first to realise this and the progress of surgery in the last fifty years is largely due to the enormous amount of experimental research which is being carried out the world over. Even though some of it may not seem to be immediatly relevant to practical surgery the widening of the horizons of knowledge is of value in itself. The history of science demonstrates that the purely academic exercise of today may find some important and even far-reaching application in the future. The combined observations of the clinical surgeons and of experimental scientists have led to a better understanding of the mechanism of surgical shock, the circulatory disturbance of burns, the metabolic disturbance of severe trauma and of the factors concerned in the healing of wounds. Certain new surgical techniques must necessarily be tried on experimental animals and prove their worth and their safety before being applied to surgery on human patients. One regards with a certain amount of scepticism however any result of experimentation which alleges to go counter to and contradict the healing powers of the body, the *vis medicatrix naturae*. I would suspect something wrong, for instance, in an experiment which alleges that the haematoma round a fracture hinders rather than contributes towards the union of fractures. The main disadvantage of experimental surgery on animals is that its results cannot always be translated to surgery on humans. Of late, there has been a tendency in some places to practice some forms of experimental surgery in various guises on human beings — these are sometimes said to be free willing volunteers but at other times they are unsuspecting human guineapigs, genuine holocausts, presumably on the altar of science. The ethics of this practice, to say the least of it, are questionable.

Having said all this on the mainstays of surgical science we should feel bound to remind ourselves of the vast amount of knowledge that has been accumulated throughout the years by the patient, painstaking and accurate observation of innumerable clinicians who have recorded their results in the surgical literature for future generations to build upon and, in their turn, extend. It was by the process of clinical observation correlated with findings at operation that Moynihan constructed the clinical picture of duedenal ulcer and of acute pancreatitis. By a similar process, in collaboration with J.E., his brother, Peter Paul recorded the surgical complications of Brucellosis and I was fortunate in that I had the opportunity of extending their observations in the field of the locomotor system.

It sounds reasonable that anay form of surgical therapy should stem from an accurate diagnosis. This is an ideal one should pursue but unfortunately we do not always attain it preoperatively. With the increase in our aids to diagnosis, however, this margin of error is progressively being reduced and the exploratory type of operation is becoming more uncommon. Surgery does not easily lend itself to conjecture; the surgeon has not only to know that a bone is broken, he has to know exactly where it is broken and how it is displaced before he can treat it; not only has he to know that there is a stone in the urinary tract but he has to know exactly where it is before he goes in for it. In P.P. Debono's early days surgical diagnosis depended largely on symptoms and physical signs and the methods of reaching it were summarised in his dictum, which I believe originated at Barts "Eyes first and foremost, hands less but little and tongue not at all". He himself was an outstanding diagnostician but that was due to his extensive experience as a doctor rather than to that miserable aphorism. An accurate history is just as important in surgery as

it is in medicine and he gets a poor history from the patient who refuses to guide the patient with his own tongue. By the time one has taken a good history he should be orientated on differential diagnosis and on the line which the special investigation should take. Physical examination is most important. I understand that in the United States this is going out of fashion and the patient may be subjected to a host of investigations without ever having been examined. This is to be deplored. Aids to diagnosis are multiplying every day and are becoming more and more sophisticated. They have undoubtedly added to the accuracy of diagnosis and in a difficult or tricky case they may be indispensable perhaps but when they become a matter of indiscriminate routine they tend to blunt our clinical insight. Every investigation should ask a question relevant to the case and there are two things we should keep in mind — one is that certain methods of investigation are only meant as tools for research and are not practical measures for day to day routine, the second that the more esoteric methods of investigation also have their pitfalls and a lot of experience is needed in their interpretation. There is no more irritating figure than the enthusiastic young doctor who gets himself bogged down by a mass of reports on radiological, haematological and biochemical tests of every description and has not used one ounce of common sense. In all surgery there is no substitute for comon sense.

Whatever means we use in diagnosing an ailment, be they clinical, chemical, haematological or radiological the conclusion is reached by inference and a long process of induction. Every detail, therefore, has to be correlated with some concrete process or condition which past experience has shown to correspond with it.

Radiology is of the greatest help to us in diagnosis and the popular mind has endowed its findings with a sort of mystical infallibility. True enough, with the refinement of its various techniques it has become extremely accurate and trustworthy but yet it should be still a golden rule that its results have got to be integrated with the clinical picture remembering we do not treat X-ray pictures but patients.

It has been speculated that soon we may be able to reach a diagnosis by computer. I have the temerity to foresee that this method may give us the name of a disease but will tell us little or nothing about the patient.

tion of antisepsis by Lister revolutionised

Infections have been among the earlist conditions that surgeons have had to treat. We find descriptions of them both in early Egyptian and Greek writings. There have been two landmarks in the history of the surgery of infections — the first concerned their prevention, the second their treatment.

In the days before Lister some of the most dreadful and dreaded infections were produced by the surgeon himself, so much so that the surgical ward was like an antechamber of death. Localisation of infection was encouraged by various means and when in the exceptional case it did occur the thick pus that resulted was greeted as *"pus bonum et laudabile"*. The introduc- the whole of surgery. Professor Debono made this the theme of his inaugural lecture when he was appointed Professor of Surgery. Hospital fever disappeared, surgical wards became a place of healing, and operative surgery became safe. But for this the tremendous surgical progress of the last century would not have taken place.

The second landmark was the discovery of penicillin by Fleming. This was the first of a long series of antibiotics all of which are being used in surgical practice; they have changed practically every aspect of the surgery of infection. Carbuncles, at one time a commonly fatal disease, are decreasing in their incidence and when they do occur they are amenable to treatment — the same may be said of other diseases such as acute osteomyelitis and lung abscess. The mortality of infections has been reduced by an incredible amount. There are a few points worth remembering — pus still needs to be drained surgically according to the old precept *"ubi pus, ibi evacua"*. The Irish counterpart is equally true — "where there is no pus, don't drain it". Secondly,

antibiotics cannot and do not penetrate dead tissue and, thirdly, the indisciminate use of antibiotics, by promoting drug resistance is probably an important factor in promoting cross infection — a problem of the utmost concern.

The value of the use of antibiotics as a prophylatic is still sub judice. Trueta has approached this problem from a different angle. He has redirected attention to the fact that a wound that is clean or has been rendered clean can resist a certain amount of infection provided that the local environment has been rendered unfavourable for the thriving of the microorganisms. This has given rise to a new concept in the treatment of wounds and was adopted with great success in the last world war.

It is possible that injuries were the first stimulus for the development of surgery. The earliest surgical writing, the Edwin Smith Papvrus, deals mainly with injuries and does this in a very practical way. Injuries also figure prominently in the Hippocratic collection — there we find writings dealing with wounds, head in juries, fractures and dislocations. Some of us may recall that the Hippocratic method of reducing a dislocation of the shoulder was a favourite one with Professor Debono. It is perhaps more rational than the more recent one of Kocher. Steady traction is applied to the arm by pulling on it; countertraction is provided by putting your foot in the axilla and when muscle spasm is overcome as a result of the traction the head of the humerus slips into place in the glenoid cavity or else you slip it in with a twist of your foot. Though war time has always provided a stimulus to the advancement of the surgical treatment of wounds there is no dearth of injured persons needing surgical treatment in peace time — indeed their number is increasing owing to industrial injuries and the increasing numbers of motoring accidents. These injuries may involve any system or, indeed, more than one system in the same accident, a lot of them are serious and need urgent and very highly skilled and specialised treatment. Therefore, when these accidents occur in large numbers it has been found necessary to establish a special accident service provided with a number of specialist surgeons available at any time of the day and night. With this organisation many lives are saved that would otherwise be lost and the injured patients are given such care as will return them to health and activity in the shortest possible time. Pari passu with this, surgical conscience has been stirred into concerning itself with all the aspects of injury: with its prevention, its immediate treatment, its after care and the resettlement into a useful occupation of those who have remained to some extent disabled. Surgery has thus intruded into the field of the legislator. the administrator and the social worker. There is much more that we wish to see accomplished — more safety measures in our homes and in industry, more safety devices in motor vehicles, stricter control of driving licenses and easier facilities for resettlement of the disabled.

Congenital abnormalities, like injuries, attracted the attention of surgeons early on in surgical history. With the exercise of some ingenuity it is possible to obtain a good deal of correction of abnormalities of the limbs by mechanical non-operative means and therefore the development of this art did not have to wait for the antiseptic era. Naturally, with the growth of operative surgery the role of the surgeon in the correction of congenital abnormalities is ever increasing and this field of surgery has become one of the most satisfying and rewarding. There are very few anomalies that cannot be corrected to some degree — many of them can be fully corrected. With open heart surgery even some of the most complicated anomalies can now be corrected. Unfortunately there is still a small residue of anomalies for which only partial restoration can be achieved and these create some of the most distressing surgical and ethical problems. I, for one, cannot as yet see my way clear to a satisfactory solution of the problem of the severe spina bifida.

Acquired deformities of the locomotor system have largely disappeared with the decline in the incidence of the diseases that produced them such as rickets, tuberculosis of bones and joints, chronic osteo-

myelitis and the badly united fractures. Scoliosis unfortunately is still with us and faces us with one of the major unsolved problems.

So much of our time is taken up with ablative surgery, the removal of diseased organs in whole or in part that it is good occasionally to think of the happiness that is brought to so many people by reconstructive and restorative surgery wherever this proves feasible — the restoration of eyesight, of hearing, of the circulation in a limb, of movement, of the act of swallowing, of normal intestinal function after obstruction, the restoration of normal appearance of the face after injury had disfigured it. Nothing but surgical measures could accomplish this, though surgery of this kind has its limitations. After all we are mere humans.

The foreseeable future will find surgeons still contending with the problem of malignant disease, i.e. cancer. If untreated, this disease will almost invariably sooner or later kill the patient. Up to a few years ago surgical operation was the only means of treating this disease; now, other measures are available such as radiation, chemotherapy aand the use of hormones. So we are often in a dilemma as to which means to adopt or as to the order in which to apply the methods at our disposal as the results of treatment are so often unpredictable and apparently capricious. In professor Debono's early days the problem was not so complex. The concept of the disease was that some tissue cells become autonomous, break loose from every restraint, multiply and disseminate at the expense of the rest of the body until eventually they sap up all the strength out of the host and the patient dies. The body was thought to be absolutely defenceless against the attack. The rational way of treating this disease appeared to be by some operation that extirpated the diseased together with a wide margin of apparently healthy tissue in continuity with the lymphatic field to which the disease could spread. This method was eminently exemplified by the radical excision of the breast as devised by Halstead and Samson Handley. Nothing could appear more rational. In the light of the evidence now becoming available it seems that the whole concept was rather naive and it is particularly in its application to cancer of the breast that it is being called into question. A lot of heart searching, fresh enquiry and reappraisal is taking place as results of treatment are being assessed on a large scale. It would seem that our fundamental concepts have to be altered and new methods of treatment tailored to the new concepts. With a few exceptions such as the hormone therapy of disease in the prostate, radiation for disease in the nasopharynx and chemotherapy for the disseminated reticuloses it seems that surgery still holds the best prospects so long as it does not damage any form or degree of natural immunity or defence mechanism that the patient may possess. The treatment of this disease is often tragically disappointing but those many cases where we are rewarded with success give us heart and make us feel that our efforts have been well worth while.

It is a popular fallacy that the surgeon practically lives in the operating theatre and the operative part of surgery is the one that is so highly glamourised. Operations, of course, form the most important and responsible part of a surgeon's work. It is in operating that the surgeon applies his skill on the patient and it is at this moment that he has to make most of his quick and crucial decisions as he meets with the unusual, the unexpected, the difficult and the critical situations. This is where hands, brain and heart are put to their severest strains and their most exacting tests. At one time speed and spectacular performance attracted the highest admiration and sometimes even loud applause. Anaesthesia has eliminated the need for speed. Without condoning the habits of those surgeons who enjoy dawdling and fiddling one can say that it is now universally recognised that skill lies in the gentle handling of tissues and organs and speed is only gained by avoiding unnecessary movements and planning each step ahead — that achieves "hurry without haste". It is a joy to watch a master surgeon turn an operation into a

work of art. Yet an operation is now regarded as only a part of a plan of treatment — an incident, albeit the most important one, in the management of the patient. The surgeon who is to give his patients the best treatment has not only to be a skilled operator but has to be highly competent in selecting his patients, choosing the right time for operating, supervising the pre and post operative treatment and managing his patient through any post-operative complications that may arise.

An operation inflicts an injury on a patient — an injury that can make him very ill and to which he may succumb. So before counselling an operation we have to ask ourselves these questions: 1) What is going to happen to the patient if he is not operated on? 2) Is this operation justified? 3) Is the operation feasible? 4) What are the risks of the operation as compared with the risks of the disease? 5) How extensive a procedure would the patent tolerate? The surgeon usually answers these questions in a flash in the light of his experience and it is in the answers that he himself gives to these questions that he shows his clinical judgment. Next he has to select the appropriate operation. "The proper operation", says Grey Turner, "even if clumsily performed, is much more likely to be successful than the wrong operation however brilliantly performed". When we come to choose the proper operation we often have to choose between several alternatives. Experience and our acquaintance with the literature will tell us which are the ones most likely to give most benefit. When it comes to details it would appear that equally good results can be achieved by alternative procedures provided they are well performed. In his Grey Turner Foundation Memorial lecture the late Professor Lambert Rogers relates that Mr. H. W. S. Wright once asked G. T. a technical question about some operation. The reply was: "It doesn't matter which way you do it, but always with great care, extreme precision and no tricks". In a similar vein P.P. often said that an operation that was appropriate in the Mayo Clinic may not necessarily have been so at the Central Hospital. Another of his tenets was that not everything new or recently popular was neces sarily better and if an operation had given him good results he would cling to it irrespective of any change in fashion.

On the other hand, without the constant trying of something new there can be no progress — surgery would become stagnant. Before that something new is generally accepted it has to prove its worth and stand the test of time. In one of his sanguine moods, Lord Moynihan once stated that surgery had attained such a degree of perfection that no further progress was possible. Time has belied that negative forecast.

Progress has engendered specialisation and specialisation in its turn has promoted progress. Surprisingly, P. P. was not keen on specialisation. He himself was so extraordinarily versatile that he did not see the need for it. Perhaps in a sense he was right. No one should specialise until he has obtained a general conspectus of surgery — in other words one should have some grounding in general surgery before becoming a specialist and preferably he should also be a good doctor.

With this increasing progress the future is a matter of conjecture and speculation but from time to time we should pause and consider whither we are going. Is organ transplantation to be the surgery of the future? From the purely surgical point of view renal transplants have proved their worth. It is doubtful if cardiac transplanation, a purely palliative procedure, has saved more life months than it has taken away.

As a conclusion to this theme it would not be out of place to ask ourselves the ultimate question: What is the object of surgery? Sir James Learmonth once gave a choice between two definitions: Wordsworth's "To make the gift of life more valuable and the men more worthy of the gift." and Macaulay's summary of Bacon's view: "The multiplying of human enjoyments and the mitigation of human sufferings." Either of these he considered to be a laudable objective; either of them emphasise the humanitarian aspect of our science and art. No one should aspire to

become a surgeon unless he has a respect for the human person. In a recent Bradshaw lecture on cancer of the breast Sir Hedley Atkins admonished us that in conducting our controlled trials each of our statistics, each of the plots on our graph is a human being, each is somebody's wife, somebody's mother or daughter; that irrespective of what little we may achieve in advancing knowledge, our first duty is to care for these people as individuals. This we can only forget at our peril and so in our consulting rooms, in the wards and in the operating theatre we do well to reflect on the precept given us by Lord Moynihan: "A patient can offer you no higher tribute than to entrust you with his life and his health, and by implication with the happiness of all his family. To be worthy of this trust we must submit for a lifetime to the constant discipline of unwearied effort in the search of knowledge and of the most reverent devotion to every detail in every operation we perform."

It is because he achieved this ideal that we regard Professor P. P. Debono to be worthy of our reverence in our com memoration this evening.

ACUTE ORGANOPHOSPHORUS INSECTICIDE POISONING

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Poisoning due to organophosphate insecticides is not infrequently fatal, as these highly toxic compounds produce irreversible inactivation of the cholinesterases. These compounds, developed during the last war, as potential chemical warfare agents, are extensively used for the extermination of insect pests. Accidental poisoning following a single or repeated exposure is a well recognised hazard among farmers and crop dusters (Rosen, 1960). Moreover, the popularity of some of these compounds as suicidal poisons, especially the highly toxic parathion, is on the increase. Wyckoff *et al* (1968) report that 48 per cent of the 50 deaths caused by O.P. insecticides over a period of 7½ years, were suicidal.

It is also claimed that the administration of atropine without the concurrent use of cholinesterase activators, such as pralidoxime, very often results in a fatal outcome in severe cases of poisoning by parathion (Quinby and Clappison 1961; Kopel *et al*, 1962; Quinby *et al*, 1963). The purpose of this paper is to report a case of acute parathion poisoning and a second asymptomatic case of poisoning due to Fitios B/77, both treated successfully with atropine alone.

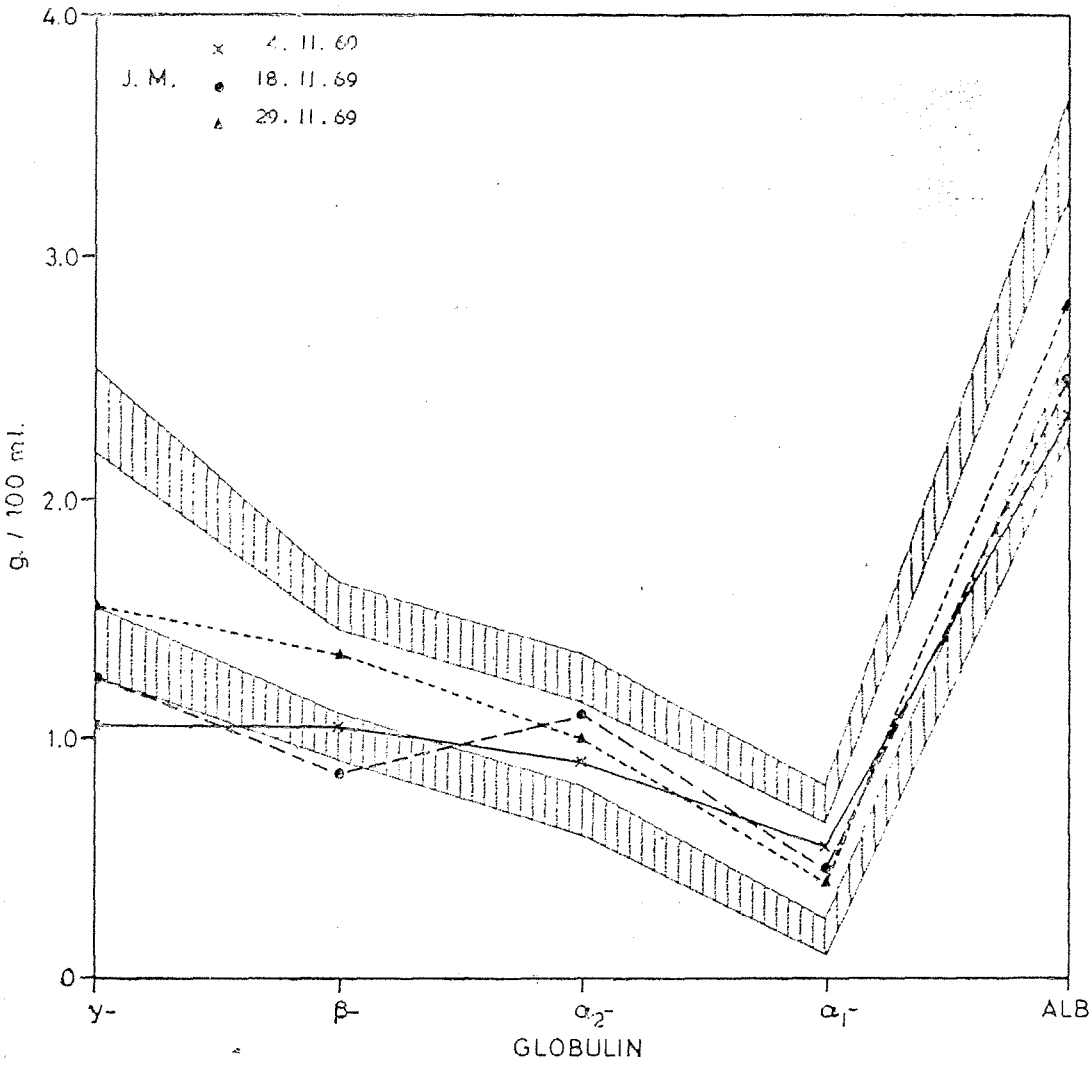

Fig. 1. Showing the changes in the serum electro-phoretic pattern in Case 1, with the upper and lower limits of normal, the shaded areas demarcating the limits of 2 S.D.

Report on Case I

L.C., male, 16 years, employed as a farm labourer for a month before hospitalisation, had been using parathion added to water for scrubbing the floor of henhouses. He wore no protective clothing and worked bare-footed. At about 5.00 p.m. on 12. 8. 68, after having used parathion, he drank water from the tap off his unwashed hands. At about 6.00 p.m. medical aid was sought because the boy was be-

having in a queer drunken manner, and by the time he was seen again by his doctor at 8.00 p.m. he was trembling, dyspnoeic and cyanotic.

On admission to hospital at 9.15 p.m., he was deeply comatose and very cyanosed. Respirations were laboured and noisy, and the R.R. was 34/min. There was marked sweating and salivation, and he was incontinent of urine and faeces. The jugular venous pressure was not raised; B.P. 160/60; pulse rate 84/min. regular and of good volume. The chest was full of coarse crepitations. The eyes were wandering; pupils pin-point and non-reactive to light. The boy was biting his lips most of the time and marked fasciculations were present. The reflexes were not elicited.

The liver and spleen were not palpable; bowel sounds were increased, and soon after admission the patient vomited.

Acute organophosphorus poisoning was diagnosed.

An intravenous infusion of 5% dextrose in normal saline was set up to facilitate the intravenous injection of atropine sulphate, 1.2 mg. at hourly intervals to attain adequate atropinisation. The criterion used to determine this effect was full dilatation of the pupils. The patient was washed thoroughly soon after admission and when the moist sounds present in the lungs had disappeared. At 1.05 a.m., the patient was still comatose and areflexic, but air entry was good with no adventitious sounds in the chest and the R.R. had dropped to 20/min. It was at this time that the pupils were noticed to be not as constricted as before. At 4.10 a.m., the pupils were fully dilated and the general condition had improved. During all this time he was receiving oxygen, but at no time did he require assisted respiration. At 5.30 a.m. he regained full consciousness and was co-operative, but his speech was rather slurred.

The patient was kept on a regime of hourly intravenous atropine, until at 11.30 p.m. of the second day in hospital, he became restless and hyperexcitable, with a very dry tongue and the pupils were still fully dilated. Hyperatropinisation was diagnosed; atropine was stopped but had to be re-started the next day when the pupils were becoming constricted again.

Laboratory Findings

E.S.R. 8 mm. in the 1st hour (Westergren); Hb 14.6 g/100 ml; WBC 7,800/ c.mm; differential count normal; blood urea 29 mg/100 ml. The urine had a pH of 5.5, contained glucose and a trace of protein, a slight excess of urobilin, no bilirubin, and no significant elements in the sediment.

The serum bilirubin was 1.0 mg/100 ml. The Van den Bergh reaction was indirect, and became negative only one month after presentation. Serum aspartate aminotransferase 15 i.u./l.; alanine aminotransferase 10 i.u./l.; alkaline phosphatase 10 (K-A) u/100 ml. The blood glucose on the day of admission was 140 mg./100 ml, and 80 mg./100 ml. the following morning. Serum electrolytes were normal; serum proteins 7.3 g/100 ml.; albumin 4.2 g/100 ml. The serum protein electrophoretic pattern was however, significantly different from the normal, and a reversal to a completely normal pattern was achieved only about 4 months later. (*Figure 1*).

The serum pseudo-cholinesterase (pChE) on admission was o u./ml. This, with the subsequent estimations are recorded in *Figure 2*.

Treatment

The dose of atropine administered in the first 24 hours was 26 mg. This was severely reduced in the subsequent 6 days according to the clinical improvement, and atropinisation was maintained using pupillary dilatation as the clinical guide. A total dose of 54 mg. was given over a period of 7 days.

Clinical improvement was noticeable as soon as full atropinisation had been attained. Although progress was maintained from the beginning, the first 7 days were marked with episodic bouts of epigastric pain and vomiting. He was able to walk

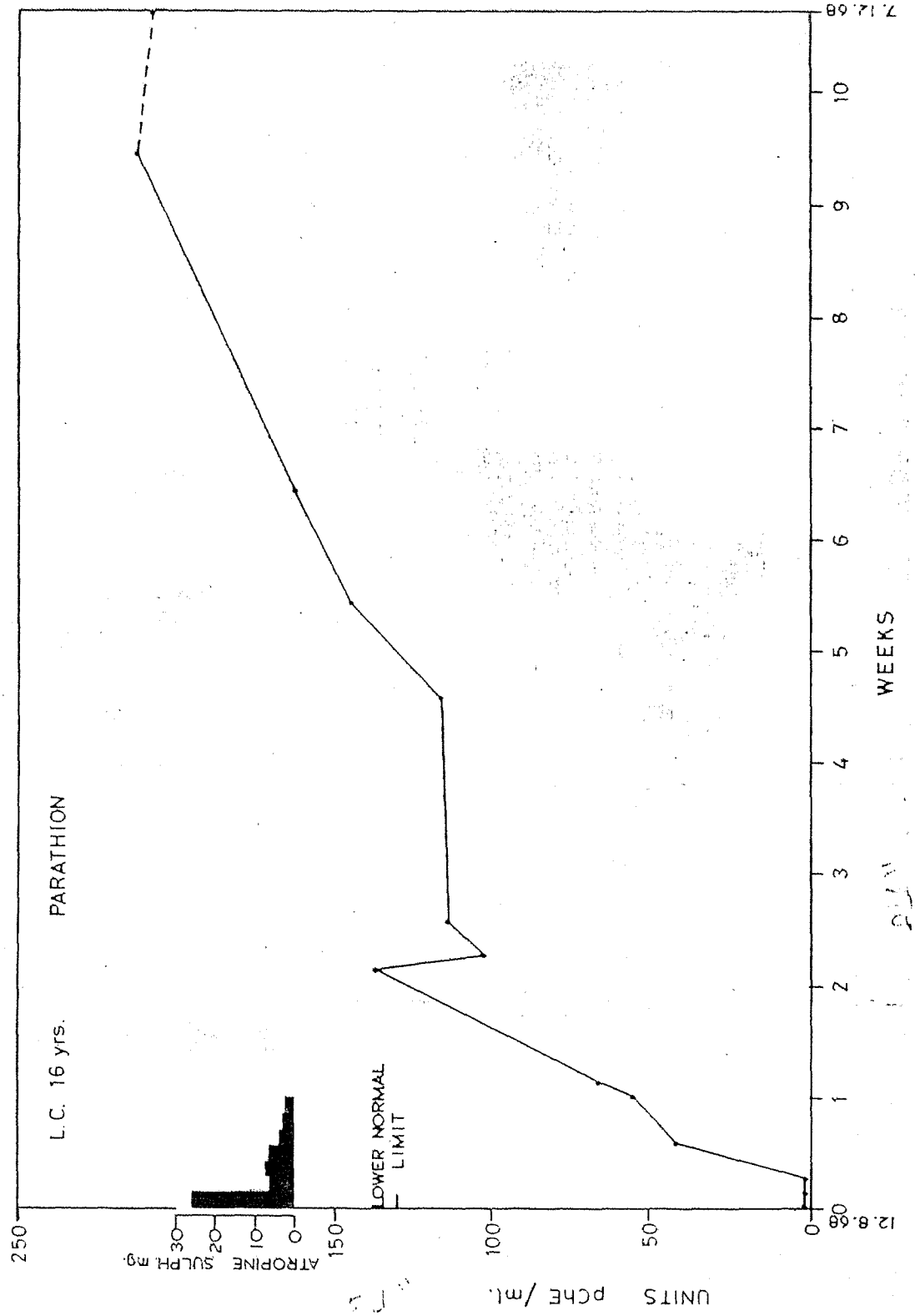

Fig. 2. Showing the limits of serum pChE and dosage of atropine sulphate in Case 1.

about on the 9th day and was discharged from hospital on the 18th day.

Report on Case 2

J.M., male, 48 years, a farmer who habitually handled Fitios B/77 (N-monoethylamide of 0.0-dimethyl dithiophosphorilacetic acid) was admitted on 21. 10. 69, half an hour after accidentally drinking about 3 ml. of a 20 per cent stock solution of this insecticide. He sought medical care not because he felt ill, but only because he realized that he had ingested a poison.

His past medical history was entirely negative, and on physical examination no abnormality was detected. Temp. 97°F, P.R. 76/min.; R.R. 20/min.; B.P. 120/75.

Laboratory Findings

The serum pseudocholinesterase (pChE) was 53 u./ml. on admission and on this basis he was treated for O.P. insecticide intoxication. Treatment with atropine sulphate was started, and serial estimations of pChE *(Figure 3)* confirmed the diagnosis.

Tests of liver function carried out during the period of observation showed only a slight rise in the serum aspartate aminotransferase to 30 i.u./l. 3 weeks after admission, while the serum alanine aminotransferase was normal throughout the period of observation. The serum bilirubin rose to 1.1 mg./100 ml. 2 months after admission.

Changes in the serum protein electrophoretic pattern were observed during this period *(Figure 4)*.

Atropine sulphate was administered i.m. for 11 days following hospitalisation, the dose being reduced progressively until the serum pChE level rose to the lower limit of normal. The total dose administered was 31.5 mg.

The patient felt well and presented no signs or symptoms whatever, except for an occasional rise in temperature up to 99.8°F. He was discharged home on the 24th day, and attended as an out-patient until he was finally discharged one month later. He continued to feel well, and on one occasion he remarked that in fact he was feeling even better than he had ever felt befort his admission to hospital. He attributer this to his having stopped handling the insecticide since hospitalisaton.

Discussion

The initial diagnosis of O.P. poisoning is usually a clincal one, and in the presence of a history of ingestion or occupational exposuer, this is not usually difficult. However, in the absence of a history of exposure and particularly in those cases affected by the highly toxic compounds, such as parathion, other conditions may be simulated. Gastro-enteritis, encephalopathy, as well as hypoglycaemic episodes may be erroneously diagnosed. The primary manifestations of O.P. poisoning arise from parasympathetic overactivity, so that excessive sweating and secretion of mucus, miosis, muscle twitchings, abdominal colic with diarrhoea, bladder contraction and bronchospasm become the principal symptoms. Though miosis is always specially emphasised, mydriasis has been observed in about 13 per cent of cases (Davies *et al*, 1967).

A hypoglycaemic episode can mimic O.P. poisoning, but hypoglycaemia has not been observed as a major clinical sign in cases of O.P. poisoning in adults. It has however been reported in an 8½ month old girl (Hruban *et al*, 1963), and the authors suggested that as pancreatic islet secretion is under parasympathetic control, over-stimulation of the pancreas may have resulted from O.P. poisoning in a child with labile control of blood glucose. As a matter of fact, ingestion of parathion by experimental animals leads to lowering of the blood glucose (Hruban *et al* 1963). However, Arterberry *et al*, (1961) and Wyckoff *et al* (1968) have reported that their patients suffering from parathion poisoning presented hyperglycaemia. In both cases here recorded, the blood glucose levels were within normal limits.

There is some evidence to suggest that other fundamental metabolic distur-

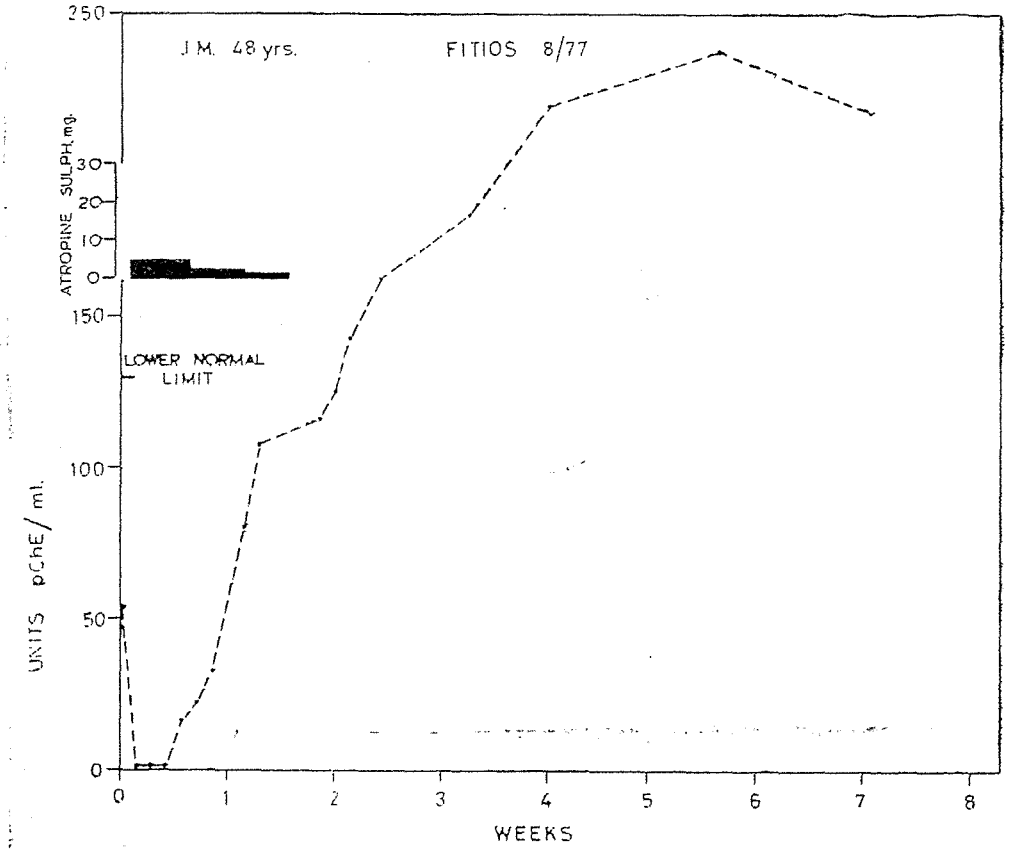

Fig. 3. Showing the limits of serum pChE and dosage of atropine sulphate in Case 2.

bances do occur in association with poisoning with O.P. compounds. Abnormal amino-acid excretion in the urine does occur (Comstock *et al*, 1967), and some degree of depression of serum enzymatic activity — alanine and aspartate aminotransferases and aldolase, besides cholinesterase — seems to become manifest following long term exposure to malathion (Grech, 1964).

The observations made on the changes in the serum protein electrophoretic pattern in our two cases are of interest. It is believed that the reduction in the beta- and gamma-globulin concentrations in the acute phase, and the gradual return to normal levels in both cases, is a true phenomenon. We are not aware that this observation has been previously recorded. It is tempting to propose that O.P. compounds might also exert an immuno-suppressant action, and if this is so their action is very rapid.

The O.P. compounds combine with the cholinesterases which become phosphorylated and therefore inactive against ace-

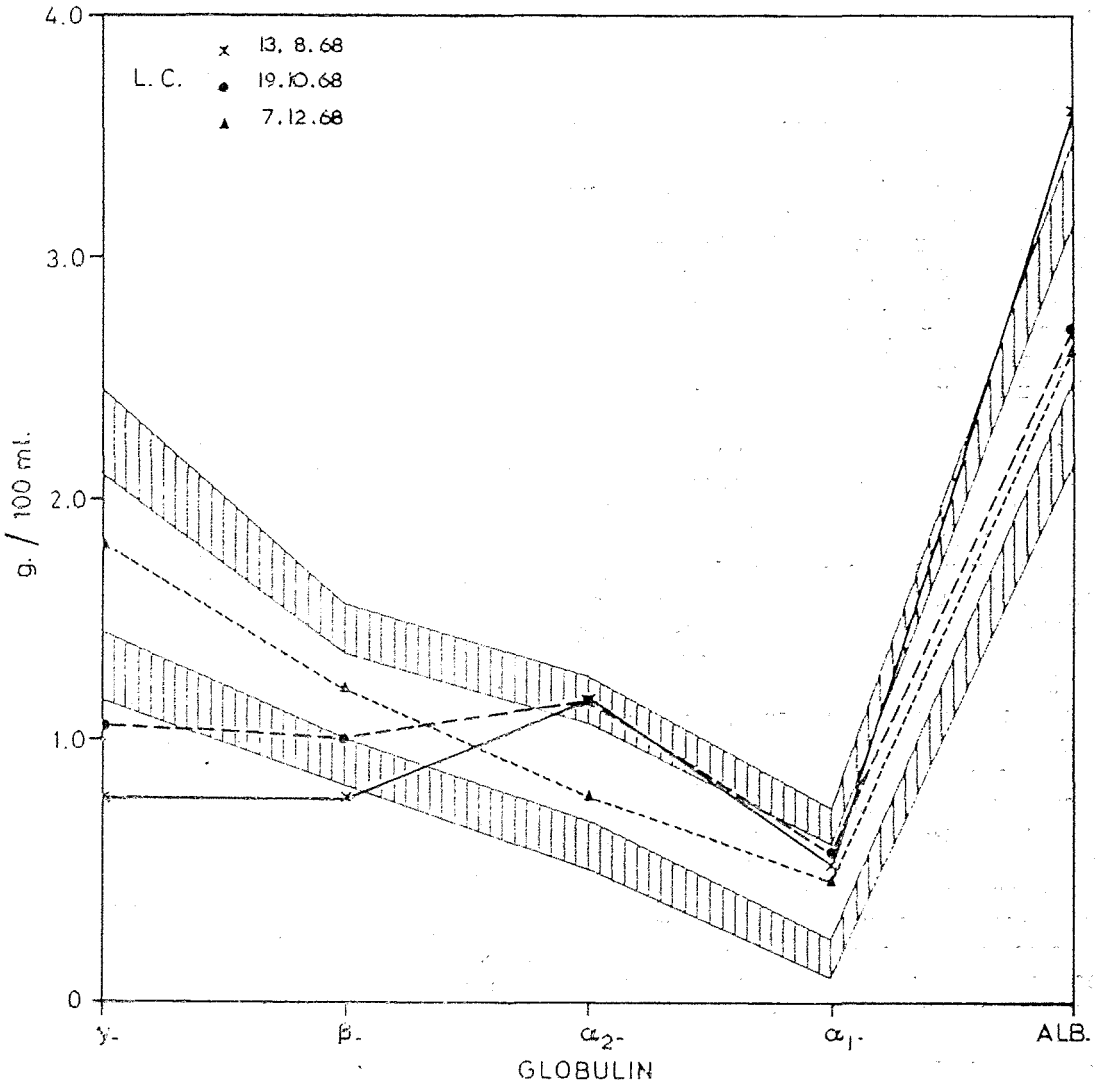

Fig. 4. Showing the changes in the serum electrophoretic pattern in Case 2, with the upper and lower limits of normal, the shaded area demarcating the limit of 2 S.D.

tylcholine, and the toxic symptoms result from the accumulation of acetylcholine at various sites. As a result of this irreversible inactivation of the cholinesterases, enzymatic activity will remain reduced until new cholinesterase is synthesised. It is claimed that non-specific cholinesterase is regenerated by the liver in about 2 weeks and at the rate of about 10% per day though it may take 12 weeks for this

to occur in the synapses and neuro-muscular junctions (Goth, 1968). In both of our cases the patient's normal level in the serum was reached before 12 weeks, rising rapidly in the first 2 weeks and more slowly afterwards.

Different O.P. insecticides vary in their toxic properties — parathion being 100 times more toxic than Fitios B/77 — the oral LD_{50} of parathion being 3 mg/kilo as compared to 340-350 mg/kilo for B/77 (Canniello, 1967). Though the degree of toxicity of these substances is different, the mode of action is the same. It appears that Fitios inactivates serum pChE much more rapidly than other cholinesterases in the body, because although no pChE activity was detected in the serum for 3 days after its ingestion, the patient remained free of symptoms.

It appears that there have been no fatalities from poisoning with Fitios (Canniello, 1969) and that this is the first case recorded in which evidence of poisoning by this insecticide has been found.

In the treatment of organo-phosphorus poisoning, the administration of atropine sulphate in full dosage, by blocking the peripheral muscarine effects and by protecting against the involvement of the central nervous system, is still the mainstay of therapy. However, as atropine exerts no protective action against skeletal muscle paralysis, as soon as signs of respiratory paralysis are evident, mechanical ventilation combined with tracheostomy, should be set-up. Naturally those drugs which potentiate the anticholinesterase effects of these insecticides such as theophylline, aminophylline and the phenothiazine derivatives are contraindicated (Arterberry *et al*, 1962). Pralidoxime and other reactivating agents may only hasten complete recovery.

References

ARTERBERRY, J.D., DURHAM, W.F., ELLIOT, J.W., and WOLFF, H.R., (1961) Arch. Environ. Health, *3*, 476.

ARTERBERRY, J.D., BONIFACI, R.W., NASH, E.W. and QUINBY, G.E., (1962) J.A.M.A., *182*, 848.

CANNIELLO, A.R., (1967) Giornate Fisiopatologiche, 81.

CANNIELLO, A.R., (1969) Personal Communication.

COMSTOCK, E.G., BICKEL, L., and MCCORMICK, R.A. Jr. (1967) Texas Med., *63*, 71.

DAVIES, J.N., DAVIES, J.E., and FISK, A.J., (1967). New York Academy of Sciences Symposium on Biological Effects of Pesticides in Mammalian Systems. N.Y.

GRECH, J.L., (1965) BRIT. J. industr. Med., *22*, 67.

GOTH, A., (1968) Medical Pharmacology, 4th Ed., Mosby Co., St. Louis, 81.

HRUBAN, L., SCHULMAN, S., WARNER, N.E., DU BOIS, K.P., BUNNAG, S., and BUNNAG, S.C., (1963) J.A.M.A., *184*, 590.

KOPEL, F.B., STAROBEN, S., GRIBETZ, I. and GRIBETZ, D. (1962) J. PEDIAT., *61*, 898.

QUINBY, G.E., and CLAPPISON, G.B., (1961) Arch. Environ. Health, *3*, 538.

QUINBY, G.E., LOOMIS, T.A., and BROWN, H.W., (1963) New Eng. J. Med., *268*, 639.

ROSEN, F.S., (1960) New Eng. J. Med., *262*, 1243.

WYCKOFF, D.W., DAVIES, J.E., BARAQUET, A., and DAVIES, J.H., (1968) Ann. Int. Med., 68, 875.

SPONTANEOUS REMISSION IN THE AHUMADA — DEL CASTILLO SYNDROME

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The association of spontaneous galactorrhoea with primary or secondary amenorrhoea is a striking clinical picture and has increasingly engaged the attention of clinicians as, during the past two decades, numerous and diverse etiological factors have been incriminated. Much stress has been laid in the past on the persistence and intractibility of symptoms in patients belonging to the group originally described by Ahumada and del Castillo (1932), and later by Argonz and del Castillo (1953). It is only natural to expect reversion to normality when an offending factor, such as a drug, is withdrawn. A case is described below where no known causative factors were present. The clinical picture showed spontaneous remission thereby giving rise to the implication that a reversible functional disturbance may exist in such cases.

Case Report

A 30-year old nulliparous woman, R.F., who had been married 11 years, was referred to hospital on 14/11/67 as a case of "acute glomerulonephritis". She had developed that day left flank ache. Her urine had become scanty and was brown in colour, and she had a temperature of 100°F. She had suffered an attack of sore throat about three weeks previously. She gave a history of recurrent attacks of tonsillitis but had never suffered from kidney trouble before. Puffiness of the face and legs had appeared over the past two days.

The patient gave a history of six months amenorrhoea and said she had noticed spontaneous ejection of milky fluid from the breasts in the latter three months. She did not give a history of headaches or episodes of unconsciousness.

Examination on admission revealed an obese woman in fairly good general condition with a puffy face. There was no acne or excessive hirsutism. She had a temperature of 100°F., a pulse of 120 beats/min., a B.P. of 120/70 mm. Hg, and a respiratory rate of 28/min. The tonsils were enlarged and inflamed. The kidneys were not palpable. Pitting oedema in the legs was present. No abnormality was detected on neurological examination.

Investigations included: Heamoglobin level - 13.6 Gms./100ml (98%); WBC - 14000/c. mm. and a PCV of 46%. Urine output per 24 hrs. varied from 100 to 300 cc. in the first few days. The urine was dark and there was massive proteinuria together with microscopic haematuria and numerous granular casts. The initial blood urea level was 92 mgms/100ml. Serum electrolytes were: Na 142 mEq./litre, K 4.7mEq./litre, and plasma chlorides 99mEq./Litre. β-haemolytic streptococci were cultured from the patient's throat and her initial anti-streptolysin-O titre was 333 Todd units rising to 625 units four weeks later.

The patient's electrocardiogram was essentially normal. Other investigations include: Serum calcium 5.3mEq./litre and plasma inorganic phosphates 3.2mgms./100ml. A glucose tolerance test showed a fasting level of 78mgms./100ml rising to a peak level of 124mgms/100ml in one hour and falling to 93mgms./100ml at the end of two hours. X-rays of the skull showed no abnormality and the pituitary

fossa was normal. Fundoscopy and fields of vision were normal. The haemagglutination-inhibition test for pregnancy was repeatedly negative.

Over the next few days her general condition deteriorated. Oedema became more marked. Her sedimentation rate, which was 22mm in the 1st hour (Westergren method) on admission, rose to 65mm/1st hour. Her B.P. reached a peak of 200/145mm Hg, and her blood urea went up to 248mgms/100ml.

The patient was started on Ansolysen injections every few hours and; later, on magnesium sulphate enemas. Her urine output slowly increased, her blood pressure returned to normal and her general condition improved over the next two weeks. Her blood urea fell to near normal limits.

As she was now convalescent as far as her kidney lesion was concerned, it was decided to pay more attention to the interesting combination of galactorrhoea and amenorrhoea which preceded her acute illness by a few months. She was adamant on questioning that she had not taken any psychotropic drugs, anovulatory steroids or any other form of medication. There had been no severe emotional stress during the previous year. The patient had, however, had a weight increase of one and a half stone during the preceding six months.

Further investigations were undertaken. Analysis of the milky fluid expressed from the breasts showed a pH of 7.0, a relatively high fat content and lactose. 17-ketosteroids and glucocorticoids were 7.0/mgms and 11.8 mgms per 24hrs respectively, i.e. within normal limits. Gynaecological examination under anaesthesia, and dilatation and curettage (Prof. A. P. Camilleri) showed a small, retroverted uterus with a cavity of $2\frac{1}{2}$ins, a palpable, not enlarged right ovary, and scanty curettings. Histological examination of the latter showed a proliferative non-secretory endometrium (Prof. G. P. Xuereb). The patient was well enough to be discharged from hospital on 22/2/68, fourteen weeks after admission.

In early May 1968 galactorrhoea stopped and regular menstruation restarted. As it was not possible to estimate urinary gonadotrophin levels at the time of her hospital stay, these were estimated in late May 1968, when she started to recover. The F.S.H. levels were then at very low limits of normal.

Discussion

The combination of galactorrhoea and amenorrhoea, together with the development of obesity in a nulliparous woman, are the striking features of this case.

Review of the literature shows numerous and very varied causes that have been incriminated over the years. These include psychiatric causes (Giraud, 1961), and intracranial pathological conditions at a number of sites especially those affecting the hypothalamo-hypophyseal region. An eosinophilic adenoma causing acromegaly is a well known cause of galactorrhoea. Other types of pituitary tumours, including chromophobe adenomas and craniopharyngiomas have been implicated (Linquette, *et al.* 1961; Forbes, *et al.* 1954), as well as pineal tumours (Oestreich and Slawyk, 1899). Other diverse intracranial pathological causes have included the odd case after brain trauma, encephalitis, and T.B. meningitis (Ravera, *et al.* 1961).

An interesting group appear related to increased afferent stimulation of the chest wall following thoracotomy, herpes zoster lesions, and burns. Drugs as an aetiological cause have recently loomed into one of the most important causes of galactorrhea. Reserpine (Somlyo and Waye, 1960), chlorpromazine and other phenothiazine derivatives (Robinson, 1957) are especially important. It has been estimated by Robinson (1957) that there is a 10% incidence of galactorrhoea in all female patients receiving chlorpromazine. If the daily dose exceeds 300/mgms then the incidence rises to 30%. Other psychotropic drugs incriminated include imipramine (Klein, *et al.* 1964), prochlorperazine and meprobamate (Hooper, *et al.* 1961). Hypotensive drugs such as alpha-methyl dopa have been

described as a cause (Pettinger, *et al.* 1963).

Particular interest has centered round the groups described where the etiological factor is unknown, and where a number of clinical features may be present. Persistent lactation following a recent pregnancy and associated with amenorrhoea, hypogenitalism, malnutrition and psychiatric disorder are usually grouped together under the term Chiari-Frommel syndrome.

Del Castillo, in a series of papers, described another group occurring usually in nulliparous women and accompanied by amenorrhoea, evidence of oestrogenic insufficiency, and low urinary gonadotrophins (Ahumada and del Castillo, 1932; Argonz and del Castillo, 1953). Three of the four cases described in 1953 were nulliparous women while one, Case No. 3, had had a pregnancy nine years previously. One of their cases had primary amenordhoea while the other three had secondary amenorrhea. These authors felt that their cases, though related to adenohypophyseal eosinophilic cell dysfunction were distinct from those described associated with clinical acromegaly (del Castillo and Lanari, 1933). Though Argonz and del Castillo felt that the syndrome they described was similar to that described by Forbes, Henneman, Grisewold and Albright (1951), the modern tendency is to separate them, and to group under the Forbes Albright heading those cases which show enlargement of the sella turcica or evidence of a pituitary tumour, such as a chromophobe adenoma, so long as there is no evidence of acromegaly. In eight of the fifteen cases described by Forbes *et al.* (1951) a pituitary tumour was present.

Our patient's clinical picture coincides with the group often known as belonging to the Ahumada-del Castillo or the Argonz-del Castillo syndrome. We feel it is more correct to refer to the syndrome as the Ahumada del Castillo syndrome rather than the Argonz del Castillo syndrome as the former two workers described it as early as 1932.

The urinary gonadotrophin levels obtained in this case can only be interpreted in the light of the clinical manifestations, and they probably reflect urinary gonadotrophins which were returning to normal. It is most interesting to note that in spite of the original claims by del Castillo *et al*, and Forbes *et al*, that urinary gonadotrophins are low, it is the view of experienced workers such as Peake and Daughaday (1968) that low urinary gonadotrophin excretion has been an inconsistent finding in patients clinically similar to those described by del Castillo and his coworkers in all other respects, and that, therefore, a low urinary gonadotrophin level is not necessary for the completion of the syndrome.

The mechanisms underlying abnormal lacatation are obscure and various theories have been proposed in the past to explain the mechanism of non-puerperal lactation. Three of the main theories advocated have been those of Nelson (1936), Meites and Turner (1942), and Folley (1956).

It is nowadays thought, however, that the all-important factor is the hypothalamus which appears to exert a restraining influence on the liberation of prolactin by the pituitary. The neuroendocrinal function of the hypothalamus in inhibiting the liberation of prolactin from the pituitary was demonstrated by Eckles and his co-workers (1958), who noted the development of persistent lactation in women with carcinoma of the breast who underwent pituitary stalk section and the insertion of a polyethylene plate between the cut ends.

It now appears that the active factors are protein or polypeptide substances of relatively low molecular weight secreted by certain parts of the hypothalamus, particularly the median eminence, and transported to the adenohypophysis where they regulate the secretion of each of the adenohypophyseal hormones. These substances may either stimulate or inhibit pituitary hormone release. The substance governing pituitary prolactin liberation is known as the luteotrophic inhibitory factor as its presence appears to diminish or suppress lactation (Achally, *et al.* 1964;

Guillemain, 1967). Hence the different syndromes mentioned above may all result from hypothalamic dysfunction causing diminution of pituitary prolactin liberation.

It should be emphasised that the usual methods of gonadotrophin assay by the mouse uterine weight method are not pure FSH determinations but measure also some luteinising hormone (LH) and luteotropic hormone (LTH) activity as well. The surprise finding in our case of a proliferative endometrium when the patient still had galactorrhoea would indicate that FSH production was not, at that time, impaired, and may imply that this endometrial proliferation was a new phenomenon and the first indication of an impending recovery. The finding of an abnormally small uterus with a uterine cavity of $2\frac{1}{2}$ ins. is consistent with longstanding low levels of oestrogens and progesterone which, in this case, would be the result of low gonadotrophic hormone secretion.

It is important to note in this respect that the use of parenteral medoxyprogesterone acetate in doses capable of inhibiting gonadotrophic hormone in patients with sexual precocity was found to be ineffective in the suppression of lactation associated with either the Chiari Frommel or Forbes Albright syndrome. Thus the inhibition of one component of the gonadotrophic triad (i.e. FSH) does not necessarily mean suppression of other units of the complex (i.e. LTH) (Kuppermann, 1967).

It was not possible to carry out a therapeutic trial in our case with clomiphene citrate (an analogue of the non-steroidal oestrogen chlortrianserine). In some cases of the Chiari Frommel syndrome it has been used with success (Kasen, 1963), as also in some cases of the Ahumada del Castillo syndrome (Whitelow, 1966). In other patients suffering from the latter syndrome, however, no beneficial results have been seen (Kempers, *et al.* 1967).

Had clomiphene been administered to our patient towards the end of her illness, the spontaneous remission that occurred could easily have been attributed to the drug. The potential coincidence between spontaneous remission and clomiphene administration must be borne in mind when assessing the benefits of clomiphene in patients with this syndrome.

Perusal of the literature on the subject shows insufficient data regarding the long term follow up of a significant number of the cases described. It is reasonable to suppose that some of these cases represented varying degrees of hormonal disturbance. It would not be a surprise to find that some of the cases with minimal dysfunction may have shown a spontaneous cessation of the galactorrhoea and amenorrhoea after an interval of time.

In the absence of a space occupying or progressive lesion, it may be postulated that a reversible functional disturbance occurred in the present case. There seems to be no reason why there should not be, on occasions, remissions in some of these cases. In our case the patient stopped lactating spontaneously shortly after her acute renal illness. One can rule out that this was solely due to the stopping of hypotensive drugs as the galactorrhoea and amenorrhoea antedated by months the use of any drug. One wonders whether the patient's renal illness affected her hypothalamic dysfunction.

The causal factors underlying the hormonal disurbance in the third case described by Argonz and del Castillo (1953) would appear to have been acquired as their patient had been endocrinologically normal before and had had a normal pregnancy nine years previously.

It is the purpose of this paper to point out that the syndrome of idiopathic galactorrhoea and amenorrhoea need not necessarily have a poor therapeutic prognosis but may show spontaneous remission.

Acknowledgements

We wish to thank Prof. A. P. Camilleri for his kind advice, and Dr. K. D. Bagshawe of Fulham Hospital for carrying out the F.S.H. estimations. We wish to thank the University Research Fund for meeting the expenses incurred in the

estimation of the urinary gonadotrophin levels.

References

ACHALLY, A. V. MEITES, J., BOWENS, C. Y., and RATNER, A. (1964) Proc. Soc. Exp. Med. 117, 252.

AHUMADA, J.C., DEL CASTILLO, E.B. (1932) Bol. Soc. gyen.y obst. *II*, 64.

ARGONZ, J., DEL CASTILLO, E.B. (1953) J. Clin. Endocr. *13*, 79. DEL CASTILLO, E.B., LANARI, A. (1933) Sem. med., *1*, 1905.

ECKLES, N.E., EHNI, G., KIRSCHBAUM, A. (1958) Anat. Rec., *130*, 295.

FOLLEY, S. J. (1956) *Physiology and Biochemistry of Lactation*; Charles C. Thomas, Springfield, III.

FORBES, A. P., HENNEMAN, P. H., GRISWOLD, G. C., ALBRIGHT, F. (1951) J. clin. Endocr. *11*, 749.

— — — — (1954) *ibid. 14*, 265.

GIRAUD, R. (1960) Bull. Fed. gynec. obst. Franc. *12*, 513.

GULLEMIN, R. (1967) Ann. Rev. Physiol. *29*, 213.

HOOPER, J. H. Jr., WELCH, V. C., SHACKELFORD, R.J. (1961) J. Am. med. Ass. *178*, 506.

KAISER, I.H. (1963) Am. J. Obst. Gyn. *87*, 149.

KEMPERS. R.D., DECKER, D.G. LEE, R.A. (1967) Obstet. Gynec., *30*, 699.

KLEIN, J. J., SEGAL, R. L., WARNER, R. R. (1964) New Engl. J. Med. *271*, 510.

KUPPERMAN, H. S. (1967). Advances in Obstetrics and Gynecology, vol. 1, Ed.b Marcus, S. L., Marcus, C. C. pp. 336. Baltimore.

LINGUETTE, M., LAINE, E., GAUTIER, P., FOSSATI, P., MAY, J.P. (1961) Ann. Endocr. Paris, *22*, 817.

MEITES, J., TURNER, C.W. (1942) Endocr. *30*, 726.

NELSON, W.O., (1936) Physiol. Rev. *16*, 488.

OESTRICH, R., SLAWK, S. (1899) Virch. Arch. Path. Anat. *157*, 457.

PEAKE, G.T. DAUGHADAY, W.H. (1968) Med. Clin. N. Am. *52*, 357.

PETTINGER, W. A., HORWITZ, D., SJOERDSMA, A. (1963) Br. med. J., *1* 1460

RAVERA, J. J., TOMALINO, D., GONZALEZ PUIG, R. (1961) Torax. *10*, 40.

ROBINSON, B. (1957) Med. J. Austral. *2*, 239.

SOMILYO, A.P., WAYE, J.D. (1960) J. Mount Sin. Hosp. N.Y. *27*, 5.

WHITELOW, J. (1696) Fertil. Steril. *17*, 584.

BILATERAL SIMULTANEOUS SPONTANEOUS PNEUMOTHORAX

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The great majority of cases of spontaneous pneumothorax involve one lung only; when this occurs in a patient with an otherwise normal respiratory tract, it usually causes no discomfort and requires no active treatment. Stradling and Poole (1966) were able to manage 83% of their simple cases in this way. The other cases are usually treated by simple aspiration of air, or by an intercostal catheter and underwater seal drainage. On the other hand, bilateral simultaneous spontaneous pneumothorax, although rare, constitutes a grave emergency when it occurs; and one of the strongest arguments in favour of prompt closed catheter drainage in the treatment of massive pneumothorax is the possibility that another pneumothorax may occur on the opposite side. The purpose of this paper is to report a case of simultaneous bilateral pneumothorax which presented as an acute medical emergency requiring immediate intervention.

Case Report

J. S., a 53-year old mill worker, was admitted to St. Luke's Hospital on 5.5.69 in severe dyspnoea and with dull substernal pain aggravated by deep breathing. He had been employed in a flour mill for the last 25 years. Slight dyspnoea on exertion and a productive morning cough with dirty, greenish, thick sputum, occasionally blood tinged dated back for 7 years. No past history of Koch's infection. Three days prior to his admission into hospital, whilst sitting in his garden, he suddenly developed a dull substernal pain accompanied by dyspnoea. The dyspnoea became progressively worse and his wife noticed that he was becoming cyanotic and restless.

On physical examination, the patient was cyanotic, apprehensive and in marked respiratory distress. His blood pressure was 140/80, respiration 40 per minute, temperature 97.4°F, pulse 110 per minute. regular. The heart-sounds were normal and the ECG was consistent with chronic cor pulmonale. An immediate X-Ray chest showed fibrotic changes in both upper zones and a 60 per cent collapse of the left lung. A rubber catheter was inserted through the eight intercostal space in the posterior axillary line and continuous suction applied. A chest X-Ray four days after admission showed marked re-expansion of the left lung and the catheter was removed a week after insertion when re-expansion of the left lung was complete.

The convalescent period was uneventful for the next four days. On the 16th of May, he suddenly developed severe dyspnoea and marked central cyanosis and became unconscious. Examination showed marked diminution of breath sounds bilaterally. The portable chest X-Ray showed bilateral pneumothorax — 30 per cent collapse on the right side and 50 per cent collapse on the left. Bilateral closed thoracotomy with under-water seal drainage was immediately instituted. Chest X-Ray taken a week later showed complete re-expansion of the right lung and marked re-expansion of his left one which was shown to be completely re-expanded three days later when both intercostal catheters were removed. He was discharged from hospital on 20th June 1969. He has been attending the out-patient department

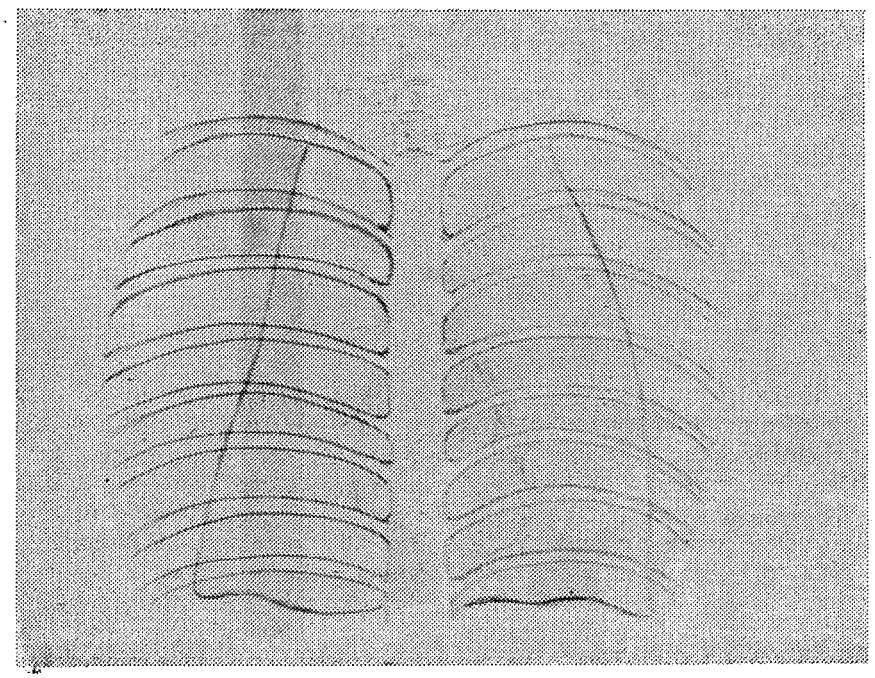

Fig. 1

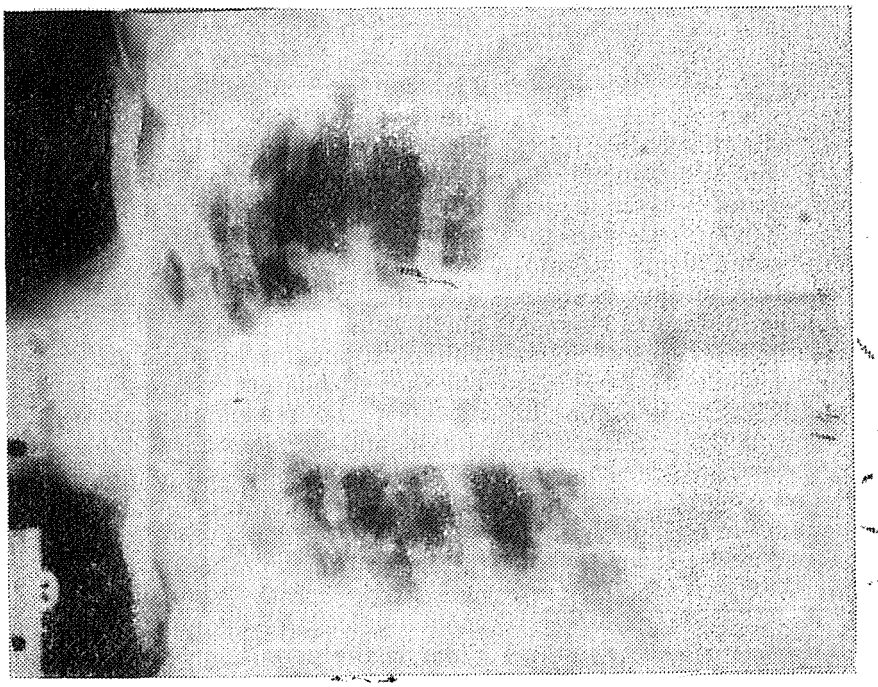

Fig. 3

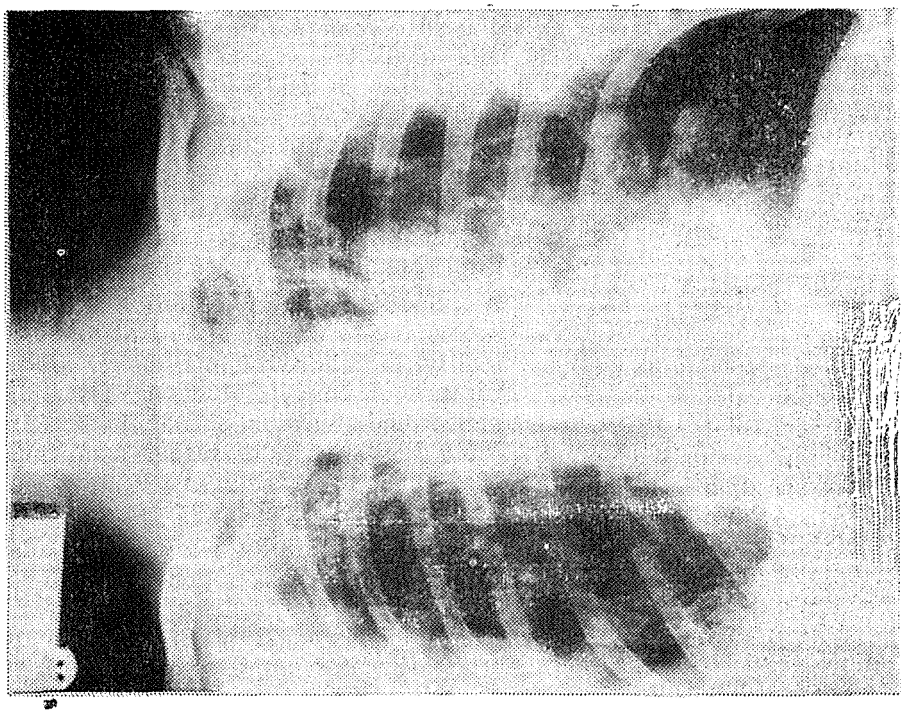

Fig. 2

since then. He was last seen on February 14, 1970, at which time both lungs were still fully expanded.

Discussion

Spontaneous pneumothorax is a fairly common malady. Wynn Williams (1957) found that there are about 7 cases a year in a population of 150,000; however, the incidence of bilateral spontaneous pneumothorax is low and this condition is inadequately reported in the literature. Thomas (1959) found 2 cases in 156 cases of spontaneous pneumothorax whilst Hyde (1962) had 2 out of 115 and Klassen (1962) one in 95 cases. *Table I* shows the incidence of bilateral pneumothorax in reports of pneumothorax; it shows that in nearly 600 patients with pneumothorax, bilaterality occurred in only 2 per cent. However, for

TABLE I

Incidence of Bilateral Pneumothorax in reports of Pneumothorax

Authors	*Pt. with Bilateral Pneumothorax*	*Total Pt. with Pneumothorax*
Thomas, P. A. (1959)	2	156
Adler *et. al.* (1961)	5	200
Klassen *et. al.* (1961)	1	95
Hyde (1962)	2	115
Peabody *et. al.* (1963)	2	23
	12	589

a pneumothorax to occur simultaneously in both lungs as a spontaneous phenomenon must be quite rare. Bilateral pneumothorax occurring simultaneously is much more likely to follow traumatic lesions to the chest. In 1960, Atkins and Smyth reported a case of bilateral simultaneous spontaneous pneumothorax, whist Payne (1965) had four cases out of 141 patients. Similar cases have been reported by Porras (1961) by Haining and Haining (1963), and by Saadi, Ruben and Massullo (1963).

Bilateral pneumothorax can occur at any age. Howie and Weed's (1957) review of the literature revealed 12 cases of bilateral pneumothorax in the newborn and they added two cases of their own. Lishman and Mansfield (1969) reported the case of a baby who immediately after birth developed a bilateral spontaneous tension pneumothorax. This condition is one of the causes of respiratory distress in the newborn and has to be differentiated from diaphragmatic hernia, eventration of the diaphragm and congenital lobar emphysema. In infancy, the diagnosis of unilateral pneumothorax is seldom missed, but that of bilateral pneumothorax in the newborn is frequently more difficult. (Ravin and Randerman, 1967).

In adolescents and adults, the finding of a hyper-resonant silent lung is diagnostic of unilateral pneumothorax; however, in bilateral pneumothorax, the presence of decreased breath sounds and distant spoken voices are the most useful physical signs as the percussion note is difficult to evaluate if both sides of the chest are affected.

The degree of collapse is usually not massive, 15 to 30 per cent being the usual amount. Saadi *et al.* (1963) did report a case of complete collapse of right lung and 80 to 85 per cent collapse of the left lung. Peabody and Luke (1963) reported a case when there was complete collapse of both lungs but in their patient the pneumothorax did not occur simultaneously in both lungs and by the time the second pneumothorax occurred, the right lung was already 50 per cent re-expanded.

Spontaneous pneumothorax is always secondary to pulmonary or pleural abnormality. In children, it may occur following rupture of congenital cysts derived from malformed terminal bronchioles (Brock, R.C., 1948) or more rarely from rupture of tension cysts in staphylococcal pneumonia (Weisel and Gorman, 1959).

In young adults, rupture of a pleural bleb is the most common cause of spontaneous pneumothorax whilst in patients over 40 it is most often due to chronic bronchitis and emphysema. Rarer causes are tuberculosis (Hyde, N.B. and Hyde, L., 1950), honeycomb lungs (Oswald and Parkinson, 1949), pulmonary malignancy,

rheumatoid disease (Davies, 1966) and cystic fibrosis (Lifschitz *et al.*, 1968).

Bilateral pneumothorax is a condition requiring prompt treatment. Immediate needle decompression of one or both sides is a life saving procedure. This has to be followed however by tube thoracotomies which have to be carried out bilaterally. High flow pumps easily expand the collapsed lungs. The trend in treatment is that every patient with spontaneous or idiopathic pneumothorax would require eventual thoracotomy (Payne, 1963). Reeves (1957) demonstrated that simultaneous bilateral thoracotomy is a satisfactory and safe procedure; and it has been suggested that bilateral thoracotomy should be done soon after pulmonary expansion has been achieved (Payne, 1963). Talc poudrage is regarded by some as the treatment of choice in the prevention of further episodes of pheumothorax (Paul *et al.*, 1951). Though recurrence rates after an intercostal tube drainage vary from 11 to 17% (Reid *et al.*, 1963; Woleott *et al.*, 1963), it was felt that open thoracotomy or talc poudrage should not be undertaken in the present case as the reactive effusion produced by the intercostal tube was such that a chemical pleurodesis was likely. The lungs have remained completely expanded.

References

ATKINS, P. C. and SMYTH, N. P. D. (1960) Dis. Chest., *37*, 702.

ADLER, R. H., MARRASH, S. and NIGUIDULA, F. (1961). New York J. Med., *61*, 570.

BROCK, R. C. (1948) Thorax, *3*, 88.

DAVIES, D. (1966) Thorax, *21*, 230.

HAINING, R. B. and HAINING, R. G. (1963) Calif. Med., *98*, 96.

HOWIE, V. M. and WEED, A. S. (1957) J. Paed., *50*, 6.

HYDE, B. and HYDE, L. (1950). Amer. Rev. Tuberc., *61*, 883.

HYDE, L. (1962) An. Int. Med., *56*, 746.

JANETOS, G. P. (1963) Amer. Rev. resp. Dis., *88*, 73.

KLASSEN, K. P. and MECKSTROTH, C. V. (1962) J. A. M. A., *182*, 1.

LIFTSCHITZ, M. I., BOWMAN, F. O., DENNING, C. R. and WYLIE, R. H. (1968) Amer .J. Dis. Child., *116*, 633.

LISHMAN, I. V. and MANSFIELD, F. (1969) Brit. med. J., *1*, 121.

OSWALD, N. and PARKINSON, T. (1949) Quart. J. med., *18*, 1.

PAUL, J. S., BEATHE, E. J. and BLADES, B. (1952) J. Thor. Surg., *25*, 52.

PAYNE, J. T. (1965) Amer. Surg., *31*, 480.

PEABODY, C. M. and LUBKE, B. W. T. J. (1963) New Engl. J. Med., *269*, 259.

PORRAS, T. (1961). Prensa. med. Argent., *48*, 2762.

RAVIN, M. B. and LANDESMAN, R. (1967) Amer. J. Obst. Gyn., *98*, 1152.

REEVES, M. M., NIAZI, S., CONNOLLY, C. and LEWIS, F. J. (1957) Ann. Surgery, *146*, 1021.

REID, J. M., STEVENSON, J. G. and MESWAN, N. (1963) Scot. med. J., *8*, 171.

RUCKLEY, C. V. and MCCORMACK, R. J. M. (1966) Thorax, *21*, 139.

SAADI, E., RIBERI, A., MASSULLO, E. (1963) Dis. Chest., *44*, 104.

SCADDING, J. G. (1967. Sarcoidosis p. 136, London, Eyre and Spotterwood.

STRADLING, P., and POOLE, A. (1966) Thorax, *121*, 145.

THOMAS, P. A. (1959). Mil. Med., *124*, 116.

WEISEL, W. and GERMAN, W. C. (1959) Surgery *45*, 335.

WOLEOTT, M. W., SHARER, W. A. and JENNINGS

WYN WILLIAMS, N. (1957). Thorax, *12*, 253.

W. N. (1963) Dis. Chest., *43*, 78.

FOETO-MATERNAL TRANSFUSION

A Cause of Anaemia at Birth

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SUMMARY

Two cases of foeto-maternal transfusion are described. The clinical picture, diagnosis and treatment are given in some detail. Other causes of anaemia at birth are also mentioned.

It has been estimated that the passage of foetal erythrocytes into the maternal circulation (foeto-maternal transfusion) occurs normally in about 50% of all pregnancies (Cohen *et al.* 1964). This is the mechanism underlying Rh-isoimmunisation of the newborn and except in these cases it is usually of no consequence because the majority of such haemorrhages are small. In some cases, however, the bleed is of sufficient degree to cause anaemia, shock or even stillbirth. This was first suggested by Weiner in 1948 and in 1954 Chown was able to demonstrate the presence of foetal RBCs in the maternal circulation thus confirming Weiner's hypothesis. We report here two such cases and discuss the condition and other causes of anaemia occurring *at birth.*

Case I

Baby I.B. A male infant born on 24. 10. 69 at Westowcroft Nursing Home, was a second child born after a normal pregnancy and delivery at 38 weeks. The placenta and vessels looked normal. Birth weight: 5lbs. 5oz. The Apgar score at 1 min.. was 8 but the baby was noticed to be pale and Hb estimation on the Haldane apparatus was found to be 77% (11 G%). He was given Synkavit 1 mg IM and at 4½ hrs. of age was admitted to the Special Care Baby Unit at Fulford Hospital, York. On examination he was a small-for-dates baby with pallor, grunty respirations, and a tachycardia of 180/min. There was no obvious external source of bleeding, no jaundice, no petechiae and no hepatosplenomegaly. Investigations carried out were as follows: Both mother and baby were group O Rh positive. Direct Coombs test — negative. Kleihauer test on the mother's blood showed a strongly positive result with more than 20 mls of foetal blood present.

He was given 70 mls of packed RBCs via the umbilical vein and prophylactic Ampicillin and Cloxacillin intramuscularly. A repeat Hb done the next day was 16.2 G %. The respiratory distress was treated successfully with intravenous Sodium Bicarbonate and Dextrose-Saline together with antibiotics. Routine check examination prior to his discharge revealed a marked pansystolic heart murmur consistent with ventricular septal defect, and a Hb of 15.7 G%. He was subsequently put on oral iron.

Case II

Baby S.S. The second baby of an Rh negative mother, she was a full term normal delivery at St. Luke's Hospital on 18.2.70 following an uneventful pregnancy. No Rh antibodies were detected at term. The baby cried well at birth after simple resuscitative measures. Birth weight was 7 lbs. 7 oz. Vaginal blood loss

during delivery was assessed as 6 ounces. She was noted to be pale soon after delivery. There was no jaundice and no petechiae, the liver and spleen were just palpable and the umbilical cord was not stained. The placenta and cord vessels were normal. There was no abnormality in the heart or lungs. Investigations on Cord Blood showed Hb. 8.8 G %, Serum Bilirubin 1.3 mg %. Van den Bergh reaction indirect. Haemoglobin F = 69 %; Haemoglobin A_2 1.4%. Screening test for G-6PD: negative; Blood Group A Rh positive. Direct Coombs test negative. Mother's blood group A Rhesus negative. Kleihauer test at 18 hrs — 10.4% of erythrocytes contained foetal Hb. On 20.2.70: Hb electrophoresis on the mother showed Hb F 2.4% A_2 2.7%; on 4.3.70: Hb F 3.3% and A_2 2.0%, Kleihauer Test was again positive. The baby was transfused with 80 mls packed RBC. Repeat Hb was 12.5 G %. Her subsequent progress has remained uneventful. She was later put on oral iron.

Discussion

It is now well recognised that significant foeto-maternal haemorrhage may present at birth in two ways. More commonly, the bleeding is acute. In such cases the infant shows the picture of oligaemic shock with severe pallor, tachycardia, weak or absent peripheral pulses and rapid, shallow and often irregular respirations. The Apgar Score at 1 minute is characteristically high in contrast with the low score found in asphyxia pallida, with which it may be confused. This differentiation is of vital importance for the severely asphyxiated neonate needs urgent respiratory resuscitation — a procedure which, with the exposure, handling and possible trauma which it may entail, may make matters worse in cases of neonatal shock due to acute blood loss.

If the haemorrhage has been prolonged or repeated during the course of the pregnancy, the foetus has a chance to adjust haemodynamically and anaemia only develops slowly. Such an infant born after chronic haemorrhage presents with unexplained anaemia at birth — an anaemia which is commonly missed. Rarely there may be added signs of congestive heart failure.

Estimation of the infant's Hb at birth may show only a slight reduction in its level if the bleeding has occurred shortly before birth. This is because of the initial haemo-concentration and as restoration of the blood volume and heamodilution takes place over the next 12 - 24 hrs serial Hb estimations will reveal a fall.

It should be emphasised that the capillary Hb level may be also spuriously high in cases of severe shock because of peripheral circulatory stasis and for this reason one should always test venous (e.g. antecubital or umbilical vein) rather than capillary (e.g. heel-prick) blood.

In acute haemorrhage the RBCs in the peripheral film will be normocytic and normochromic, while in chranic blood loss a hypochromic microcytic picture may be seen. Other evidence of iron deficiency — low serum iron level and no stainable iron in the bone marrow — have also been demonstrated in the latter cases (Eshaghpour *et al.* 1966).

Proof that the foetus bled into the mother can be obtained with certainty only by demonstrating the presence of foetal red cells in the maternal circulation. This can be done by one of several techniques including direct differential agglutination (Jones and Silver 1958), fluorescent antibody techniques (Cohen *et al.* 1960), examination of the buffy coat for foetal RBCs (Goodall *et al.* 1958); the alkali denaturation method (Singer *et al.* 1951) and the acid elution method of staining for cells containing foetal Hb (Kleihauer *et al.* 1957).

The simplest and most widely used of these is the Kleihauer test in which methanol-fixed maternal blood films are treated with an acid buffer at pH 3.4. Foetal RBCs resist lysis by the buffer solution so that they subsequently react with the ordinary Hb stains, whereas the adult maternal RBCs are lysed and appear as "ghosts". The foetal erythrocytes are then counted and a rough calculation is made as to the degree of haemorrhage that has

taken place. The result may be conveniently reported as the ratio of foetal to maternal RBCs expressed as a percentage. The Kleihauer technique can be relied upon with certainty for diagnosis only when other conditions capable of producing a rise in maternal Hb F levels (e.g. thalassaemia minor, sickle cell anaemia) are absent. In such cases the tests based on differential agglutination should be performed.

Diagnosis of foeto-maternal transfusion may be missed in cases where the mother and infant are ABO incompatible. Here, the baby's A or B cells are rapidly cleared from the mother's circulation by maternal anti-A or anti B, and thus are not available for staining by the Kleihauer technique. This test should therefore bedone as early as possible after birth.

The exact mechanism by which the foetal blood enters the maternal circulation is obscure and in most cases there are no gross placental abnormalities. The placenta should be examined carefully because the haemorrhage from the infant may not have entered the mother's circulation and instead may have accumulated in the substance of the placenta. (Chown 1955) or retroplacentally (Kevy 1962). Rarely, the placenta may be damaged during high rupture of the membranes (Apley *et. al.* 1961) and in one case the condition was associated with a chorion-carcinoma (Benson *et al.* 1962).

The differential diagnosis of anaemia at birth is not usually difficult and a list of causes is shown in Table 1. There are two main groups of conditions causing obvious anaemia *at birth.* The first and by far the commonest is haemolytic anaemia due to Rh, ABO or other rare group incompatibility. The presence of Rh antibodies during pregnancy, direct Coombs test and serum bilirubin on cord blood, testing for incompatibility between mother's serum and baby's RBCs and blood film examination, are routinely undertaken to diagnose this group. Various infections are a less common cause of haemolytic anaemia at birth.

The second group is anaemia caused by intrauterine haemorrhage. Foetal haemorrhage should be suspected during labour or during the operation of artificial rupture of membranes if there is a sudden gush of bright red blood from the vagina. The foetal origin of the blood can be confirmed in the labour ward by testing for foetal Hb which resists denaturation with alkali (Apt test). The placenta should be examined to exclude rupture of anomalous vessels, retroplacental clot, etc. If there is no obvious source for the haemorrhage, foeto-maternal transfusion should be excluded by an immediate Kleihauer test. Pallor in one of a pair of monozygotic twins with relative polycythaemia in the other, points to twin-to-twin transfusion (Vassallo Agius 1967). Congenital hypoplastic anaemia is extremely rare and is confirmed by a low reticulocyte count and bone marrow studies.

Treatment depends on the degree of anaemia and the general condition of the baby. When the infant is in shock or if the pallor is very marked, plasma should be given rapidly initially (via an umbilical catheter) to expand the intravascular compartment. When blood becomes available a transfusion of 10 cc/lb (20 cc/kg) body weight packed cells should be given. Infants who are mildly anaemic and who show no distress do not require blood and should be given oral iron for three months to replenish the depleted iron stores. Iron is also needed for the infant who receives a blood transfusion because this is not generally sufficient to replace the iron lost from the haemorrhage. McGovern *et al.* (1958) reported iron deficiency anaemia in a three month old infant that had foeto-maternal haemorrhage and was transfused at birth.

Acknowledgement

We thank Dr. W. Henderson, Consultant Paediatrician York, England and Dr. E.A. Cachia, Consultant Paediatrician, St. Luke's Hospital, Malta for permission to publish details of the two cases.

TABLE I
CAUSES OF ANAEMIA
AT BIRTH

A. INTRAUTERINE HAEMOLYSIS

1. ISO-IMMUNISATION (Erythroblastosis foetalis)
— Rh incompatibility
— ABO incompatibility
— Rare group incompatibility
2. INTRAUTERINE INFECTIONS
— Bacterial — Septicaemia
— Viral — Rubella; Cytomegalovirus
— Protozoal — Toxoplasmosis
— Spirochaetal — Syphilis

B. INTRAUTERINE HAEMORRHAGE

1. HAEMORRHAGE IS INVISIBLE
— Foeto-Maternal transfusion
— Twin-to-Twin tranfusion
2. HAEMORRHAGE IS USUALLY VISIBLE
— Incision of anteror placentia praevia at C.S.
— Placenta Praevia
— Abruptio Placentae
— Rupture of anomalous vessels
— Rupture of umbilical cord
— Damage to placental vessels at A.R.M.

C. IMPAIRED RBC PRODUCTION

Congenital Hypoplastic Anaemia
(Erythrogenesis imperfecta)

References

APLEY, J., COLLEY, P.A.N. and FRASER, I.D. (1961) Lancet 1: 1375.

BENSON, P.F., GOLDSMITH, K.L.G., and RANKIN, G.L.S. (1962) Brit. Med. J., 1: 841.

CHOWN, B. (1954) Lancet 1: 1213.

CHOWN, B. (1955) Am. J. Obst. Gynec. 70: 1298.

COHEN, F., ZUELZER, W.W., and EVANS, M.M. (1960) Blood, 15: 884.

COHEN, F., ZUELZER, W.W., GUSTAFSON, D.C., and EVANS, M.M. (1964) Blood, 23: 621.

ESHAGHPOUR, E., OSKI, F.A., and NAIMAN, J.L. (1968) J. PEDIAT., 69: 806.

GOODALL, H.B., GRAHAN, F.S., MILLER, M.C., and CAMERON, C. (1958) J. Clin. Path., 11: 251.

JONES, R.A., and SILVER, S. (1958) Blood 13: 763.

KEVY, S. (1962) J. Pediat., 60: 304.

KLEIHAUER, E., BRAUN, H., and BETKE, K. (1957) Klin. Wsch. 35: 637.

MCGOVERN, J.J. DRISCOLL, R., DUTOIT, C.H., GROVE-RASMUSSEN, M., and BEDELL, R.F. (1958) New Eng. J. Med. 258: 1149.

SINGER, K., CHERNOFF, A.I., and SINGER, L. (1951) Blood 6: 413.

VASSALLO AGIUS, P. (1967) St. Luke's Hosp. Gaz. Malta. 3, 124.

WEINER, A.S. (1948) Am. J. Obst. Gynec. 56: 717.

PEUTZ-JEGHERS SYNDROME IN CHILDHOOD

Report of a case

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Peutz-Jeghers Syndrome (Peutz 1921, Jeghers *et al.* 1949) is a condition characterised by intestinal polyposis associated with typical pigmented spots around the mouth and on the oral mucosa. The syndrome is rare and to date about 300 cases have been reported in the world literature. It is much rarer in children than in adults.

Case Summary

The patient, an 8-year old boy, was admitted to the Paediatric Ward, Kettering General Hospital, with a 12 months history of recurrent episodes of anorexia, abdominal pain and vomiting. The pain was colicky and localised to the epigastrium, usually coming on a few minutes after meals. It was followed after a variable interval by projectile vomiting which was often bile-stained and which relieved the pain slightly. During these attacks, which lasted for a few days, the boy's appetite was generally poor and he looked miserable. The bowels were regular throughout and the stools were never noticed to be blood-stained or 'tarry'. Over the month before admission, the pain had occurred almost every day and had also become constant, losing any relation to meals. The boy had lost about a stone in weight over a period of 4 months. The only other complaint was recurrent oral ulceration. The patient's parents were both well as was an elder sister. The mother had facial freckles.

On examination the boy looked pale and thin, weighing 41 lbs. (on the 3rd. percentile). He had numerous freckles on the face, especially on the nose and cheeks ('butterfly' distribution) and around the mouth *(Fig. 1)*. The pigmentation extended over the vermilion of both lips and there were everal bluish-black pigmented spots on the labial and buccal mucosa *(Fig. 2)*. He also had scattered freckles on the dorsal aspects of both hands and feet and some 'beaking' of the fingernails, but no obvious clubbing. The abdomen was scaphoid and a sausage-shaped, smooth, slightly tender mass was easily palpable in the left iliac fossa. The bowel sounds were augmented and on rectal examination there was some tenderness on the left side. There was no blood on the examining finger.

Laboratory investigation gave the following results: Hb. 5G/100ml., P.C.V. 22%,

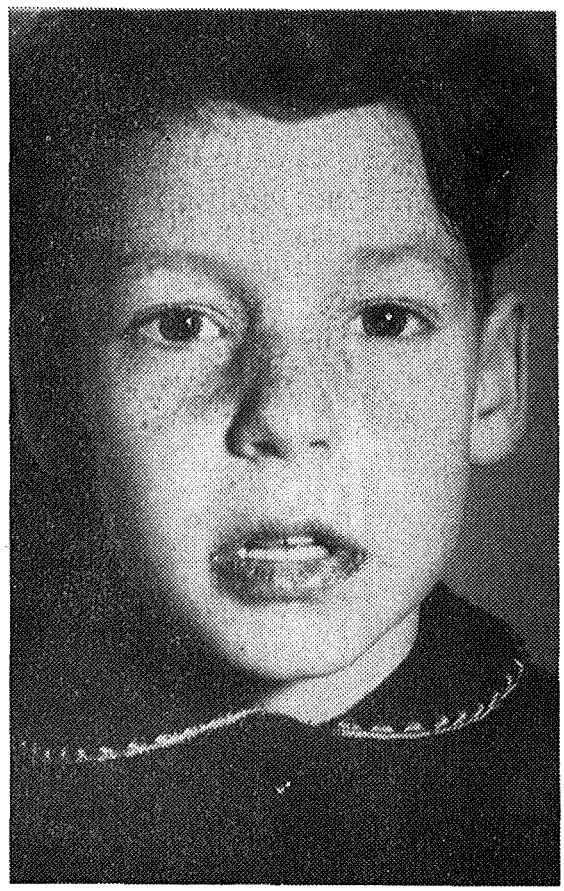

Fig. 1

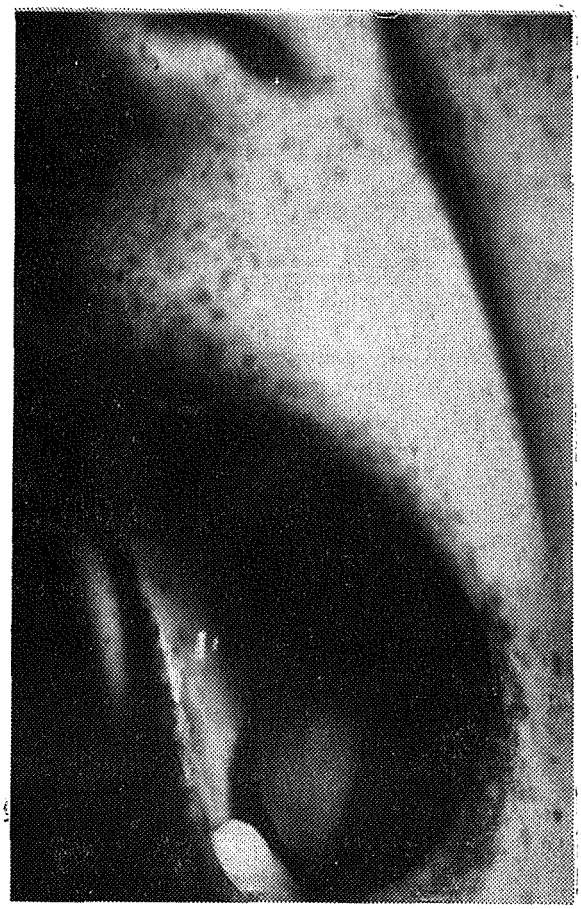

Fig. 2

M.C.H.C. 23%, M.C.V. 58cuμ. The peripheral blood film showed anisocytosis, poikilocytosis, microcytosis and hypochromia. Reticulocytes: 2.1%, E.S.R. 24mm in 1hr (Westergren). The W.B.C. count, Urinalysis, Blood Urea and serum Proteins were normal. The serum Electrolytes were: Na 127mEq/lit., Cl 93mEq/lit., K 3.2mEq/lit. The Heaf test was negative. Stool examination for occult blood was positive on three occasions. A plain X-Ray of the abdomen was normal. On barium study there was no evidence of hiatus hernia or oesophageal reflux and no ulcers could be seen in the stomach or duodenum. Folow-through for small intestine showed a large dilated loop of jejunum. The rate of transit of the contrast medium was normal. There were numerous, small filling defects in the ileum which were very suggestive of small polypi and two other large ones in the jejunum. The colon was normal. The overall impression was that of intermittent intussusception (although no actual apex for this could be seen) and multiple small intestine polyps.

During the first week in hospital, the boy had several episodes of abdominal pain with vomiting and examination on different occasions showed visible peristalsis, tenderness in the epigastrium and an evanescent abdominal mass which shifted in position from day to day. The bowel sounds were increased. The motions were normal. In view of the decision to operate, the anaemia was corrected by blood transfusion.

Sigmoidoscopy up to 15cms. was normal. At laparotomy (Mr J. H. C. Phillips) there was no small bowel dilatation but six polyps were found in the upper jejunum *(Fig. 3)*. Approximately 25cms. of involved jejunum were excised and an end-to-end anastomosis performed.

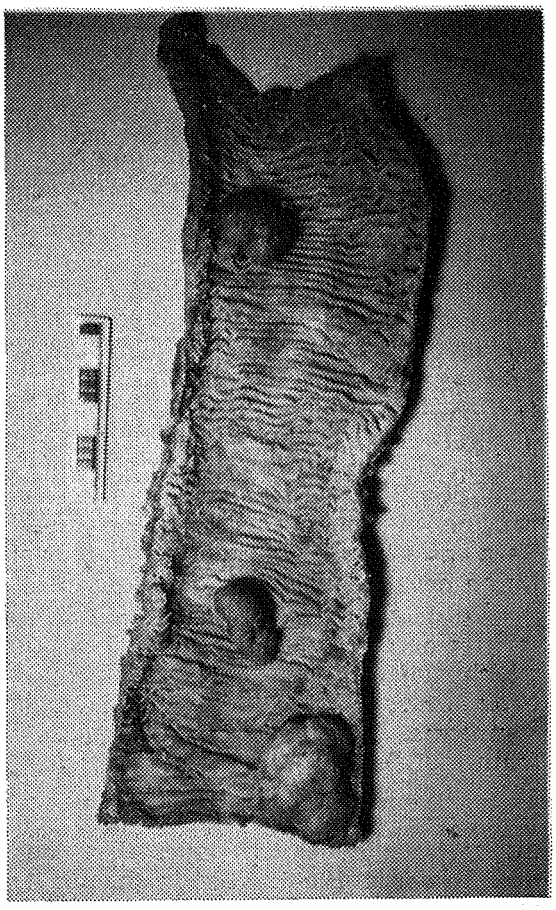

Fig. 3

The pathologist's report (Dr. P. S. Andrews) was as follows: "23 cms of small intestine with six polyps. The largest is sessile 3.2 x 2cms in size; others, ranging in size from 2.5 x 1.2 cms down to 0.2 x 0.1cms. No glands were found in the pedicle. Histology showed benign jejunal adenomatous polypi with abundant collections of histiocytes in parts of the stroma". The histology of a freckle excised from the skin was normal except for some irregularity of the melanin pigmentation in the basal-cell layer.

The post-operative period was uneventful and the patient was discharged home twelve days after operation with a Haemoglobin of 11 G %. He has been followed up as an out-patient and has up to now remained well and symptom-free.

Comments

Peutz-Jeghers Syndrome can present at any age but reports of it in the paediatric literature are sparse (Massimo 1959, Wenzl *et al.* 1961). Cases occurring in childhood usually come to light after the condition has been discovered in one of the patient's parents or older siblings.

The condition is inherited as an autosomal dominant of high penetrance and the majority of cases have therefore been found to involve several members of one family (Christiaens *et al.* 1959, Bartholomew *et al.* 1962). Sporadic cases do however occur and the case here reported is probably one of these. The boy's mother had facial freckles at first suggestive of the condition, but she was symptom-free and had no pigmentation inside the mouth. Rare cases where either polypi or pigmentation occur alone have been described.

In diagnosis, it is usually the characteristic peri-oral and buccal pigmentation which suggests intestinal polyps as the basic cause of the patient's abdominal symptoms. A peculiar and often puzzling feature of the syndrome is the presence of an evanescent palpable mass which shifts to different positions in the abdomen during separate colicky episodes (Dormandy and Edwards 1956). This is due to the self-reducing intussusception and, as happened in this case, it may be mistaken initially for a faecal mass and therefore thought to be of no significance.

The condition can closely mimic the syndrome of cyclical vomiting, which is very much more common and is not associated with buccal pigmentation.

The polyps are notoriously difficult to visualise radiologically and barium studies are very often negative (Dormandy 1958). In most cases therefore, the absolute diagnosis can only be made at laparotomy when multiple polyps are found in the intestine, usually in the jejunum and ileum.

The question of possible malignant change occurring in these polyps is still somewhat controversial. In a review of 67 published cases, as high an incidence of malignancy as 19% was recorded (Bailey 1957). Dormandy attributed this to misinterpretation of the histological findings and pointed out that clear-cut cases of metastases had never been reported (Dormandy 1958). A definite case of Peutz-Jeghers syndrome with metastases in a 52-year old woman has however been subsequently recorded (Williams and Knudsen 1965). Nevertheless, most authorities seem to agree that such a malignant change is extremely rare and histologically the polyps are usually hamartomatous malformations (Dormandy 1958, Bartholomew *et al.* 1962). Because of this, most surgeons prefer conservative treatment and perform multiple enterotomies and polypectomies rather than gut resections. In the case here reported it was thought justifiable to resect the involved part because the polyps were localised to a small stretch of jejunum.

The prognosis of the condition is, on the whole, good though these patients are prone to develop anaemia from intestinal blood loss and have repeated episodes of intussusception from further polyps which tend to crop up in spurts over the years and which often require further surgical treatment.

Acknowledgements

I would like to thank Dr. R. Wigglesworth, Consultant Paediatrician in the Kettering and Northampton Areas for permission to publish this case.

References

ANDREWS, L. G. (1954). Arch. Dis. Child., *29*, 455.

BAILEY, D. (1957), Brit. med. J., *2*, 433.

BARTHOLOMEW, L. G., MOORE, C. E., DAHLIN, D. C., and WAUGH, J. M. (1962) Surg. Gynaec. Obst., *115*, 1.

CHRISTIAENS, L., FONTAINE, G., DEFOORT, G. (1959). Arch. Fr. Paed., *16*, 963.

DORMANDY, T. L., and EDWARDS, J. H. (1956). Gastroenterologia, *86*, 456.

DORMANDY, T. L. (1957). New Engl. J. Med., *256*, 1093.

DORMANDY, T. L. (1958). In Modern Trends in Gastroenterology, edited by F. Avery Jones, 2nd series, p. 118. Butterworth, London.

JEGHERS, H., MCKUSICK, V. A., and KATZ, K. H. 1949). New Engl. J. Med., *241*, 993; 1031.

MASSIMO, L. (1959). Minerva Ped., *11*, 1116.

PEUTZ, J. L. A. (1921). Nederl. Maandrschr. v. Geneesk, *10*, 134.

WENZL, J. E., BARTHOLOMEW, L. G., HALLENBECK, G. A., and STICKLER, G. B. (1961). Paediatrics, TB, 655.

WILLIAMS, J. P., and KNUDSEN, A. (1965). Gut, vol. 6, *2*, 179.

PHARMACISTS AND POLITICS IN MALTA IN THE 18th and 19th CENTURIES

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The autocratic rulers of the Order of St. John of Jerusalem allowed no overt political activity during the two-and-a-half centuries of their domain over the Maltese Islands. Signs of unrest first occurred in 1560 when a number of citizens met secretly and drew up a petition to Philip II, King of Spain, to whom they appealed to induce Grand Master Jean de la Valette to respect their political rights and privileges among which was the question of the imposition of taxes. The author of the document was, allegedly, Dr. Joseph Callus, the first Maltese physcian known to us, who was arrested with his collaborators, condemned to death and hanged (Cassar, 1965).

No other political stirrings on the part of the Maltese came to ruffle the regime of the Knights of St. John until two hundred years later when preparations for a revolt were hatched. On the 31st December 1772 a certain Giuseppe Zahra, one time teacher of mathematics to the pages of the Grand Master, together with a priest from Floriana, Don Gaetano Mannarino, assembled in the vicinity of the church of St. Publius with four hundred followers. The pretext was that of rendering thanks to the Almighty by Don Gaetano Mannarino for the recovery of his brother from a very grave illness but in reality the intention was to take possession of Valletta. The projected rising was, however, called off at the last moment when the leaders learned that the government had got wind of the whole affair and taken the security measures that the situation called for (Laferla, 1926).

Among the conspirators there were a physician from Valletta, who remains anonymous, and who lived in Floriana but later moved to Birkirkara (Callus, 1961 a); and an apothecary from Floriana, Pasquale Balzan.

We first hear of Pasquale Balzan in

February 1764 when he applied to the Grand Master for permission to run a pharmacy at Floriana under the direction of "an approved and matriculated pharmacist". His request was granted as he had assured the Medical College that he would do so with the assistance and under the direction of the pharmacist Aloisio Cocchi, until he himself had finished his studies and "passed the usual examination" in pharmacy.

Balzan had begun his apprenticeship with the pharmacist Giuseppe Felici at Floriana, then went to continue his studies at Palermo, Naples and Rome where he was examined and awarded the certificate of pharmacist *(privilegio d'aromatario)* by the thirteen pharmacists and three physicians composing the College of Rome, on the 21st June 1766. On his return to Malta in August of the same year he obtained the licence to exercise his profession and keep a pharmacy in Floriana in his own name (Archives 1190 and 1191, RML).

A second attempt at a rebellion was made in 1775. Pasquale Balzan with an unnamed pharmacist from the Holy Infirmary again appears among the followers of Don Gaetano Mannarino during the so-called "Rising of the Priests" who demanded the restoration of national privileges and a reduction in the price of bread. Pasquale Balzan, with a handful of men, succeeded in taking possession of St. James Cavalier in Valletta, while Mannarino with another group of insurgents captured Fort St. Elmo. The uprising was quickly quelled by the Grand Master and Knights of St. John. Pasquale Balzan was arrested and imprisoned in the Castellania (now the office of the Health Department) and charged with high treason, but a legal point cropped up with regard to the court procedures.

Balzan, besides being a pharmacist, was also a cleric. Having received minor orders, he enjoyed ecclesiastical immunity and could not, therefore, be prosecuted by the Civil Tribunals. The Grand Master, however, refused to hand him over to the Episcopal Court for trial and ordered his execution with the other rebels. Balzan was strangled to death in the Castellania, and beheaded. His head was impaled on a pike on St. James Cavalier on the 13th/14th September 1775 (Callus, 1961 b).

The next political episode in our history occurred in 1798. In that year the Order of St. John was expelled from Malta by the French under Napoleon, who captured the Island.

The French period was brief and turbulent. The Maltese soon became dissatisfied with the new regime and rose against the French whom they blockaded in Valletta and the three cities for two years. The apothecary M. Falzon of the village of Attard, who lived through those confused times, complains of the "sickness, mortality, desolation, lice, debts, anxieties and sadness" which he had to contend with. He describes the state of the Island as being so chaotic as to be nothing less than *una Babilonia tra tutti, in tutto e per tutto* (a Babel among us all, in everything and everywhere). He not only had to bear the brunt of personal tragedy through the loss of his brother and of his wife and the ruin of his business but also suffered poltical persecution at the hands of the French and their partisans (Ms. 756, RML). He has left us no detailed records of this persecution but we possess other documents relating to similar charges which another colleague had to face at this period.

He was the pharmacist Francesco Pisani, the owner of a pharmacy in *Strada Reale,* Senglea. The informers against Pisani described his pharmacy as a "club" where persons met during the night in summer "to disturb the neighbours with the playing of musical instruments and singing". The place was also the resort of priests, disgruntled French officers, "bad characters and many discontented and unbridled youths". In this "club", Pisani was alleged to have plotted, together with the physicians Michele Adriano, Giovanni Bruno and Gaetano Pisani, to assassinate General Vaubois and oust the French from Malta. These conspirators were said to have planned to send a Maltese boat in search of the British naval units that were cruising in the vicinity of the Island to invite them to enter our ports on the 10th August 1798. The sight of the British Fleet was to serve as a signal for an armed

revolt against the French. The ultimate aim of the conspirators was to set up a new independent republic.

Francesco Pisani and Michael Adriano were arrested and submitted to trial. Both of them protested their innocence of the charges brought up against them. They were not only pro-French but they were proud of being members of the National Guard *(Archivio Corte Civile,* Malta). Unfortunately we do not know how this trial ended and what happened to Pisani and Adriano as the records of the legal proceedings are incomplete. It appears, however, that they escaped a judicial death as their names have not been traced in the Registers of Deaths of the Parish Church of Senglea (Burlo', 1963).

More is known about another pharmacist who has left his imprint on the history of this epoch. He was Stanislaus Gatt who at first accepted public office under the French but later turned against them. Born about 1744, he studied pharmacy at the Holy Infirmary of Valletta. After qualifying in 1770 he set up in practice at Qormi, having bought the pharmacy of the *aromatario* Ignazio Cascin of that village (Arch. 1192, RML) where Gatt lived for the next forty years.

He entered public life in 1770 when he was appointed Jurat of Qormi. By 1798 he had risen to the rank of Syndic. When the French soldiers occupied Qormi they ransacked his home but he was retained in office with the title of President of the Municipality of Qormi and Luqa. His sympathies, however, were never with the French and when the Maltese insurrection broke out he was chosen by the insurgents to be President of the Blockade Committee and Commander of the Qormi Battalion. In his new role as leader of his village, he incurred heavy financial expenses in his efforts to obtain the necessary grain from Sicily to feed his soldiers and the people of Qormi. He realised that it was not enough to expel the French from Malta but that it was equally vital to bring the Island under a powerful protecting power. For this reason he put his signature to a petition addressed to the King of Sicily in which the Maltese leaders asked for the transfer of the sovereignity of Malta to Great Britain.

For his services during the blockade he was awarded the *Patria liberata* gold medal by Sir Alexander Ball and also a scroll testifying to his zeal and bravery in the defence of the Island. After retiring from public life owing to ill health (Stellini, 1962 a), he went back to his pharmacy but did not cease to take an active interest in the social and political life of his village. Indeed between 1801 and 1803 he was engaged in defending the rights of the people of Qormi against the autocratic administration of the *Luogotenente* Manwel Gellel. Gatt died on the 4th March 1811 (Cardona, 1952). His pharmacy passed into the hands of the apothecary Giorgio Galdes whose father had married a Gatt. This pharmacy was still in existence at No. 1 St. Catherine Street, Qormi, until about 1853 (Stellini, 1962 b).

Politics again obtruded themselves into the life of apothecaries towards the mid-century when some of the pharmacaies of Valletta came very prominently in the public eye. A characteristic feature of our times is the great number of clubs in our towns and villages that cater for a variety of tastes and interests. No such development had yet taken place in the mid-nineteenth century. In the absence of such facilities for companionship and for the exchange of views, the rudiments of political club-life were being fostered by the pharmacies of the time. Indeed it has already been seen how, at the close of the 18th cntury, a Senglea pharmacy was described as a "club". Pharmacies continued to play this role in the succeeding century when they formed the *rendez-vous* of groups of professional and cultured men who wended their way to the apothecary's in the evening to while away their leisure hours and to discuss the news and political topics of the day. Those were times of social and political unrest and turmoil in Europe. Events on the continent, on which Malta depended for its commerce and sustenance, were followed with avid interest in the Island. Attention was particularly focussed on southern Italy and on Sicily — these states being the nearest to us geographic-

ally, culturally and commercially. The Italian peninsula was then the scene of frequent armed risings. Many Italians and Sicilians were driven away from their homes by fear of persecution. Both revolutionary and reactionary refugees made Malta their temporary residence between 1821 and 1861 and found staunch sympathisers among both the liberal and the conservative elements of Maltese professional men. It is not to be wondered at, therefore, that the pharmacies patronised by these professional *habitues* gained notoriety as the meeting places of Italian and Sicilian refugees and propagandists for the liberation and unification of Italy.

The pharmacies that came into the limelight for their political activities were those of Giovanni Bardon at 167 Merchants Street; of Vincenzo Duclos at 285, of Arpa at 240 and 241 and of Dr. C. Schinas at 56 Kingsway, Valletta (Laurenza, 1932).

Bardon's pharmacy was one of the haunts of the renowned Italian liberal refugee Nicola Fabrizi (1804-1885) (Mangion, 1962). As head of the association *Giovane Italia* he operated from Malta between 1837 and 1864 forging links and communications between Mazzini in London and a number of Italian political emigrees in various parts of the Mediterranean (Laferla, 1938). Though opposed by reactionary elements and dogged by Bourbon spies in Malta he never ceased to fight for the unity and independence of Italy and in the 1864 was among those who welcomed Garibaldi to Malta (Bonello, 1963).

Schinas's pharmacy, also known as *Farmacia della Carita'*, was run by the pharmacist Emanuele Maria Borg "a man of proved ability and for many years assistant pharmacist of the Civil Hospital" *(Il portafoglio maltese,* 1840). He was a member of the *Associazione Patriottica Maltese* which had been founded on the 5th November 1848 for "the advancement of the people" in politics and public morality. Under the presidency of Dr. Gio Carlo Grech Delicata M.D., it survived until the 31st July 1852 when it was dissolved. (Fiorentini, 1966). It supported the Italian liberals and the unity of Italy and opposed the temporal power of the Papacy. It published the paper *L'Avvenire* between 1849 and 1852 when it ceased to appear following the Bishop's censure.

Schinas's pharmacy fell under a cloud in 1850. Those were the days when political grievances on the part of citizens were made known to government by means of public petitions and memorials for which their promoters sought to obtain the greatest number of signatures. The *Farmacia della Carità,* the *Farmacia della Pietà* (known also as *Missierna)* and the *Farmacia Unione* were the favourite places for the signing of petitions sponsored by the *Associazione Patriottica Maltese (L'Ordine,* 1850 a). Because of its liberal principles the *Associazione* provoked the antagonism of the reactionary Italian elements who had found refuge in Malta and of their Maltese sympathizers. One of the loudest opponents of the *Associazione* was the newspaper *L'Ordine* which pleaded the cause of the Bourbons of the Two Sicilies and supported the temporal power of the Pope. This paper directed its tirades against the *Farmacia della Carità,* and although it never attacked Dr. Schinas, it did not spare the pharmacist. The doctor was abroad at the time but when he returned to Malta in October, *L'Ordine* grasped the opportunity to remark that Dr. Schinas, being a government employee and a person esteemed for his gentlemanly character, had every interest to see that his pharmacy was managed with honour and decorum. The paper also expressed the hope that he would send away from his establishment all those persons who had made it their "club". Though Schinas was of a liberal frame of mind, he had no intention of getting involved in the political agitations of his time. Weeks later, therefore, he took a more drastic step than that suggested by the newspaper — in fact nothing less than the closing down of his pharmacy in December of the same year *(L'Ordine,* 1850 b).

With the unification of Italy in 1861 and the return of Italian and Sicilian refugees to their country, Maltese pharmacies ceased to be the foci of Italian propaganda and political activity; but echoes of those days still reverberated in 1872. Indeed we read that in that year a

man was cudgelled by a doctor in Arpa's pharmacy for allegedly being an "impostor and a supporter of Garibaldi" *(La Fenice,* 1872).

In subsequent years a number of pharmacies eventually got involved in the web of Maltese party politics. This alignment into opposite ideological camps lasted well into the present century and was only brought to an end by the outbreak of the Second World War in 1939 and by the changed social, economic and political orientations of the post-war years.

References

Archives 1190, fol. 461, Royal Malta Library.

Archives 1191, fol. 69, RML.

Archives 1192, fol. 86, RML.

Archivio Corte Civile, Sezione Reg. Francese, Incarichi Criminali 1798-99, Armadio 39, Malta.

BONNELLO, V. *et al.* (1963). *Echi del risorgimento a Malta,* Malta, pp. 68 and 138.

BURLO', J. C. (1963). The Very Rev. Archpriest, Senglea. Personal communication, 26th February.

CALLUS, P. (1961 a). The Rising of the Priests, Malta. p. 97.

CALLUS, P. (1961 b). Op. cit., pp. 23-32, 88-89.

CARDONA, G. (1952). *Il-Malti,* March, p. 10; *Times of Malta,* 4th March p. 4.

CASSAR, P. (1965). Medical History of Malta, London, p. 19.

FIORENTINI, B. (1966). *Malta rifugio di esuli,* Malta, p. 148.

Il portafoglio maltese (1840), 15th June, p. 927.

La Fenice (1872), 7th September p. 2 and 14th September p.1.

LAFERLA, A. V. (1938). British Malta, Vol. I, Malta, pp. 63, 186 and 251.

LAFERLA, F. (1926). *Una giustizia storica,* Rome, pp. 15-20, 60-68 and 79.

L'Ordine (1850 a), 28th September p. 450 and 5th October p. 458.

L'Ordine (1850 b), 20th July p. 370 and 27th July p. 378, 14th September p. 433, 19th October p. 473, 28th December p. 554.

LAURENZA, V. (1932). *Archivio storico di Malta,* Vol. III, Rome, p. 143. *Fior del mondo,* Vol. VI. Torino, p. 466.

MANGION, J. (1962). Personal communication quoting a letter from Giorgio Catania to Nicola Fabrizi preserved in the *Musco del Risorgimento* at Rome.

Ms. 756, no pagination, RML.

STELLINI, P. (1962 a). Document in his possession.

STELLINI, P. (1962 b). Personal communication, 12th May.

Looking Backwards

THE MALTA PLAGUE EPIDEMIC OF 1675 — 1676

SAVIOUR PISANI
M.D.

The epidemic began on the 24th December, 1675 when one of the daughters of a certain merchant from Valletta named Matteo Bonnici, was afflicted by a strange disease the chief characteristics of which were its acuteness, red petechial haemorrhages and the enlarged lymph nodes in the right groin. The suspicions of the family doctor, Dr. Cassia, were quickly aroused and he immediately informed the protomedicus, Dr. Domenico Sciberras. The death of the young girl on the seventh day of her illness was followed by the illness of a brother and of a slave who developed a swelling in the groin. Up to then the disease was being considered as a simple acute febrile illness, until another sister fell ill being covered with petechial haemorrhages and showing enlarged lymph nodes in her armpits. The girl died after four days. Consequently under pressure from the general public the authorities closed the merchant's house together with that of a soldier relative of the family who had a daughter who had died with swollen lymph nodes.

Still, it seemed that the closure of the two houses was not enough, for cases began to appear everywhere whose main characteristics were enlarged lymph nodes, papules and petechial haemorrhages. At this stage the Protomedicus began to reconsider his position. Therefore on the 28th January, 1676, a meeting of the health authorities was held in secret, not to alarm the people, at which it was concluded that plague had probably appeared in the island. Therefore the protomedicus recommended the transport to the isolation hospital of all affected persons and infected objects.

Another result of this meeting was the appointment of four Knights Grand Crosses to act as Plague Commissioners. To these officers was given absolute power to safeguard the public and "the Religion", as the order of St. John was customarily referred to. A tribunal met in the Chancellery twice daily — in the morning from 6 to 10 and in the afternoon from 3 to 5.

This tribunal was responsible for collecting news about the plague and for providing the needy with all requirements. To the four Knights Grand Crosses were added two Counts and the usual commissioners for public health. The counts and the Public Health officials were described as men of great skill. Their duties were to see that the orders given by the Knights Grand Crosses were obeyed and to distribute alms when necessary. Two other Commissioners were later added to supervise the transport of the diseased from their villages.

The virulence of the disease increased rapidly so that even men commissioned to combat the disease contracted the infection and died of it. All measures designed to limit the spread of the illness were proving ineffective and, as the disease progressed, more drastic measures began to be put into effect. The number of Public Health officers and isolation hospitals was doubled and all suspected and infected houses were closed. Doctors who willingly or through negligence failed to report cases were severely punished. A number of gallows were erected to deal

with people who disobeyed orders. To set an example three men were hanged.

The course of the disease appeared to be variable for after the phase of acute virulence a milder phase appeared and it seemed that the efforts of the Public Health authorities were bearing fruit. However, a new phase of acute virulence was heralded by the death of a child at Fort St. Angelo when the disease began to spread throughout the three cities, first in Vittoriosa and Cospicua then on to Senglea and to the country. The familiar features of the disease reappeared, namely the haemorrhages and the buboes so that the protomedicus was constrained to declare the island to be infected and accept international quarantine measures.

On the 26th February the special committee met again. In this meeting the Grand Master promised that everything necessary, both as regards medical and general help, would be provided to the island which was then in a state of chaos. Some people were thinking that the measures taken were sufficient while others were thinking that they were not severe enough. The opinion of the latter prevailed so that more vigorous measures were taken.

From the 24th March the movements of the people were very rigorously restrained while the diseased and the suspected were totally isolated from the community. The people of the Mandragg, the "Archipelago" and French Street — regions very severely affected — were told not to leave their houses. The Commissioners saw to it that butchers, cheesemongers, bakers, etc. were available to give proper service to these people shut in their homes. The order was repealed on the 16th June. Another order prohibited barbers from cutting the hair of the sick and of relatives of people who had died of the disease.

The plague was proving to be a very heavy burden on the community. Therefore it was not surprising that certain quarters began to question whether such vigorous measures were necessary. At this stage the Maltese School of Medicine was still not decided and while some medical men were thinking in terms of plague others believed the island was being visited only by a high febrile illness. Therefore foreign opinion was asked for. Five physicians, from Marseilles, Rome, Florence, Valencia, Paris and Naples respectively were of the opinion that the island was affected with plague.

After the triumph of the first school of thought measures were made even more rigorous. Therefore the use of Holy Water was prohibited, and gatherings in churches, squares, hotels and streets were made illegal. The isolation hospitals were enlarged, barricades were constructed and finally the city was closed.

Three surgeons were called to Malta, one a Neapolitan and two French, the first on the 29th May, the second on the 9th June. All of them had had great experience of plague. The Italian was a volunteer who worked day and night with the sick. The other two came from Marseilles and were given travelling expenses, free board and lodging and 700 French pounds a month each. All agreed with the measures taken by the Public Health authorities in isolating the sick and those suspected of being so. In all 116 "barracks" were constructed on the shores of Marsamxett to house those suspected of being ill.

The galleys were provided for by depositing the food and other necessities in a special place known as the *Ristello della Marina* from where it was taken by the sailors. At night the ships had to anchor two to three miles out at sea until break of day, a guard being provided all the time on the prow and on the poop of the ship.

On the death of a diseased person the Public Health authorities had to be informed. These were responsible for giving the order for burial to the grave diggers and undertakers. The dead were buried in common graves which were situated in places recommended by the medical profession. The grave-diggers were responsible for beating the earth down very thoroughly. After the disappearance of the plague the graves were sprayed with

scent and their invironments kept absolutely clean.

Meanwhile, Mdina and Gozo remained free from the disease. After the first invasion by families from Valletta, the *Capitano della Verga* closed the city, so that by the middle of April it was isolated from the whole island. The Captain provided a door and a guard of four men to guard it and used to supervise it himself. Food was deposited near the gate. Travel to Gozo was also discouraged. A commission was responsible for the storage of grain and of wheat and a small ship was used to carry supplies and to bring news.

The last phase of the illness was heralded by an extensive spread after a relatively quiet period. The island was now on the verge of despair. All that was humanly possible had been done and now panic began to appear. Some people went to live near the sea, nobody daring to approach the cities. There was a phase of religious revival. Everybody recited prayers and performed penance. The Blessed Sacrament and holy relics

Table I. Number of deaths (Estimated population: 60,000)

	Men	*Women*	*Total*
Valletta	757	1300	2057
Vittoriosa	727	1063	1790
Senglea	-	-	1885
Cospicua	511	809	1320
Qormi	122	187	309
Zebbug	74	95	169
Zabbar	102	168	270
Other places	-	-	932
Total	-	-	8732

Table 2. Number of "Illustrious persons" who died of the plague

	Valletta	Senglea	Vittoriosa	Cospicua	Villages
Knights Grand Crosses	1	-	-	-	-
Knights	8	-	-	-	-
Parish Priests	7	1	1	-	1
Canons	1	-	-	-	-
Priests	23	18	37	7	10
Monks	21	-	8(1)	4	1
Physicians	3	1	2	-	3
Surgeons	-	1	6	-	4

(1) All Dominicans

were exposed for special veneration. The Grand Master seing the plight of his people paid frequent visits to the affected areas both in the cities and in the country distributing alms and trying to help the needy.

The Commissioners' meeting on the 14th June came to the conclusion that there were enough medical supplies in the island. By the 27th August the disease seemed to be over at last. The happy people now began to clean up the island by getting rid of all rubble and waste material. All joined in thanksgiving to God.

On the 24th September, 1676 the final disappearance of the plague was publicly celebrated by the firing of guns and the ringing of bells. A *Te Deum* was sung and a most splendid procession was made. The isolation hospitals were closed, the barricades removed and the gentlemen of the Public Health were very generously rewarded and praised throughout the island.

(From manuscript 6402 of the Royal Malta Library)

Burial grounds used during the epidemic:

Valletta: Manoel Island
Vittoriosa: Il-Hisieli
Cospicua: Outside the fortifications
Senglea: Ditto
Birkirkara: Village cemetery
Gudja: Village cemetery
Qormi: Vilage cemetery. Later closed.
Zurrieq: Disused church of St. Thomas
Kirkop: Disused church of St. Giacione
Rabat: Disused church of St. Mark
Mosta: Don Martino Vella's Church
Bubaqra: Disused church of St. Nicholas
Attard: St. Michael's Church
St. Angelo: Ditch

Isolation Hospitals used during the epidemic:

Valletta: Manoel Island
Vittoriosa: Magazine near the "Manderaggio"
Senglea: Quarters of St. Philip.
Cospicua: Quarters of St. Paul.
Birkirkara: The Captain's Tower.
Attard: Giacomo Muscat's Palace.
Gudja: House.
Luqa: the house of Gio Domenico Sciriha and Vincenzo Abela.
Rabat: Hal Bajjad.
Kirkop: Ta' Galea's House.

CLINICOPATHOLOGICAL CONFERENCE
St. Luke's Hospital, April 1970

In October 1969, professor V.G. Griffiths inaugurated monthly clinicopathological conferences at St. Luke's. We publish two of the cases presented at the April meeting. A guest participant was professor Linell, of the University Institute for Pathology, associated with the Almanna Sjukhuset of Malmo, Sweden, who was then visiting the medical school.

Professor V.G. Griffiths: Today's conference is on tumours of the kidneys and ureters.

Case presented by Mr. J.B. Pace.:

The patient was a man aged 64 years. In 1926, the patient then 26 years of age, contracted gonorrhoea. In Januaary 1956, he presented with difficulty in starting micturition, dysuria (burning at the end of micturtion) and increased frequency (D/N = 3/2). Urine was occasionally "smoky". The urinary stream was apparently normal. In February 1956, he was admitted to the medical ward (MMA) of "St. Luke's" for "acute pyelonephritis". In August 1956, he was referred to the surgical department (prof. A.J. Craig) for "Haemorrhagic cystitis? Calculosis". He gave a two-day history of "reddish threads" in turbid urine. On admission to the surgical ward (MS2), no clinical abnormalities were noted. The urine was turbid and contained traces of albumen and a small number of erythrocytes and polymorphonuclear leucocytes. Urine culture was negative. The haemoglobin was 90% and the W.B.C. count 8100/c.mm.

After a lapse of 11 years, in August 1967, he was in hospital again, having been referred to Mr. R. Attard's surgical unit for a "Mass R. loin — Enlarged kidney". Through the previous eleven years, the patient had had intermittent attacks of dysuria,difficulty in starting the act of micturition with intermittent stream, dribbling and passage of blood clots and, sometimes, with strangury. These attacks, recurring every 8 or 9 months, had been often accompanied by rigors and pyrexia. The patient's appetite and weight had remained unaltered. Three weeks before admission the patient had noticed a swelling in his right loin.

On examination, the man looked well although very thin. A mobile, tender, enlarged right kidney was palpable. Urine analysis and culture were negative; blood urea was 31/100 ml. Excretion pyelography was reported upon as follows: "No opaque calculi seen. Good concentration of the dye on both sides. The right kidney is larger than the left and there is displacement of the pelvis medialwards with disappearance of the calyceal system, suggesting neoplasm or cyst. Right ascending pyelogram is suggested" Right ascending pyelogram was refused by the patient, who again took his own discharge from hospital.

In January 1970, (that is 28 months later), the patient was readmitted (MS2 — prof. V.G. Griffiths) because of severe haematuria with passage of clots, intense hypogastric pain and dysuria. He had been complaining of a dull pain in the right flank for the previous 6 months.

On examination, there was some evidence of loss of weight, the pulse rate was 64/minute, B.P. 130/60. The chest was clinically normal. Examination of the abdomen revealed a hard, mobile mass, about 6 inches in diameter in the right loin, easily palpable from the anterior lumbar region of the abdomen and bimanually. The bladder was distended and the patient could not pass urine adequately. The clot retention was relieved by catheterisation and bladder washout, marked haematuria per-

sisting. Haemoglobin was 75%; blood urea 33 mg./100 ml. R.P.C.F., V.D.R.L. and Kahn tests were negative. Chest X-ray revealed no abnormalities. Cystocopy showed a possible papilloma (or blood clot) near the right ureteric orifice, but a good view was difficult to obtain owing to the presence of blood The presence of urethral stricture was excluded.

In view of the strong clinical and radiological evidence of right renal neoplasm, exploration of the right kidney was undertaken without delay. This was done on the 23.1.70, through a right paramedian incision. The presence of a large tumour of the lower twothirds of the right kidney was confirmed and a right nephroureterectomy was carried out (prof. V.G. Griffiths); the precaution was taken of ligating the renal vein at the outset.

The patient's recovery from the operation was uneventful and he was discharged home on the 10.2.70. When reviewed in the outpatients' department on the 17.2.70, he was found to be well and was asked to return in a month's time, but he did not turn up on the relevant date.

Prof. G. Xuereb: There are two points from the clinical aspect that I find worth noting: (1) that the history goes back to about $2\frac{1}{2}$ years before operation, and (2) the history of material extruding from the right ureteric orifice has a bearing on the results of examination of the specimen.

The specimen is the right kidney with a neoplastic mass arising from its middle third. It measures 12.5 cm. across, 12.5 cm. from upper to lower pole and 7.3 cm in depth. Externally some normal tissue is seen at both poles and a neoplasm is present affecting the convex border, growing more laterally than medially although the region of the hilum is also enlarged and occupied by tumour. Low power section of the pelvis shows a similar picture. Longitudinal section of the tumour shows typical yellowish-orange tumour tissue with areas of necrosis and haemorrhage, normal renal tissue being preserved at upper and lower poles. Microscopical examination shows clear-cell carcinoma with a papillary arrangement of tumour cells in some areas and with an acinar arrangement of carcinoma cells in other areas. The periphery of the specimen consists of a thin shell of compressed normal renal tissue. The tumour was growing into the renal pelvis; the renal vein and ureter were normal. Papillary tumours often seed into the lower ureter and the extruded material seen on cystoscopy may have been such a seedling.

Prof. Linell: The patient had many admissions to hospital. What was the matter with him in 1956?

Mr. Pace: In that year, the patient was referred twice — once for "pyelonephritis" and later, for "haemorrhagic cystitis". Thorough investigation had not been possible as the patient had left hospital at his own request, but it had been thought he had urethral stricture, though this diagnosis was not borne out by subsequent observations.

Prof. Linell: He may have had a tumour which regressed and later recurred in a more malignant fashion. This can only be a hypothesis, but partial regression in renal parenchymatous tumours has been shown to be possible.

Prof. Xuereb: We had been attributing his symptons to his past gonorrhoea.

Prof. Linell: He did not have a stricture at the last admission.

Mr. Pace: Perhaps the lesion was initially benign, an adenoma, which later underwent malignant change. Renal adenomas are known to be pre-malignant.

Prof. Linell: Many so-called adenomas are really carcinomas. Sometimes histological distinction between adenoma and papillary carcinoma is not possible.

Prof. Xuereb: Small adenomas are frequently seen at postmortem in older age groups; carcinoma is seen in younger people usually.

Prof. Linell: Adenomas over 2-3 cms. diameter are considered as carcinomas and, in fact, they sometimes metastasize. This causes one to consider adenomas as "carcinoma-in-situ", and the causes which bring about spread are not known.

Mr. Pace: This tumour must have been present in 1967 since there was then a palpable kidney and an abnormal pelvicalyceal pattern in the excretion pyelogram.

Prof. Linell: Renal arteriography at that time would have been helpful in diagnosis as it would have shown the abnormal arterial pattern caused by the presence of the tumour.

Prof. Griffiths: This case was presented at a recent clinico-pathological meeting as "an abdominal mass, probably carcinoma of the kidney". In 1967 the patient had an easily palpable mass and the tumour must have been there for a long time, although we cannot say if it had been there as far back as 1956. I had a case of carcinoma of the kidney filling three quarters of the abdomen with a 14-year history of haematuria. These tumours can exist for a long time without causing wasting or metastases and without local spread to prevent complete excision.

Cystoscopy, postoperatively, should now be carried out in view of the possible seeding of pelvic tumours in the lower ureter.

Mr. J. Muscat: Was a diagnosis of the type of carcinoma made prior to operation?

Prof. Griffiths: No.

Mr. Muscat: Can such a pre-operative diagnosis be made?

Prof. Griffiths: If the radiographic picture is that of pelvic tumour, one would be on the lookout for ureteric seedlings. It may be very difficult to be sure from pyelograms whether the tumour is arising from renal parenchyma or from renal pelvis.

Mr. Pace: Renal angiography might help in doubtful caases.

Prof. Linell: I do not think it possible for a differentiation to be made easily by renal angiography, although this investigation can be helpful in diagnosing the presence of a tumour when pyelography leaves us in doubt.

Case presented by Mr. J. Muscat.

The patient was a man of 50. He was admitted to St. Luke's Hospital on the 5th. February 1970 with a 10-year history of bilateral renal colic, pain in both loins radiating to the groins. There had been intermittent episodes of haematuria through the past 3 years, the last being 3 days before admission. There had been nocturia (3) but no dysuria, no hesitancy of micturition and no recent loss of weight. There was no past history of prolonged immobilisation in bed.

On examination: the patient appeared lean and his general condition was fairly good. B.P. 140/80, pulse rate 85/min. The respiratory system was clinically normal. Examination of the abdomen revealed only slight tenderness in the right lumbar region.

Investigations: Urinalysis on 5/2/70:

Colour — smoky, S.G. 1010; protein +, glucose absent; R.B.C. + + +, W.B.C. + +. Haemoglobin: 75%, W.B.C.: 16500/c.mm. Blood urea: 32 mg./100ml.

On 29/1/70: I.V.P. showed bilateral renal calculi; right kidney very poor function; left kidney hypernephrotic. On 10/2/70 the right kidney was exposed through a lumbar approach and was found to be enlarged, the lower pole being very hard and adherent. A nephrectomy was carried out. On 24/2/70 the patient was discharged, after an uneventful recovery from the operation.

Prof. Xuereb: This type of lesion we had not seen hitherto. The enlarged and distorted kidney, when sectioned, showed a hydronephrosis with a darkish calculus impacted in the mid-pelvis and a tumour at the lowermost loculus. The specimen measured 16.5 x 9 x 6 cm. The tumour did not have the usual appearance of the kidney; it was proliferative, papillary, firm and had a pearly appearance. Section showed squamous metaplasia of the lining of the calyces and a characteristic squamous cell carcinoma permeating the renal structures. The high power view showed typical malignant squamous cells. The whole neoplasm consisted of malignant-squamous cells with keratinisation, and the diagnosis was therefore squamous carcinoma of kidney pelvis associated with pelvic calculus and hydronephrosis.

Mr. Muscat: The patient is now in hospital with a bad infection of the other kidney to which he may well succmb. It was not possible to carry out investigations of calcium metabolism to establish the presence of hypercalcemia (because of lack

of the necssary facilities).

Prof. Xuereb: Professor Linell is it unusual to find such an extensive squamous carcinoma and do these tumours metastasize?

Prof. Linell: Squamous carcinoma in bladder and renal pelvis is not rare and is often combined with other kinds of carcinoma. The etiology of such pelvic tumours is now being postulated as due to phenacetin. In Sweden and Switzerland many people were found to die of uraemia after chronic ingestion of phenacetin. In the late 19th. century workers in a factory producing phenacetin/caffeine combinations were dying of uraemia after about 20 years. Among these patients with "phenacetin kidneys" there were large numbers of pelvic carcinomas. The phenacetin habits of patients with pelvic carcinomas are now being investigated to establish the truth of the matter or to dispose of tse idea.

Prof. Xuereb: What is the picture of "phenacetin kidney"?

Prof: Linell: Papillary necrosis and chronic intersitial nephritis. Formerly they were described in the U.S.A. and in Switzerland as "chronic pyelonephritis".

Prof. Griffiths: Why was the ureter left behind in this case?

Mr. Muscat: At the time of operation I was sure this was not a papillary tumour, as was subsequently proved. The patient had pain over the last 20 years. I do not know if he had taken any phenactein.

Prof. Linell: Obtaining a history of drug ingestion is difficult in most cases.

Prof. Griffiths: In winding up this meeting I thank all the participants, particularly professor Xuereb and the department of pathology. Our special thanks go to professor Linell for his most valuable contributions to the discussions.

INCIDENCE AND TREATMENT OF CANCER OF THE LIP IN MALTA

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Cancer of the lip is a condition which can be diagnosed at an early stage. If treated efficiently it carries an excellent prognosis. The following is a brief account of its incidence in the Maltese Islands and of the mode of treatment currently being adopted.

The figures given should be factual. They include all patients treated at St. Luke's, at Victoria Hospital, Gozo, and at the two private nursing homes. These were checked against the pathology records at St. Luke's and at the Blue Sisters Hospital and were also chcked against notifications to the Health Department. They cover the 5 year period 1963 to 1967. Only newly diagnosed patients were included; in other words recurrences, even if they were at some distance away from an area which had been treated in previous years, were not included. Also, these figures refer only to true cancers of the lip, i.e., cancers which originate on the vermilion surface of the lip. Many cases notified as cancer of the lip, especially of the upper lip, are, on close examination, found to be cancers of the skin close to and invading the lip. These have all been excluded.

Table 1

Ca LIP

Incidence by Age and Sex

	M	F	30–39	40–49	50–59	60–69	70–79	80–89	90+	Yearly Total
1963	15	1	0	3	6	3	3	1	0	16
1964	13	3	0	2	3	6	4	1	0	16
1965	16	2	0	2	3	3	8	1	1	18
1966	22	1	1	4	7	7	3	1	0	23
1967	17	0	2	1	3	8	2	1	0	17
Total	83	7	3	12	22	27	20	5	1	90

Incidence

During this five year period there were 90 new cases diagnosed. *Table I* shows their distribution by sex and age. There is nothing unusual in these figures. The male/female ratio is about 11.1 in favour, or rather, against, men. The highest incidence occurred in the 50's, 60's and 70's. There were only 3 patients below the age of 40. I must however here confess to one inaccuracy. When this table was prepared, I did not include a young lad of 18 who had been referred to me early in 1964 by Professor Craig. This lad had a hard nodule on the right side of the lower lip. Not being convinced that this was a malignant condition, the proper procedure should have been to refer him back to the Surgeon with a view to excision biopsy. Unfortunately, this was not done, and the lip was irradiated half-heartedly. This means that although the full cancericidal dose was given, treatment was limited to a very small portion of the lip just enough to cover the nodule and a few millimeters around it. The lesion gradually softened and eventually cleared up completely. The patient defaulted from follow-up after 18 months and failed to turn up in spite of repeated requests. He reappeared quite recently with a similar lesion just medial to the treated area. This time a biopsy was done and the pathologist reported the lesion as showing 'Carcinomatous change in a labial epidermal cyst'. The patient has now undergone a wide excision of the lip and is well. I do not wish to give the impression that I consider a biopsy to be essential; far from it because diagnosis is usually extremely simple. A biopsy however should always be done whenever there is any doubt. In this series, histological confirmation was obtained in one third of the cases. Almost all the lesions were squamous cell carcinomas; there were only 2 adenocarcinomas originating from the glandular elements of the lip. None were basal cell carcinomas.

Clinically, the majority of lesions presented as the typical "button-like epithelioma". The proliferative cauliflower type of growth was less common accounting for 8% in this series. Cancer of the lip is a moderately slow growing tumour. In our patients, the average interval between the appearance of an ulcer and the date of diagnosis was 9 months. 14% of the patients gave a history in excess of two years.

Lymphnode metastases is nearly always a late feature. In our patients only 6% had clinically involved glands when first seen. This compares well with figures reported from other centres which usually vary from 10 to 15% (Stoll 1952). Distant metastasis was never seen.

Ninety cases over a five year period gives an average incidence of 18 new cases every year. If we take our population as beein 300,000, we therefore have an incidence of 6 per 100,000. This is a comparatively high figure when compared to other parts of the world. Most of the figures have been obtained from a Monograph called "Cancer incidence in five continents". In Asia and Africa the condition is almost nonexistent, whereas in the Northern Provinces of Canada, can-

cer of the lip is extremely common (9 per 100,000). Malta comes second in the list (6 per 100,000). Investigation into possible aetiological factors has not been profitable. None of our patients had ever smoked clay pipes; only five of them were wooden-pipe smokers. The majority were moderately heavy cigarette smokers, but no more so than the general healthy population. 75% of the patients held, or had held for many years, fulltime outdoor occupation, and the commonest incidence was in farmers, fishermen and stonemasons.

This would appear to confirm that excessive exposure to actinic rays plays an aetiological part. It would be interesting to have statistics from Sicily, Cyprus and other central Mediterranean areas to see how they compare. The fact that many of the patients gave a long history of cracked, scaly lips prior to the development of ulceration suggests that the actinic rays themselves do not directly cause cancer, they act as a chronic irritation which provokes a constant reparative process. At some stage, this controlled reparative process breaks down, and the autonomous "angry" cancer cells take over.

Treatment

It has been repeatedly shown that cancer of the lip is a curable disease. Equally good curative results have been obtained both by surgery and by radiotherapy. It is a popular belief that radiotherapy should be preferred because it gives a better cosmetic result. This is true in most cases but not always. For the small early lesion, a wedge resection gives an excellent cosmetic result and this is also true for the more advanced lesions but only if one has facilities for good plastic repair. The cosmetic results obtained by radiotherapy are usually good but are not always as good as we would like to believe. Some years after irradiation, it is not unusual to see deformity due to fibrosis and also patches of telengectasis. Where radiotherapy scores over surgery is in the treatment of a carcinoma of the lip when the rest of the lip shows premalignant changes such as hyperkeratosis and leocoplakia. In such cases, one can easily treat the whole of the lower lip and prevent recurrences or fresh lesions from developing at a later date. From an analysis of the results of the 90 cases under review, I would conclude that Surgery should always be preferred in the case of the young patient with an early lesion without premalignant changes around it. For the older patient surgery and radio therapy are equally efficient but if radiotherapy is to be done, treatment should always be directed to take in the whole of the lip.

Table II shows the treatment modality employed in our 90 patients. The swing to radiotherapy is quite impressive. All the 53 patients who had radiotherapy were treated by external irradiation using 140Kv X-rays with filtration to give a half value layer of 8 mm al. The dose given was 4500r to 5000r in 2 weeks. Fig. I is a drawing of the technique used. A piece of lead is placed between the inner aspect of the lip and the gums and another piece of lead with a cut-out is placed in front of the lip. This limits the beam of X-rays to

Table 2

YEAR	RADIOTHERAPY	SURGERY	SURG. & RAD.
1963	1	15	0
1964	9	7	0
1965	13	4	1
1966	16	6	1
1967	14	3	0
TOTAL	53	35	2

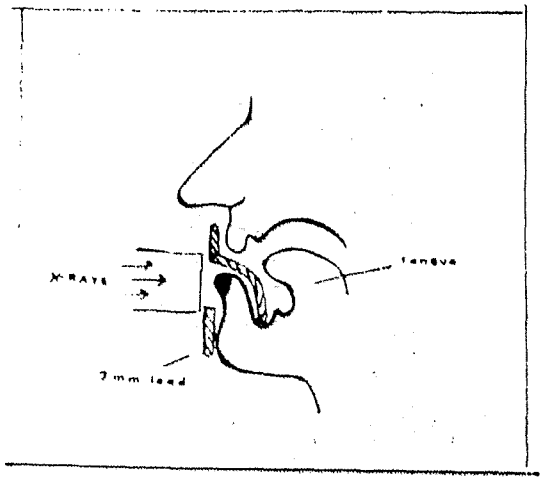

Fig. I

the requisite size. *Fig II* shows a patient set up for treatment. The lead cut-out allows the whole lip to be treated while protection is afforded to the surrounding skin, the gums, and the oral cavity. This is most important as we are all aware of the damaging results which may follow irradiation of the oral cavity. This is well seen in Fig. III. Apparently the degeneration is not due to a direct effect of the ionizing rays on the teeth but is a consequence of a diminution in the amount of saliva, and a change in its chemical composition. None of our patients were treated by the application of radioactive sources. This method as practised in Manchester is probably superior to treatment by X-rays in that it gives equally good curative results and better cosmetic results. Unfortunately, however, it is time-consuming and it increases the radiation hazards to the staff. With X-rays therapy, at the end of treatment, the patient develops quite a severe radiation reaction, the lip becomes swollen, raw and uncomfortable. A white membrane forms over the vermilion surface and this becomes covered over by a crust. It usually takes about 3-4 weeks before the crust falls off and healing becomes complete. The application of a 2% sol. of Gentian Violet seems to protect the lip and hasten the healing process. Patients are then followed up at monthly intervals for the first six months, 2 monthly intervals for the next six months 3 monthy intervals for the next two years, and then six monthly indefinitely.

Results

53 patients were treated by radiotherapy alone. At the end of 1 year 50 (94%) were alive and showed no evidence of residual disease. Two had died with residual disease at the primary site and with metastasis in glands. These two were old patients who had presented with advanced disease which was deeply penetrating into the alveolar sulcus and involved the jaw *(Fig IV)*. The third patient had a large proliferative type of growth *(Fig V)*, which was extremely radiosensitive and melted

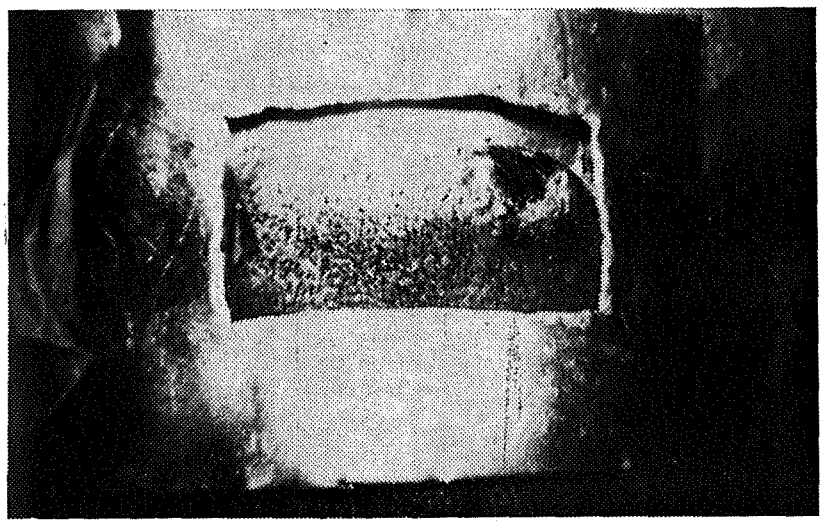

Fig. II

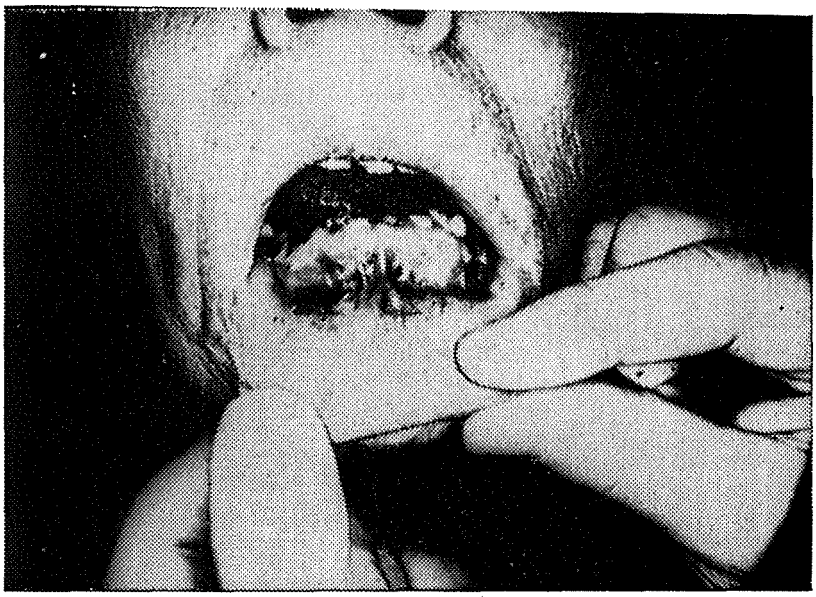

Fig. III

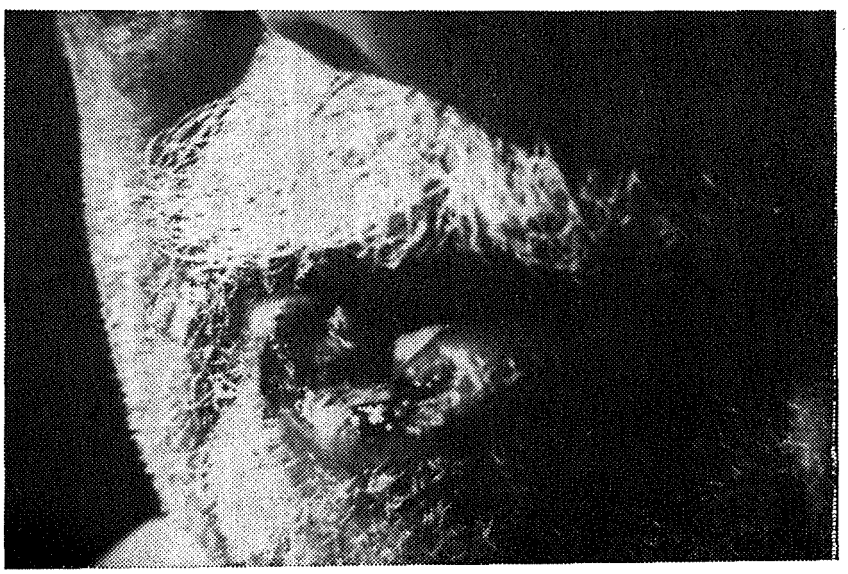

Fig. IV

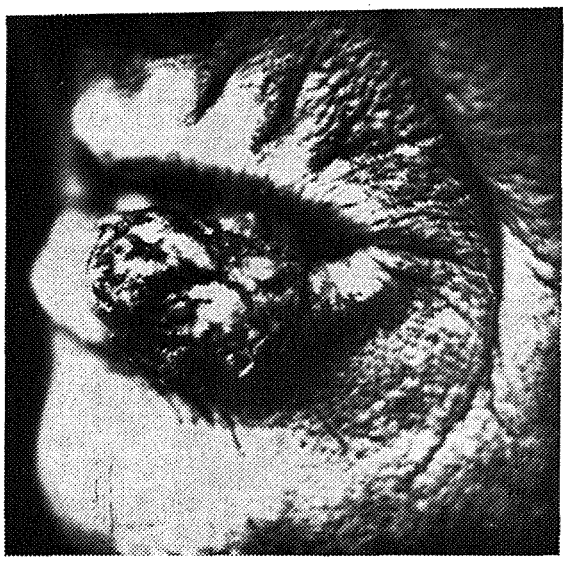

Fig. V

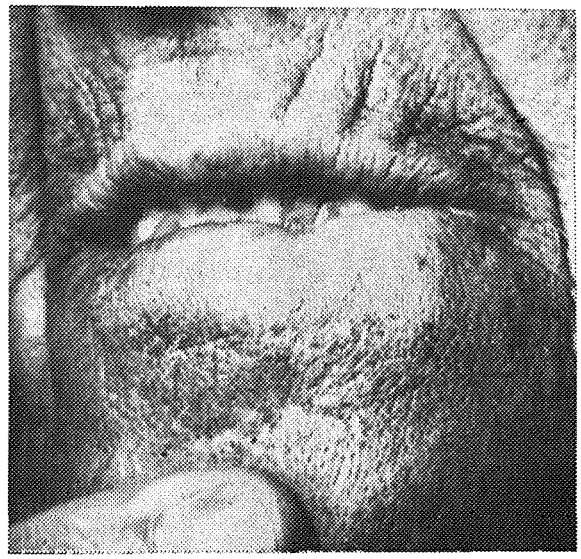

Fig. VI

away during treatment *(Fig VI)*. Unfortunately she defaulted from follow-up and turned up after 4 months with fixed submental glands. A submental block dissection was done but this was incomplete and she died shortly afterwards with fungation in the neck and through the floor of the mouth.

None of the patients have been lost sight of. So far there has only been one other death but this was from an unrelated cause. Only one recurrence at the primary site has occurred and this was in the upper lip. One other patient, who originally had only had one side of his lip treated, has had to have treatment on the other side for an early lesion. The numbers are too small and it is too early yet to try to analyse the 3 year and 5 year results but it is anticipated that these will be good. It has been shown that recurrences, if they are to occur usually do so within the first three years.

References

STOLL B.A. *"X-ray and Radium Therapy"*. H.K. LEWIS & Co. Ltd. 1952 *"Cancer Incidence in 5 Continents"* UICC Monograph 1957.

GLADSTONE W.S. *et al.* Am. J. ROENTGENOL. *79*: 101-113. 1958

CERVICAL METASTASIS FROM OCCULT NEOPLASM

13 Year survival after treatment

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Summary

In about 8% of cases presenting with metastatic disease in cervical lymph nodes, there is initial failure to find the primary lesion.

Whatever the stage at which the metastatic disease is recognized, and whatever the treatment employed, the prognosis for most of these patients is poor. Long survival is rare. (Comess, Beahrs and Dockerty, 1959; France and Lucas, 1963; Greenberg, 1966; Jesse and Neff, 1966; Marchetta, Murphy and Kovari, 1966; and Shaw 1970).

A case is here reported of metastatic carcinoma in cervical nodes in a patient who is alive and well 13 years after treatment, the site of the primary tumour remaining unknown.

Case Report

The patient, a woman aged 30, presented on 27/5/57 with a non-tender, right-sided neck swelling, the size of a golf ball, of about two months duration. On examination the swelling was noted to lie under the upper half of the right sternomastoid muscle, and was not attached to superficial or deep structures. Examination of the mouth, tongue, throat, nasopharynx, oropharynx, laryngopharynx and larynx revealed no abnormalities. A W.B.C. and differential W.B.C. were within normal limits, and the lungs, on X-Ray, were clear.

The site of the swelling was explored and an enlarged lymph node was excised. Biopsy showed carcinomatous metastasis of the 'lymphoepithelioma' type. Another E.N.T. examination was performed; again no evidence of a primary lesion could be found.

On 5/9/57 more nodes were palpable at the site of the previous excision. The patient was referred to the Royal Marsden Hospital. The histology of the excised node was there labelled as undifferentiated polygonal cell carcinoma. She was fully investigated, including a biopsy from the nasopharynx, but no evidence of the primary neoplasm could be found. A large lower abdominal mass was noted; laparatomy revealed a massive fibromyoma of the uterus and a sub-total hysterectomy and right salpingo-oophorectomy were carried out. Following this operation, a hard nodule was found in the right lobe of the thyroid gland. It was decided to continue with the Telecobalt 60 treatment to the neck and to explore the thyroid after completion of the irradiation. Exploration revealed a normal-looking thyroid gland and biopsy confirmed this. The response to irradiation was excellent.

A period of 13 years has now elapsed. The patient still shows no evidence of malignant disease. The site of the primary lesion has never been determined.

Discussion

A recent, progressive, painless swelling in the neck of an adult is a very significant symptom. If the swelling, whether unilateral or bilateral, is thought clinically to be an enlarged lymph node (or nodes), the condition should be regarded as malignant, unless proved otherwise.

Correct management of such a case consists in searching for a primary lesion in the head and neck and, if unsuccessful, elsewhere. In about one in ten of cases a primary tumour may not be evident initially. A thorough E.N.T. examination will be indicated, bearing in mind that the nasopharynx is the commonest site of occult primary neoplasms. The subsequent frequency of primary site involved is variable but an accepted order is: naso-

pharynx, tonsil, tongue base, thyroid, larynx (not cordal) floor of mouth, palate, laryngopharynx, (Shaw 1970). Other primary sites are the bronchus, oesophagus, breast, stomach, kidney, large intestine, rectum and prostate.

It is useful to note the location of the involved node, or nodes, in the neck, as this may give a clue as to the site of the primary lesion. Node enlargement high in the deep cervical chain suggests a primary in the nasopharynx, tonsil, or tongue base. If bilateral, or along the spinal accessory chain, one should suspect the nasopharynx. Lesions of the tongue and floor of the mouth usually metastasize to the submaxillary group. Single node enlargement in the mid or lower zones of the jugular chain should lead one to suspect the larynx, pharynx, cervical oesophagus, or thyroid. Supraclavicular node involvement may be metastatic from almost any site in the body, but most commonly bronchi, breast, stomach or lower oesophagus, the latter two chiefly to the left side. (Shaw, 1970).

Excision biopsy of cervical nodes should not be used as a short cut to diagnosis. It should certainly not precede an E.N.T. examination. It is no credit to arrive at a diagnosis by node biopsy when an obvious head and neck primary tumour had been present and could easily have been found had an E.N.T. examination been carried out.

Nevertheless, it is accepted that lymph node excision is often necessary. Histology of enlarged cervical nodes will in most cases distinguish between disorders arising in the lymph node itself — such as Hodgkin's disease, lymphosarcoma, reticulosarcoma, etc. — and metastasis in a node. However, histology of cervical metastases is often inconclusive as regards the determination of the primary site, unfortunately; the picture is in most cases that of squamous or anaplastic carcinoma. Nodal histology can at times, however, provide direct evidence for suspecting the true site of the primary carcinoma — metastases from a papillary thyroid carcinoma is the best example.

Perusal of the relevant literature reveals that the prognosis for these cases of cervical metastases from occult tumour is not good. A neoplasm that has metasatasized when first seen is less amenable to control than one that has remained localized. The great majority of cervical metastases are squamous or undifferentiated carcinoma, and the ultimate prognosis is poor regardless of type of therapy. There is almost universal agreement that treatment of any kind can only be effective if the primary lesion is detected early and treated. However, Jesse and Neff claim a higher cure ratio where the primary site was never found. This sounds paradoxical to other authors. It could be explained though, by the possible inclusion of the primary tumour in the field of irradiation, or by its spontaneous regression.

Similar cases of long survival after treatment for cervical metastases from an unknown primary tumour have been reported in the literature, but they are few in number. Long survival is definitely uncommon, and the 13-year survival in this case is a rare occurrence.

Acknowledgements

Mr. Pierre Damato gave me full liberty to look up the records of his department. He suggested an important reference concerning the above subject. I found his experience, especially of nasopharyngeal carcinoma, stimulating and useful.

Professor George Xuereb read and criticized this article.

Dr. H. Sultana suggested another of the references.

References

Comess, M.S., Beahrs, O.H., and Dockerty, M.B. (1957), Surg. Gynec. Obstet; *104*, 607.

France, C.J., and Lucas, R. (1963), Amer. J. Surg. *106*, 835.

Greenberg, B.E., (1966), Cancer; *19*, 1091.

Jesse, R.H., and Neff, L.E. (1966), Amer. J. Surg. *112*, 547.

Marchetta, F., Murphy, W., and Kovaric, J. (1966), Amer. J. Surg. *106*, 974.

Shaw, H.J., (1970), J. Laryngology. Otology. *3*, 249.

MALIGNANT LYMPHOMA OF THE INTESTINE:
A report of three cases.

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Tumours arising in the small intestine are uncommon; those of them originating in the lymphoid tissues are said to be even less frequent than adennocarcinomas. This infrequent incidence, together with the particular problems they pose with regard to their pathology and diagnosis, seems to us to warrant the report and comment on three cases which we have treated over the past eight years.

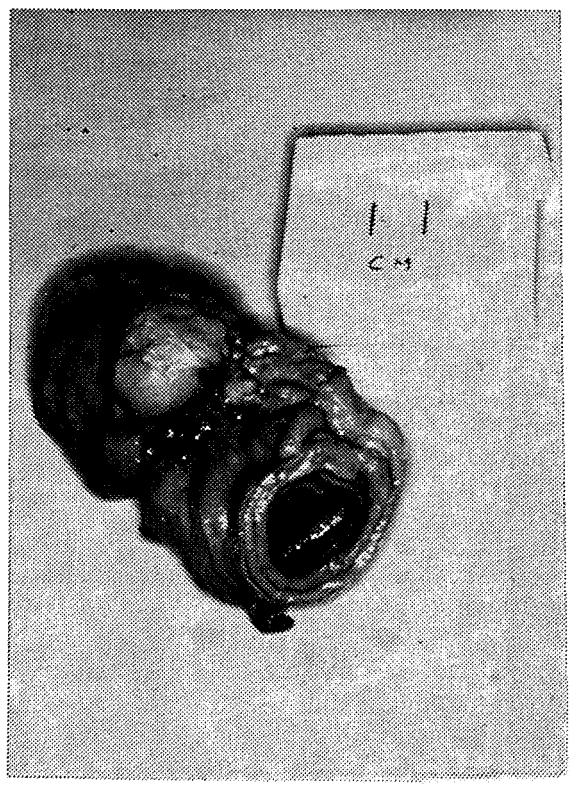
Case Reports

Case 1. Male aged 46, seen first on the 26.7.62, complaining of bouts of colicky abdominal pain and increasing constipation over a period of two months. There was occasional neausea, a fair appetite and no vomiting but the patient was afraid to eat as food seemed to precipate the onset of pain. There was some loss of weight. About twenty months previously he had had an attack of intense diarrhoea lasting some ten weeks.

On examination he was a well nourished man of good physique. There was no facial flush and no finger clubbing. His chest was clear. His abdomen was full, and there was some slight, ill defined tenderness in the right lower quadrant. Bowel sounds were hyperactive.

He was seen again on the 22.8.62. The pain was now getting worse, and a swelling had appeared in the right axilla which was getting larger, but was not causing pain. Examination confirmed the presence of a soft, enlarged, non-tender lymph node about 4cm in diameter, in the right axilla. The neck, left axilla, and both groins were free from enlarged nodes. The liver and spleen were not enlarged.

A blood count showed a haemoglobin of 76%, white cells 9,000, with no im-



Case 1. — Resected segment of small bowel.

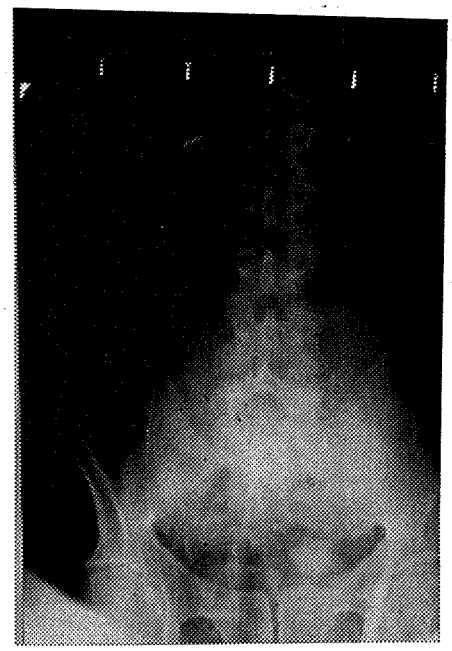
mature white cells. ESR was 38mm in the first hour. Barium meal and follow through showed some hold up and dilatation of the lower ileum.

Laparotomy (J.A.M.) was performed on the 25.8.62 under general anaesthesia. The abdomen waas explored through a right paramedian incision. There was no free fluid. The small intestine was the seat of five lesions, four of which were in the ileum, and one in the jejunum. The lesions were well defined, thickening the bowel wall, narrowing its lumen, and presenting a whitish, pearly appearance on the serosal aspect. There were numerous, moderately enlarged, firm glands in the root of the mesentery. The liver and spleen were palpably normal. An ileo-transverse colostomy was performed, short-circuiting the ileal lesions, and the abdomen was closed. The enlarged node in the right axilla was excised. Histological examination of this node was reported "Lymphosarcoma — the picture is uniformly dominated by the presence of small round lymphocyte-like cells. Infiltration of the capsule is a prominent feature." (Dr. F. Calleja). The operation wound healed satisfactorily, but the patient developed diarrhoea.

In October 1962 he was referred to London, where he had radiotherapy to the right axilla and right groin (2000r in 14 days). Between the 17th and 29th October 1962, he was given 12 m.c. of P_{32} by intravenous injection. He returned to Malta in December 1962. His diarrhoea had lessened, but his general condition was not good. However he slowly began to show a remarkable and progressive improvement, recovering his apetite and putting on weight. His energy was also returning, and he was back to a full day's work after about three months. He was subsequently lost sight of for two years.

On the 13.3.65 he was seen again, when he complained of severe colicky abdominal pain and vomiting which had started some nine hours previously. Absolute constipation was present. General examination showed a well nourished, but dehydrated man, with a slightly distended and tense abdomen, and hyperactive bowel sounds. Plain X-Ray of the abdomen on the 14.3.65 showed fluid levels in the small intestine.

Laparotomy performed that same day revealed the seat of the obstruction to be an infiltrated, short segment of ileum, which was adherent to the anterior abdominal wall; this was mobilised and resected, and continuity restored by end to end anastomosis. He made a fair recovery from this operation. His subsequent course was marked by episodes of abdominal pain and diarrhoea. At first he responded to cyclophosphamide and corticosteroids, but eventually took a downhill course, and died on the 6.10.65.



Case 2. — 14. 3. 65. Plain X-ray abdomen showing multiple fluid levels.

Case 2. Male aged 51 was referred to the Surgical Outpatient clinic on the 5.5.62 for Ca Rectum by his General Practitioner. He gave a history of intermittent attacks of diarrhoea sometimes lasting a week, over the previous six months. The stools were at times blood stained, but there was never any constipation or tenesmus. His appetite had lessened, but there was no nausea or vomiting. There was some loss of weight. There was no previous illness of note. He said he had noticed increased

growth of three cysts in the scalp which he had had for many years.

On examination, his general condition was fair. He was high-coloured, his tongue was clean and moist, and there was no cervical lymph node enlargement. His jugulars showed no engorgement. Temperature was 98°F, pulse 72 per minute, blood pressure 110/60 mm Hg. The chest was clinically clear. The abdomen was soft; there was slight tenderness in the Left Iliac Fossa. Slightly enlarged, discrete, non-tender lymph nodes were noted in the groins.

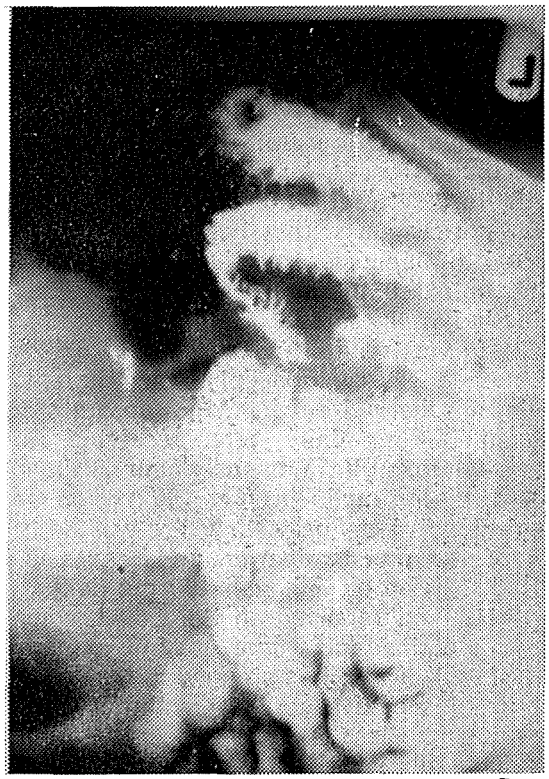
Investigations: haemoglobin 98%; white cells 4,000; urinalysis: negative; blood urea: 26 mg%; faecal occult blood was positive. Barium enema on the 22.5.62 showed an irregular filling defect of the caecum.

Laparotomy (J.A.M.) was performed on 25.5.62. There was a large growth affecting the ileocaecal region of the bowel, tgether with diffuse mesenteric lymphadenopathy. Right hemicolectomy was performed. Post-operative recovery was satisfactory, the wound healed, and normal motions were passed on the 6.6.62. He was discharged to Surgical Outpatients on the 10.6.62.

The histological report (Prof. G. P. Xuereb) was as follows: A portion of distal ileum, ileo-caecal junction, appendix and colon, measuring 40cm in length, and 6.5cm in diameter at the ileo-caecal junction. Numerous enlarged lymph nodes are embedded in fat and in omentum, the largest of these measures 3.4 x 2.7 x 2.5cm, and on section it presents a grey surface with several haemorrhagic areas. The smaller lymph nodes show replacement of their normal architecture by glistening translucent tissue. Transverse section through ileum and caecum shows greyish-white tumour tissue growing into the lumen of the intestine and reducing it to slit-like dimensions. The tumour occupies 7cm length of the caecum and extends proximally into ileum for 6.8 cm. Microscopical examination shows a lymphosarcoma arising in the caecum and extending to the terminal portion of the ileum. The tumour consists largely of well differentiated lymphocytes, compactly arranged with scanty connective tissue support. The sarcoma cells are within the submucosa, and have produced atrophy and replacement of the mucosal lining. There is little evidence of muscle infiltration. Mitotic divisions are not abundant; cellular pleomorphism is not a feature. There is diffuse metastasis of lymphosarcoma within lymph nodes. Histological diagnosis: Lymphosarcoma of the caecum extending into ileum and metastatning in lymphy nodes.

He was readmitted on the 18.6.62 for a course of cyclophosphamide therapy, being discharged on the 2.7.62 on oral endoxan 100 mg daily, after receiving 1.5 gm of endoxan intravenously over 11 days. He was seen again in July 1962 when he said he was keeping well. There was nothing of note on examination, and he was advised to keep on endoxan 100 mg daily.

He next reported on the 4.8.62, when he complained of vague abdominal pain. He stated that he had stopped taking endoxan of his own accord some three weeks previously. On the 29.9.62 he was found to have developed gross enlargement of the cervical lymphnodes, and notable enlargement of the glands in both groins. He complained of sore throat, and his voice was nasal in character. He was readmitted to hospital. Further treatment with cyclophosphamide resulted in marked subsidence in the size of the cervical nodes. A chest X-ray in this period showed the presence of a mass in the right hilum (5.10.62). He was discharged to outpatients on the 3.11.62. He kept reasonably well till the 15.12.62 when he complained of sore throat, hoarseness, and renewed enlargement of the cervical nodes. A severe bilateral conjunctivitis was also observed. On the 16.12.62 he was put on intravenous cyclophosphamide for the third time. His subsequent course was gradually downhill, though a chest X-ray on the 24.11.62 was reported 'Lungs are clear'. On the 28.1.63 he was noted to have stridor. His tonsils were enlarged and his fauces inflamed. The cervical nodes were again enlarging. On the 31.1.63 tracheostomy was performed under local anaesthesia. In spite of further chemotherapy with leukeran and cyclophosphamide, his decline was not arrested, and he died on the 15.2.63.



Case 3. — Barium study of small intesting showing a narrowed segment.

Case 3. Female aged 62 years, presented in January 1970 with a history of low grade pyrexia and intermittent abdominal pain since April 1969. In October 1969 she had a bout of vomiting lasting one week. She was anorexic, but her bowels were said to be regular. There was no diarrhoea, some weigth loss, and no dysuria. She had a past history of Undulent Fever in 1927, and haemorrhoidectomy in 1956.

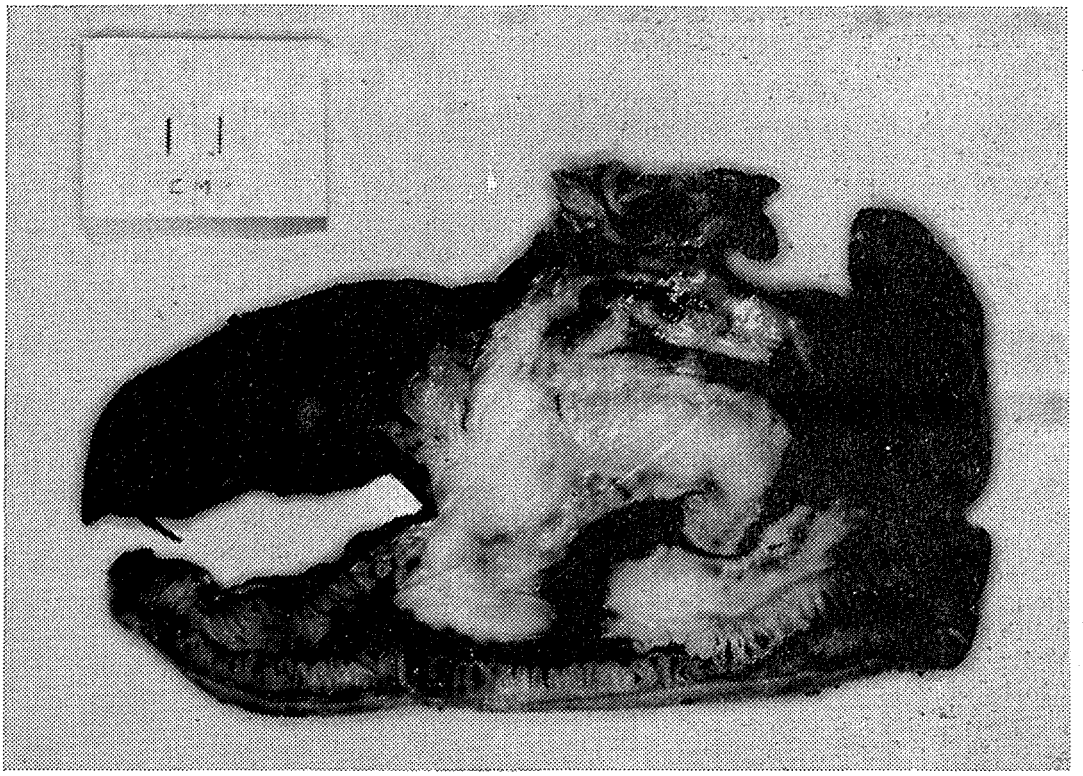
On examination, she was found to be pale and listless. Her pulse rate was 80 per minute, and blood pressure 140/90mm Hg. Abdominal examination revealed an ill defined mass in the left lumbar region.

Investigations: on the 31.5.69: haemoglobin 72%; white cells 8,000: Polymorphs 67%; Lymphocytes 28%; Monocytes 4%; Eosinophils 1%. There were no immature or abnormal white cells. ESR: 31 mm in the first hour. On the 19/5/69, tests for Brucella melitensis, Salmonella typhi, and Proteus OX19 were negative. On the 12.9.69, faecal occult-blood was negative.

Radiological investigations: Chest X-ray on the 3.6.69 showed slight linear atelectasis in the right mid zone. No evidence of active lesions. Heart not enlarged. Barium meal and follow through on the 12.11.69: Oesophagus normal; stomach and duodenum: no lesions seen. Small intestine: there is a narrowing about one inch in length in jejunum, which shows in many but not all films. As it is not persistently present, we have to assume that it is spastic, possibly inflammatory. If clinical signs of obstruction supervene, one has to repeat examination of the small bowel. Cholecystography on the 10/1/70: no opaque calculi seen. Good concentration of the dye by the gallbladder, very little contraction after a fatty meal. Intravenous pyelogram on the 26.1.70: Preliminary film: no opaque calculi seen. Excretion urography: good concentration of the dye on both ces of the rikht kidney are dilated — varsize, shape and position. Some of the calyces of the right kidney are dilated — variation of the normal. The left kidney, ureter and bladder show no abnormality.

Laparotomy (J.A.M.) was carried out on the 29.1.70, through a right paramedian incision. This revealed a tumour mass involving three dilated loops of ileum, and omentum. There were numerous enlarged nodes in the mesentery. No free fluid. The liver and spleen were normal. The three affected loops of small bowel and omentum were resected, and continuity restored by three end-to-end anastomoses. The post-operative recovery was uninterrupted, and the patient was discharged home on the 9.2.70.

Biopsy report was as follows: "When sectioned the tumour is seen to extend over an area 8 × 7 cm involving the wall of both excised segments of upper ileum. A fistulous track containing bile stained faecal material lies in the tumour mass. The small loop of lower ileum is adherent but not infiltrated by tumour. Lymph nodes in the mesentery are enlarged. Microscopy shows Lymphosarcoma permeating ileum. Lymphnodes show sinus catarrh. There is no evidence of metastasis.



Specimen from Case 3. — Three loops of small bowel resected. Tumour mass involving the two lower loops with a fistula connecting the two loops.

Discussion

By 1932, when Ullman and Abeshouse published their classical paper on this disease, some 440 cases had been reported in the literature; this number rose to some 600 cases by 1961. Since 1932 no striking advance has been made in the study of its pathology, diagnosis, or treatment, however certain facts have emerged from the study of the mounting number of cases reported. The method of selection of cases for study has varied with the author. Dawson, Cornes and Morson have been the most specific in this respect, and exclude from their study, all those cases in which lymphomatous change was present at any site other than the intestine and regional lymphnodes. We have considered it more useful from the clinical standpoint to select these three cases on the basis adopted by Burman and Van Wyk, who included in their series all those cases in which the symtom producing lesion was situated in the small bowel or caecum, and excluded those in which generalised lymphoid sarcomatosis happened incidentally to involve the lymphoid tissues of the small intestine. We agree with these authors in including caecal growths along with those affecting the terminal ileum, as it is often impossible to determine the exact site of origin of a tumour that affects both caecum and terminal ileum.

All our three cases were diagnosed histologically as Lymphosarcoma. It is interesting to note that in published series, Lymphosarcomas and Reticulum Cell Sarcomas have been about equally represented, and together accounted for the vast majority of cases. Hodgkin's Lymphoma and Giant Follicular Lymphoma have been very rare as primary intestinal pathological changes. This contrasts sharply with the high overall incidence of Hodgkin's Lym-

phoma, which is said to account for about 50% of all cases of Lymphoma in all tissues (De Gruchy).

Various gross features have been reported, the commonest being polypoid, annular, ulcerative and aneurismal. An important feature of these tumours is that they have little connective tissue stroma, as indicated in the biopsy report of our Case 2. This, together with infiltration of the muscle coat, is said to account for the aneurismal varieties of the growth. (Azzopardi and Menzies, 1960). Polypoid growths have shown a tendency to intussuscept. (Faulkner and Dockerty, 1953). Multiple growth, as occurred in our Case 1, have frequently been reported. The occurrence of fistulous tracks, as in our Case 3, seems to be rare.

Of our three cases, two were males and one was female. This is in keeping with the sex incidence in published series, that give a sex ratio varying from 3 to 2, to 3 to 1 in favour of males. Age incidence studies show that most cases occur in the age group 45 to 60 years, but no age group is exempt.

As for signs and symptoms, it is true to say that no definite syndrome is produced by this disease. In general, it may be said that cases have presented either as surgical emergencies or insidiously. In the former group, the picture has been that of acute, or acute on chronic intestinal obstruction, or of perforation with peritonitis. A few cases have presented with massive bleeding per rectum. As for those cases presenting insidiously, the picture has been that of vague malaise, anorexia, mild abdominal pain that was usually colicky, some disturbance of bowel habit, anaemia and weight loss. On examination, there has often been noted some indication of partial obstruction. The finding of a palpable mass has been frequent. This was present in our Case 3. It occurred in half the cases described by Allen *et al.*, 19 of the 25 cases described by Burman and Van Wyk, and 19 of the 33 cases described by Faulkner and Dockerty. Irvine and Johnstone mention this finding in only three of their 17 cases, and attribute this low incidence to the fact that a sizeable proportion of their cases presented as surgical emergencies with perforation and peritonitis.

The sheet anchor of therapy remains what it was in 1932 when Ullman and Abeshouse wrote "Surgery in the form of resection of involved gut offers the best results from a curative or palliative standpoint. These results are still such as to 'inspire widespread pessimism'. The long term survivals are the exceptions, and this despite the advances in the fields of radio- and chemo- theraphy. Case 2 was given a course of deep X-rays and the isotope P_{32} He survived two and a half years.

Even in the presence of marked and widespread enlargment of the mesenteric nodes, surgical extirpation of the intestinal lesion or lesions is the best course. Enlarged nodes may not necessarily be the seat of metastasis, as in our Case 3. This latter consideration has lead Azzopardi and Menzies to recommend that in the face of a non-resectable growth, a biopsy of the actual neoplasm is essential to establish the diagnosis and submit the patient to radiotheraphy if necessary. There is general consensus regarding the value of post-operative radiotherapy in unresectable growths, and in those with regional lymph node metastasis. What is uncertain is the value of radiotherapy where no evidence of lymph node spread is present.

SOME FACTS ABOUT LEUKAEMIA IN MALTA

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This analytical study of the records available of all reported cases of Leukaemia during the period January, 1966 to December, 1969 aims at pointing out the inter-relationship between type, age, sex, month and year incidence.

The presenting signs and symptoms are not the aim of this study but it is worth mentioning that in the great majority of cases there was severe anaemia, marked purpura and bleeding gums, and generalised lymphadenopathy with splenomegaly. However a few cases were referred to the Surgical Out-Patients' and wards for as wide a variety of causes as a back abscess, ? N.G. stomach, abdominal pain and abdominal tumour.

A classification of the reported cases of leukaemia shows clearly the relative frequency of the various haematological types. All the cases under study have been classified according to the predominant cell-type, whether mature or immature, and whether myeloid, lymphatic, monocytic, etc. Peripheral blood films and marrow smears were examined after Leishman and peroxidase stains.

The frequency of occurrence of the main types of leukaemia and the relationship between the age and the type of leukaemia is apparent from table I.

Lymphoblastic leukaemia, though occurring at all ages, has a peak incidence in the first decade of life; lymphocytic leukaemia occurs almost exclusively in people above 60 years; the incidence of myeloblastic and myelocytic leukaemia is

Table I

Decade	Lymphoblastic	Lymphocytic	Myeloblastic	Myelocytic	Monocytic
1st	12	-	-	1	2
2nd	2	-	1	-	-
3rd	4	-	-	1	-
4th	-	-	1	-	-
5th	1	-	1	-	-
6th	-	-	-	1	2
7th	1	4	2	3	2
8th	2	2	-	-	-
Total:	22	6	5	6	6

spread out over all age groups; and finally the monocytic type has a small peak in persons above 50 years. One may add that in this 4-year period there was one of each of the following types: Stem cell leukaemia, megakaryocytic leukaemia and plasma cell leukaemia.

The sex distribution is interesting as shown in Table II. The ratio of incidence is approximately twice as high in males as in females.

Table II

Year	No. of Males	No. of Females
1966	9	3
1967	7	4
1968	7	3
1969	11	9
Total:	34	19

Study of the age incidence among these cases of leukaemia bring forth the following deductions. The highest incidence is equally in the first and seventh decades of life, whereas the lowest incidence is in the fourth and fifth decades.

During these four years 1966/69 the records show 53 confirmed cases of leukaemia with an approximate average incidence of 13 cases per year. During 1969 the number of diagnosed cases of leukaemia increased twofold. There were 12 cases in 1966, 11 in 1967, 10 in 1968 and 20 in 1969.

Incidence by month is given in Table III.

The highest incidence is in July while the lowest is in May and June. What may be worth finding out is whether the peaks in October, 1968, in March/April, 1969, and in July, 1969, were related to any outbreak of infectious disease. Cases arise sporadically over the island; at times, however, two, three or even four cases occur at about the same time of the year

Table III

Month	1966	1967	1968	1969	Total
Jan.	3	1	-	-	4
Feb.	1	2	1	1	5
Mar.	2	-	-	3	5
Apr.	-	2	-	3	5
May.	1	-	-	-	1
June	1	-	-	-	1
July	-	2	2	4	8
Aug.	1	1	1	1	4
Sept.	1	1	1	1	4
Oct.	-	1	4	1	6
Nov.	1	1	-	1	3
Dec.	1	-	1	2	4

in the same region or district as can be seen from the following examples:—

Jan. '66 to June '66 — 5 cases of leukaemia were diagnosed from Zejtun / St. Lucia / Paula Region.

Feb. '69 to April '69 — 4 cases of leukaemia were confirmed from Sliema / St. Julian's Area.

The worst hit places over the four year period were Zejtun, Sta. Lucia, Valletta and Sliema.

This report is limited to a short period and the number of cases are few. There is, however, an increasing incidence of leukaemia in Malta as elsewhere. A more detailed study is indicated; this should possibly be inclusive of all reported cases of malignant disease of the blood-forming tissues.

My thanks go to Professor G. P. Xuereb and Dr. J. Mifsud for their advice and encouragement.

REFERENCES

ALLEN, A.W., DONALDSON, G., SNIFFEN, R.S. and GOODALE, F. (1954) Ann. Surg., *140*, 428.
AZZOPARDI, J.G. and MENZIES, T. (1960) Brit. J. Surg., *47*, 358.
BURMAN, S.O. and VAN WYK, F.A.K. (1956) Ann. Surg., *143*, 349.
DAWSON, I.M.P., CORNES, J.S. and MORSON, B.C. (1961), Brit. J. Sur., *49*, 80.
FAULKNER, J.W. and DOCKERTY, M.B. (1952) Surg., Obst. and Gynaec., *95*, 76.
IRVINE, W.T. and JOHNSTONE, J.M. (1955), Brit. J. Surg., *42*, 611.
LAME, E.L., VELAT, C.A. and CUSTER, R.P. (1954), Ann. Int. Med., *40*, 57.
ULLMAN, A. and ABESHOUSE, B.S. (1932), Ann. Surg., *95*, 878.

BREADTH OF ATTENTION AND SOCIAL WITHDRAWAL IN HALLUCINATED AND NON-HALLUCINATED CHRONIC SCHIZOPHRENICS

MICHAEL ORR

Summary

1 The relationship between the degree of social withdrawal and breadth of attention in 24 cronic non-paranoid schizophrenics was investigated by relating clinical ratings of withdrawal to performance on a card sorting task.

2. The results obtained by Venables (1963) confirming this relationship could not be replicated for the whole group. The experimental design differd in some aspects from the Venables design.

3. Results were suggestive of a qualitative difference between hallucinated and non-hallucinated schizophrenics. In the hallucinated group, more withdrawn patients showed a narrower span of attention than less withdrawn patients; this relationship could not be seen in the non-hallucinated group.

Recent research in schizophrenia has been repeatedly focussed on the nature of disturbances in cognitive function and on the correlation of measures of these disturbances with measures of physiological arousal and of social withdrawal. A number of studies have submitted evidence that chronic schizophrenics show a defect of attention characterised by an inability to attend selectively to a relevant stimulus dimension (Weckowitz and Blewett, 1959; McGhie and Chapman, 1961; Chapman and McGhie, 1962; Lawson *et al.*, 1964; Sutton *et al.*, 1961; Lawson *et al*, 1967; Chapman, 1966.)

It is also generally agreed that chronic schizophrenics have higher basal levels of physiological arousal than normal controls. (Malmo and Shagass, 1949a; Whatmore and Ellis, 1958; Reynolds, 1962; Malmo *et al.*, 1951; Goldstein *et al.*, 1965.) Venables and Wing (1962) have shown that more withdrawn patients show a higher degree of cortical arousal than less withdrawn patients, and Venables (1963), using performance on a card sorting task as a measure of selectivity of attention, has shown that more withdrawn, and hence more highly aroused, chronic non-paranoid schizophrenics show a narrower span of attention than non-withdrawn patients. These findings are compatible with the suggestion that increases in arousal levels lead to a decrease in the utilisation of peripheral cues. (Easterbrook, 1959; Callaway *et al.*, 1958.)

The concept of heightened arousal and impaired selectivity of attention, though undoubtedly attractive, has not been fully accepted and a number of related hypotheses have been proposed

which acount for a large number of observed phenomena. (Broen and Storms, 1961; 1966; Storms and Broen, 1969; Silverman, 1964; 1967; Shakow, 1962.)

Most of the studies listed above were carried out on chronic non-paranoid schizophrenics; although the paranoid non-paranoid subdivision of a chronic schizophrenic sample for experimental investigation is a useful and vital one, it was felt that other clinical aspects of the illness should be taken into consideration; " . . . something is lost in lumping this (non-paranoid) group" (Shakow, 1969.) and Raeburn and Tong (1968) have shown that certain notions on schizophrenic performance do not necessarily correspond with the intensity of a delusional state.

For this reason selectivity of attention and social withdrawal were measured in a small group of chronic non-paranoid schizophrenics and the results then analysed in terms of the presence of auditory or visual hallucinations at any time during the patient's recent history. Social withdrawal was measured by appropriate clinical rating scales and selectivity of attention was measured by means of a card sorting task.

Methods

A. **Subjects :** Twenty four chronic non-paranoid schizophrenics were tested. Each patient had a history of hospitalisation of three years or more and the clinical course of the illness was well documented. The following criteria were defined for each patient : age, sex, duration of illness, the absence of a coherent, systematised delusional state, the presence or absence of hallucinations in any modality, and the nature and dosage of any drug therapy over the previous six months.

There were twelve males and twelve females in the sample, mean age being 37 years. Ten patients admitted repeated recent hallucinatory experiences and their statements were confirmed by members of the nursing staff.

All patients tested had received varying doses of trifluorperazine (Stelazine) within the six months preceding the experiment.

B. **Measurement of Withdrawal :** Each patient was rated by his or her charge nurse on items 6, 7, 9, 10 from the scale devised by Venables (1957) and items 1 to 5 from the scale devised by Venables and O'Connor (1959). The same items used by Venables (1963) were adopted in order to maintain as close a similarity between the two studies as possible.

The small size of both the hallucinated group and the non-hallucinated group makes it hazardous to attribute the differences between them solely to the presence of hallucinations as other factors may have been operative; however the findings reported above serve to emphasise the importance of taking into account as many features of the clinical picture as possible in the selection of a sample of schizophrenics.

C. **Measurement of Breadth of Attention :** Each patient was asked to sort one of two packets of 36 cards each into two categories on the basis of the presence of either of two relevant letters set against a background of eight irrelevant letters. The relevant letters in each of the two packs were B and Z; the irrelevant letters in one pack were, as in Venables' (1963) experiment, C, G, J, L, Q, Z, Y, W, and D, F, H, K, R, T, V, X in the other.

Each subject was given five sorts on one of the two packs and then given one sort on the other pack. The degree of impairment of performance brought about by a change in the irrelevant background was taken as an index of the breadth of attention. Half the subjects were given one pack for their first sorts, the other half were given the other pack.

In order to determine whether results could be baised by differences in the speed of letter recognition secondary to differences in the degree of schooling received, data on the education level in years were obtained from the case notes and subjects were also given a similar card sorting task in which both the relevant and the irrelevant stimuli were coloured circles.

Results

The difference between the time taken to sort the second pack of cards and that

taken on the last sort of the first pack was taken as a measure of the degree of impairment caused by a change in the irrelevant background stimuli. It was assumed that the less the impairment caused by background, the narrower the span of attention.

This measure differs from that used by Venables (1963), who used the difference between the estimated time of a fifth sort on the first pack after four practice sorts and the measured time of the sort on the second pack; since the trends for the first sorts were not linear, and since it is unlikely that the degree, and indeed the direction, of change in the early stages of practice can be predicted with any accuracy, this measure could not be adopted.

From the scatter diagram *(Fig. 1)*, it can be seen that results for the whole group do not support the relationship between withdrawal and breadth of attention reported by Venables (1963).

It can be seen, however, that the relationship between the two variables for the hallucinated group tends to be in the opposite direction to that for the non-hallucinated group and both these relationships appear to be significant.

The correlation for the whole group was 0.051 (not signficant, $n = 24$). The correlation between the two variables in the hallucinated group was, however, 0.784 ($p < 0.01$, $n = 10$); the correlation in the non-hallucinated group was -0.634 ($p < 0.05$, $n = 14$).

The results obtained with the colour cards showed no significant relationship in any group and measures of attention span were not related to the education level in years.

Discussion

The results obtained by Venables (1963) could not be replicated in a

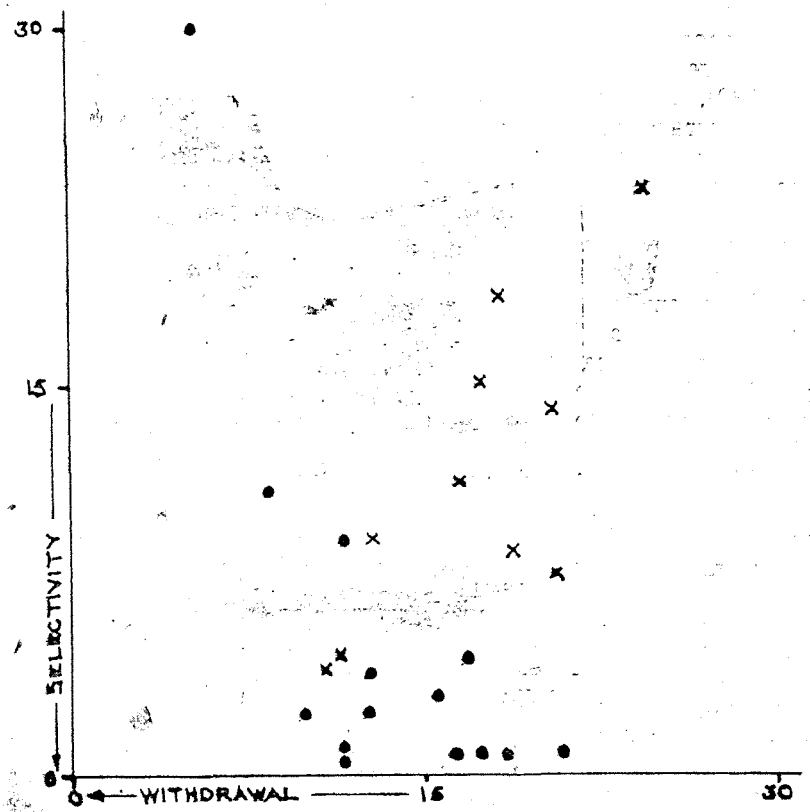

FIG. 1.

HALLUCINATED GROUP = X-X-X NON-HALLUCINATED GROUP = ●-●-●

similar, but not identical, experiment. The findings for the whole group do not provide evidence supporting a relationship between social withdrawal and the breadth of attention.

These findings suggest that more withdrawn patients show a decreased span of attention if they are subject to auditory or visual hallucinations, and that, in the absence of hallucinations, the opposite effect can be seen.

There is no record of any attempt at determining the qualitative and quantitative effects of hallucinations on the performance of chronic schizophrenics in choice reaction time tasks; there are many difficulties involved, the main one being that it is impossible to determine the time of occurrence, duration and extent of a hallucination with any accuracy, and it is equally difficult to ensure that a subject is actively hallucinating at the time of testing.

Venables (1963) interpreted his findings as providing some evidence against the concept of overinclusiveness in schizophrenics (Cameron, 1938), and suggested that the decreased distractibility seen in more withdrawn patients could be due to selective processes occurring at a cortical level.

It is not unlikely that selective proceses may be affected by the general level of 'noise' in the perceptual system, and that the effects of such 'noise' on levels of arousal would be related to its "arousal value". 'Internal sources of 'noise' have been described and one could speculate that hallucinations could act as 'internal sources of noise' with a high "arousal value".

It has in fact been suggested that hallucinated schizophrenics may differ from non-hallucinated schizophrenics in more than just momentary perceptual experiences (Forgus and Dewolfe, 1969).

The work reported was undertaken as a final year project in part fulfilment of the requirements for the Oxford B.A. in the Final Honours School of Psychology, Philosophy and Physiology, and was carried out at Mount Carmel Hospital, Attard, by kind permission of the Physician/Superintendent, Dr. J. Pullicino.

Thanks are due to the consultant staff at Mount Carmel Hospital for permission to test patients under their care, and to the nursing staff for their cooperation.

References

Broen, W.E. and Storms, L.H. (1961) Psychol. Rev. *68*: 405.

Broen, W.E., and Storms, L.H. (1966) Psychol. Rev. *73*: 265.

Callaway, E., and Dembo, D. (1958) AMA Arch. Neurol. Psychiat. *79*; 74.

Chapman, J.P. (1966) Br. J. Psychiat. *112*: 225.

Chapman, J.P., and McGhie, A. (1962) J. Ment. Sci. *108*: 487.

Easterbrook J.A. (1959) Psychol. Rev. *66*: 183.

Forgus R.H., and Dewolfe, A.S. (1969) J. Abnorm. Psychol. *74*: 288.

Goldstein, L., Sugerman, A.A., Stolberg, H., Murphree, H.B. and Pfeiffer, C.C. (1965) Electroenceph. clin. Neurophysiol. *19*: 350.

Lawson, J.S.., McGhie, A. and Chapman, J. (1964) Br. J. Psychiat. *110*: 375.

Lawson, J.S., McGhie, A. and Chapman, J. (1967) Br. J. Psychiat. *113*: 527.

Malmo, R.B., and Shagass, C. (1949a) Psychosom. Med. *11*: 9.

Malmo, R.B., Shagass, C. and Smith, A.A. (1951) J. Personality *19*: 359.

McGhie, A. and Chapman, J. (1961) Br. J. Med. Psychol. *34*: 103.

Raeburn, J.M. and Tong, J.E. (1968) Br. J. Psychiat. *114*: 43.

Reynolds, D.J. (1962) Unpubl. doct. diss. Univ. of Pittsburgh.

Shakow, D. (1962) Arch. Gen. Psychiat. *6*: 1.

Shakow, D. (1969) Arch. Gen. Psychiat. *20*: 618.

Silverman, J. (1964) Psychol. Rev. *71*: 352.

Silverman, J. (1967) Psychosom. Med. *29*: 225.

Storms, L.H. and Broen, W.E. (1969) Arch. Gen. Psychiat. *20*: 129.

Sutton, S., Hakerem, G. and Zubin, J. (1961) Amer. J. Psychol. *74*: 224.

Venables, P.H. (1957(J. Ment. Sci. *103*: 197.

Venables, P.H. (1963) Arch. Gen. Psychiat. *9*: 74.

Venables, P.H. and O'Conner, N. (1959) J. Ment. Sci. *105*: 895.

Venables, P.H. and Wing, J.K. (1962) Arch. Gen. Psychiat. *7*: 114.

Weckowicz, T.E. and Blewett, D.B. (1959) J. Ment. Sci. *105*: 909.

Whatmore, G.B. and Ellis, R.M. (1958) Amer. J. Psychiat. *114*: 882.

THE PLACE OF CLINICAL DEMONSTRATIONS IN THE TEACHING OF ANATOMY

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Anatomy has been defined as "the branch of science which deals with the macroscopic and microscopic structure of living things, with the way in which structure is related to function and with the processes by whch structure has evolved in the species and developed in the individual*". Anatomy as a Science is a broader discipline than Anatomy in its relation to Medicine. Medical Anatomy is that aspect of Anatomy taught to medical students with the purpose of providing for their future needs as medical practitioners.

Preclinical teaching of Anatomy should strive to achieve, as its main aims, the realisation by the medical student that through the understanding of the normal structure of the body any interference with normal morphology at once becomes apparent, so enabling one to anticipate any functional disturbances which may result therefrom; and, lastly, that the clinical signs and symptoms of diseases as well as the rational use of the methods for their examination and treatment are founded on an anatomical basis.

In the preclinical teaching of Anatomy emphasis should, therefore, be laid on the fact that:

1. Anatomy deals with the living body.
2. Structure must be correlated to function.
3. Anatomy is the basis for the understanding of disease processes.

What follows is a discussion of the use of clinical demonstrations in the teaching of Anatomy, an assessment of their benefits and possible pitfalls, and an account of the problems involved in the organisation and selection of cases for such demonstrations.

At clinical demonstrations in Anatomy suitable patients from the clinics or wards are demonstrated to students at the preclinical level. The anatomist, in conjunction with other preclinical and with the clinical teachers and making use of hospital records, clinical examination, X-Rays and other specialised investigations, demonstrates the various abnormalities of structure and function and then illustrates and emphasizes the anatomical aspects of the clinical problems involved, without however referring to the pathological significance of the conditions and without in any way involving the student in matters of differential diagnosis or treatment. The student thus faced with a living subject, is enabled to correlate structure to function and to appreciate the relationship which Anatomy has to the problems of clinical medicine. It is because clinical demonstrations fulfil so completely all three main aims sought for in the teaching of preclinical Anatomy that, I feel, their use finds an important place amongst the various methods employed for this purpose.

The use of clinical demonstrations benefits the preclinical student in various ways. The student is made aware that Anatomy deals with the living functioning body. Faced with dead bodies in this dissecting room and with histological preparations in the laboratory, the student is apt to forget that the cadaver is dissected only as an approximation of the

* Memorandum of evidence to the G.M.C. on the medical curriculum by the Council of the Anatomical Society of Great Britain and Ireland (1965).

living body and that the human body is not solely a series of histological sections or a number of charts. Clinical demonstrations bring the preclinical student face to face with living functioning patients so making him apply and visualise the anatomical knowledge he has acquired from the cadaver to the living subject opposite him. What was a static science dealing with lifeless structures thus becomes the dynamic morphology of intact man.

An opportunity is given to the student at such demonstrations to integrate structure and function. Using clinical patients one can demonstrate disturbances of structure and, as a natural consequence, one can then illustrate the functional disturbances which result from such altered morphology. The student is thus unconsciously made aware of the fact that, just as in disease so in health, structure must always be correlated to function. Such horizontal integration helps to break down the artificial barrier which very often exists between Anatomy and Physiology.

The integration achieved is, however, not only horizontal but also vertical; I refer to the integration which clinical demonstrations promote between the preclinical and clinical stages of the student's medical school career. The student comes to realise that Anatomy is the basis for the later understanding of disease processes, the scaffolding on which the structure of disease is built. He becomes aware that disease represents but a deviation from the normal and realises that the range and limits of normal variations must be known if he is to appreciate his later studies of abnormal, that clinical phenomena can be understood and remembered on simple anatomical grounds, and that therefore his subsequent understanding of disease will largely depend on the anatomical knowledge gained in the preclinical period.

Unfortunately there is very often a relative isolation between the preclinical and clinical disciplines so that the student often comes to think of these subjects as isolated branches of knowledge and not different facets of one study. Clinical anaatomy demonstrations serve to emphasize for the student the importance of cohesion and unity which should underlie these two stages. Their use prepares the student to make a smooth and unbroken transition from the familiar and normal of the preclinical stage to the unfamiliar and abnormal of the clinical stage. They therefore help to bridge the chasm which often exists between the preclinical and clinical sections and instil into the student's mind a sense of the unity of Medicine.

The student often finds that he makes his first acquaintance with the method of history-taking and with the technique of the clinical examination of patients at clinical demonstrations. Students are occasionally asked to elicit a history from a patient during a demonstration; more often however they learn the method of history-taking by listening to the clinician interrogating the patient.

The student is also introduced to the clinical methods of examination by the use of inspection, palpation, percussion, sometimes auscultation, and occasionally to the use of special methods of examination and investigation (as the examination of the eye, the interpretation of normal and abnormal X-Ray pictures, E.C.G.'s, etc.).

Early contact with patients at clinical demonstrations and the observation by students of how clinicians treat their patients, helps to lay down a good early groundwork in doctor-patient relationship. The student thus early on gets into the habit of being sensitive not only to the patient's medical requirements but also to his non-medical needs and comforts.

More important to the immediate needs of the preclinical student is the help which clinical demonstrations afford him in actually acquiring the factual knowledge of Anatomy. This they do in several ways.

The study of Anatomy becomes more enjoyable as these demonstrations orientate preclinical Anatomy to a vocational or productive purpose. One must admit that Anatomy is a dull subject for a student who knows nothing else but Anatomy. Clinical demonstrations give the student an opportunity of understanding the purpose behind some, at least, of the material he has to learn so that his approach to

Anatomy becomes motivated to a purpose and its study therefore rendered more interesting. He no longer feels, as is often the case, that Anatomy is but a hurdle to be cleared before the 'real' Medicine is started in the wards; a glimpse of the clinical life ahead of him, on the other hand, instils into him a professional spirit which makes the study of Anatomy relevant to the outside world.

At clinical demonstrations, the student is encouraged to take part in the lively discussions which often follow and to pose questions on relevant points. He thus becomes an active participant rather than an observer and such active participation helps the student to absorb more anatomical facts than could possibly be the case by being a passive observer at routine lectures.

Clinical demonstrations teach the student how to integrate anatomical knowledge. Faced with a patient he has to recall what he has learned in the lecture hall and in the dissecting room and integrate the relation and relevance of such knowledge with the clinical material he is confronted with. Too many students seem to think of Anatomy as a collection of systems and organs corresponding to what is found in the textbook — thousands of facts all distinct from each other and all to be independently memorised. Nothing can be farther from the truth. The study of Anatomy can be rendered intelligent and easy only through the integration and coordination of anatomical facts to each other and to the whole.

Clinical demonstrations also often help the student understand aspects of Anatomy which would otherwise be difficult to appreciate. Nowhere is this more so than with Neuroanatomy. Greater emphasis is being laid nowadays on this branch of Anatomy, a sound knowledge of which is absolutely essential for the differential diagnosis of certain clinical disorders. It is impossible to learn the facts of neuroanatomy only by reading textbooks and impracticable to learn such facts by dissection which is a highly skilled and time-consuming task; furthermore, mastering the morphological aspects of neuroanatomy is only a basis for the more fundamental problem of correlating structure to normal and abnormal function. It seems therefore that the ideal method of teaching neuroanatomy is through the use of clinical demonstrations. Neuroanatomy in fact presents unrivalled opportunities for the integration of Anatomy with Physiology and the clinical subjects.

The Anatomy taught to the medical student must be that wich provides a basis for the understanding of the clinical subjects. The importance of this was recognised as far back as 1730 when Cheseldon in his 'Anatomy of the Human Body' wrote: "I endeavoured to be more explicit about those (things) which are of the greatest use in Philosophy, Physic and Surgery; and I would wish the dividing and distinguishing of parts were usually done with more regard to these valuable ends". Clinical demonstrations highlight for the student those features of Anatomy which are of clinical importance and out of a vast number of facts help the student select the material which forms the necessary anatomical scaffolding for the clinician and which he will be expected to recall throughout his life.

Clinical anatomy demonstrations prove also of benefit to the teaching staff. Having as they are to be jointly organised by both preclinical and clinical teachers, they promote not only cooperation and liaison but also personal contact and goodwill between these two groups of teachers, so helping to break down the artificial barrier which very often exists between them. Such a barrier is often not only on the personal, but also on the teaching level. It produces the so-called "integrated teacher", individuals who are ready to cross departmental barriers and bring their individual knowledge on a common subject under study. Such integrated efforts are most effective in advancing enquiries, whether practical or theoretical, both on the preclinical and clinical sides. They also serve constantly to remind teachers that the preclinical training in Anatomy must take heed of its purpose to provide instruction for the student's medical needs and not as a preliminary to advanced work in

the science of Anatomy — that the student must be a good doctor rather than a good anatomist. Teachers would then understand, more fully than they have perhaps done in the past, that the Anatomy they teach must contribute well-defined information to the student as an individual who later on is going to be a doctor caring for patients.

Invaluable as clinical demonstrations are to the teaching of Anatomy, one must be constantly aware of the possible pitfalls which could result from their use.

It has been suggested that clinical demonstrations might distract the student from his preclinical studies. The student might concentrate prematurely on clinical material so that he is weaned away from Anatomy and the other basic sciences. This possibility can be avoided partly by laying the right emphasis on what the student should attain in the preclinical period, namely a mastery of the fundamental skills and basic principles rather than the use of professional methods and materials, and partly by devoting to clinical demonstrations the right amount of time such as to stimulate without overburdening the student with clinical material.

It is possible that by integrating Anatomy with the use of clinical demonstrations, the preclinical student might fail to realise the relative importance of each and, having to contend with too much, might treat both too superficially. This leads to uneasiness on the part of the anatomist for fear that Anatomy might be too narrowly conceived and on the part of the clinician for fear that the medical student might get too superficial a view of the importance of a patient. The problem can similarly be solved by making the right emphasis on the right principles.

Clinical demonstrations have been criticised in that they take too much time, not only on the part of the teachers who have to organise them, but also of the students who have to attend them, with a consequent added burden on staff and students who are already both overworked. One must see that too much time is not devoted to this method of teaching.

It has been suggested that the preclinical period might be too early a stage to bring the student in contact with clinical material; the student is still clinically immature at this stage and therefore lacks the foundation for benefitting from seeing clinical patients. This may be true from the clinical aspect but is certainly not so from the anatomical sense.

Demonstrations, it has been said, might break up the continuity of instruction and interfere with the development of proper cohesion and unity in the teaching of Anatomy. Here again, however, a proper balance is essential in the time devoted to the use of clinical demonstrations and that devoted to other activities in the Anatomy curriculum.

Many clinicians who are excellent at demonstrating cases to clinical students, very often cannot adapt themselves successfully when they are trying to teach preclinical students; they talk at a level which the student is quite unable to reach. Apart from this, specialists often fall into the temptation of going into the aspect of their subject intensively and of emphasizing facts, which though academically interesting, have little or no value in preparing the ordinary preclinical student for his future work. Moreover, clinicians often emphasize the details of treatment which the student at this stage is unable to appreciate; especially so is the emphasis on operative techniques which might give the erroneous impression to the student that Anatomy is closely and solely linked with the techniques and interests of operative surgery. The student thus often finds himself at clinical demonstrations in a confused state of mind. It is only a matter of good judgement on the part of the teachers concerned which will help preserve the balance.

And as a last note of warning — the preclinical teacher must not lean too much on the use of clinical demonstrations to stimulate the student in his study of Anatomy and neglect to inject interest and stimulation in his own lectures and dissection classes. Clinical demonstrations supplement but do *not* replace the more orthodox methods of teaching Anatomy.

The organisation of clinical demonstrations should ideally be in the hands of a small committee on which are repre-

sented the clinical departments, including the specialised units, and the Departments of Anatomy and Physiology.

The time allotted to clinical demonstrations should be cut to a stimulating minimum so as to prevent the danger of distracting the student from his preclinical studies. The practice of some American medical schools of giving one demonstration a week is overgenerous and tends to encroach too much on the time allotted to the study of Anatomy. Ideally three to five demonstrations, of approximately ninety minutes each, should be given each academic term. This implies a total of 14 to 23 hours per academic year; taking the mean total number of hours allotted to the teaching of Anatomy as 573 hours per academic year, 3% of this would be devoted to clinical demonstrations.

It has been suggested that clinical demonstrations should be given as a 'crash' course in the later part of the preclinical period rather than being spread over the two preclinical years; the reason advanced is that the student, having by then covered most of the Anatomy, would be in a better situation to correlate his anatomical knowledge and apply it to the clinical material shown. I feel, however, that spread over a longer period clinical demonstrations would produce a more effective interweaving of the preclinical and clinical stages than would a more formal, shorter bridging course.

Clinical demonstrations tend to be time consuming for student and teacher alike if a judicious selection of cases is not made to preserve a proper balance. The cases selected should be those which give an opportunity to emphasize anatomical points of importance and to clarify the understanding of anatomical points which otherwise would be obscure. The cases chosen should have signs and symptoms easily interpretable in terms of the student's preclinical knowledge of Anatomy; they should if possible be chosen to correspond with the regions being dissected at that period and to illustrate clinically the conditions which correspond to what the student is studying at the time.

Conclusion

The use of clinical material should play an important part in the preclinical teaching of Anatomy to medical students. Greater use should be made in the future of clinical demonstrations to supplement the more orthodox methods used in the teaching of Anatomy.

There is no doubt that preclinical subjects should be given a clinical orientation. For this to be possible not only is greater cooperation and liaison called for between the preclinical and clinical departments, but preclinical teachers should be given part-time appointments in the teaching hospital, as was strongly recommended by the General Medical Council in a recent report to the Royal University of Malta, and as, after all, has long been the practice in medical schools in the United Kingdom. Only in this way could the preclinical subjects become linked with the clinical studies so providing better integration of the medical curriculum.

THE USE OF METHYL METHACRYLATE FOR THE PREPARATION OF CASTS OF THE CEREBRAL VENTRICLES

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Introduction

Dissection is the best way to study the anatomical relations of the cerebral ventricles; a resin cast, however, illustrates more accurately their actual size, shape and intricate anatomy.

Materials

Crystic resin is the conventionally used resin for corrosion casts; it is chemicalley a polyester cross-linked type of resin available as intermediates in the form of thick syrups to which setting agents are added (Tompsett, 1956). Epoxy resins are also sometimes used as casting resins (Roff, 1956). Vinyl resin commercially known as Vinylite and introduced by Narat in 1936 as a substitute for cellulose acetate then in use, is to-day employed in the United States with special reference to the study of liver tumours (Healey, 1960). A study of the resins available in Malta showed that methyl methacrylate, much used in dental mechanics, could be availed of to produce a detailed, beautifully coloured, rigid cast of the comparatively large cerebral cavities. Shrinkage after processing is negligible so resulting in a markedly true and well marked impression of all the structures immediately related to the ventricles. The cast produced does not warp even in warm surroundings, can be washed, and is resistant to a number of corrosive agents. The resin is easily available (being so much in use in the dental field), has a relatively long shelf-life in warm climates and above all it is very easy to mix.

Method

The method used is divisible into three distinct phases:

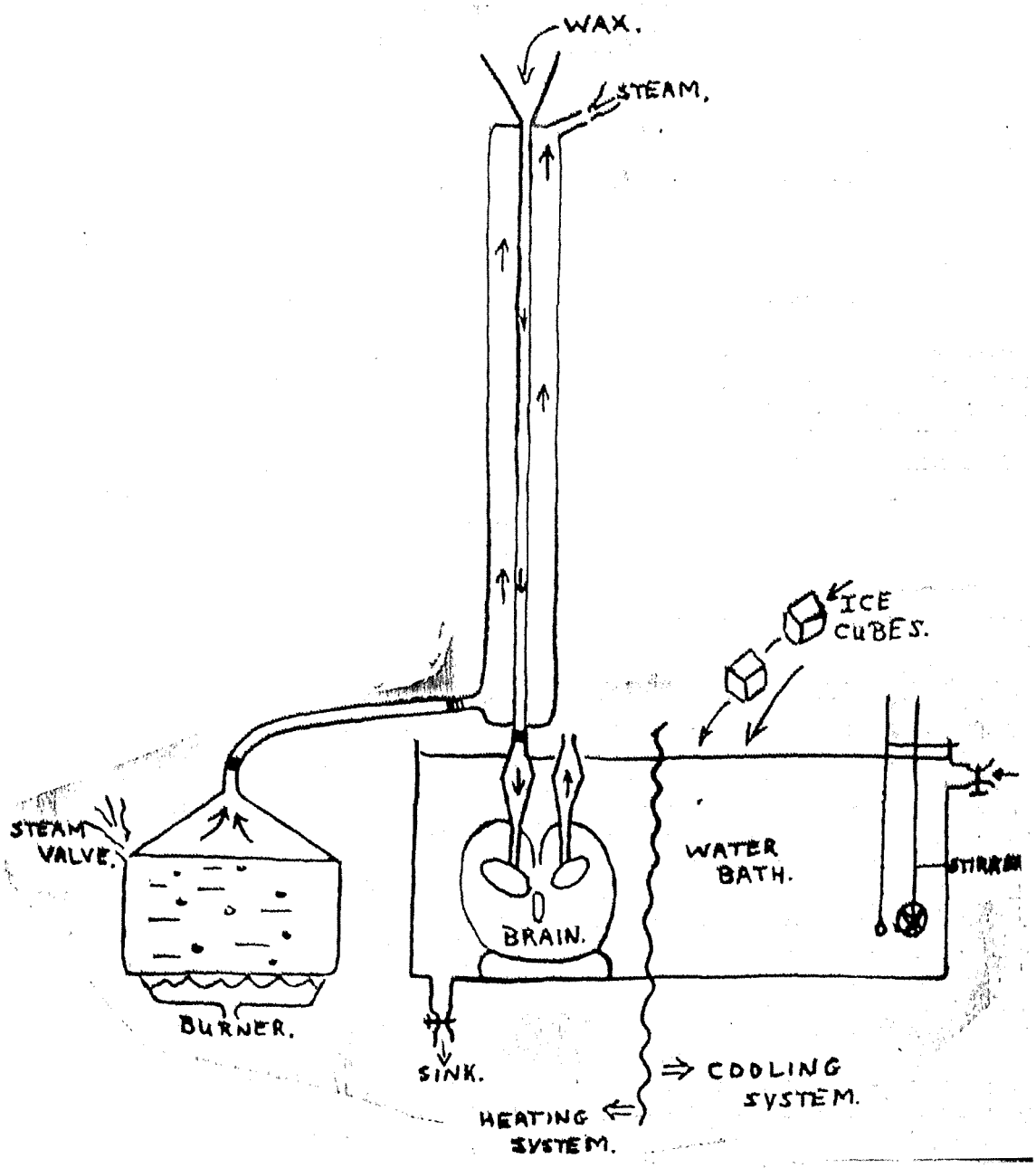
Phase A: Wax injection and subsequent dissection to remove the wax cast;
Phase B: Construction of a plaster of Paris negative of the wax cast, followed by the resin cast;
Phase C: Final pruning, spraying and mounting.

Phase A: This phase essentially entails introducing liquid wax (melting point 59°C.) into all the ventricles via the tiny interventricular connections and then cooling the wax to below 59°C. To ensure the vital fine control on the wax temperature, a simple apparatus was constructed whereby the brain's *internal* temperature was raised to 85 C.; the liquid wax at 90° C. was then injected using gravity as pressure and when the ventricular spaces were full, the whole internal system was quickly cooled to 50° C. and then gradually to 20° C. (This avoids unwanted shrinkage and cansequent cracking of the wax.)

The apparatus used (shown below) consists of:-

(a) a heating system made up of a small modified water bath (a minimum water volume renders easier complete temperature control) to raise the brain internal temperature, and a boiler-condenser system to provide a way by which molten wax can be injected under pressure into the brain;

(b) a cooling system which comes into operation to lower the brain's internal temperature; this includes running cold water and the use of ice blocks.



This phase is crucial because:

(a) if the temperature of the wax within the brain falls down prematurely at any one time to 59° C., blockage of the ventricular systems would occur; the brain is therefore left for seven hours in water at 90° C. until its internal temperature reaches 85° C.

(b) rapid cooling is necessary to ensure that no wax trickles out so leaving empty spaces after the injection process is stopped. To achieve this the brain on the outside is cooled down to 10° C. using ice blocks and very cold circulating water;

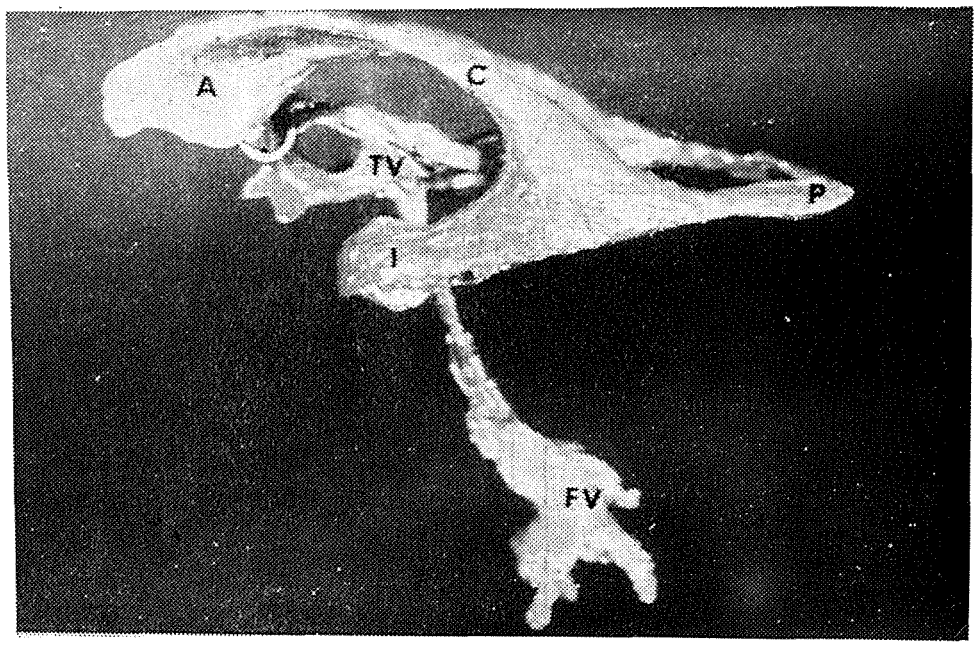


Figure I: Lateral View showing the anterior (A), posterior (P), and inferior (I) horns as well as the central part (C) of the lateral ventricle. TV indicates the third ventricle and FV, the fourth ventricle.

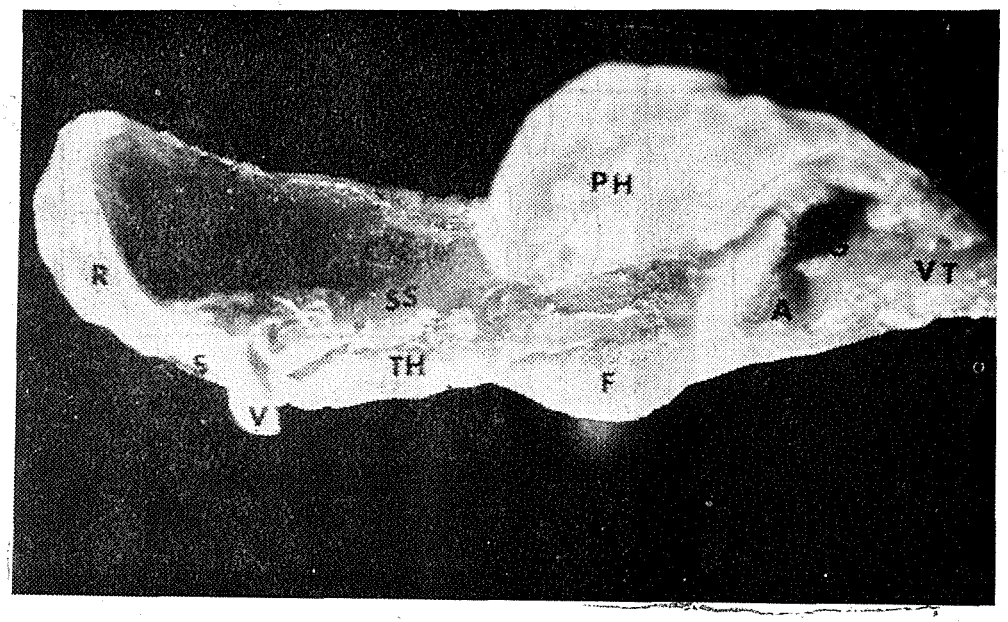


Figure 2: Inferior View of Lateral Ventricle showing impressions of calcar avis (A), caudate nucleus (CN), fornix (F), glomus chorioideum (G), pas hippocampi PH, rostrum of corpus callosum (R), septum lucidum (S), stria semi-circularis (SS), thalamus (TH), interventricular connection (V) and ventricular trigone (VT).

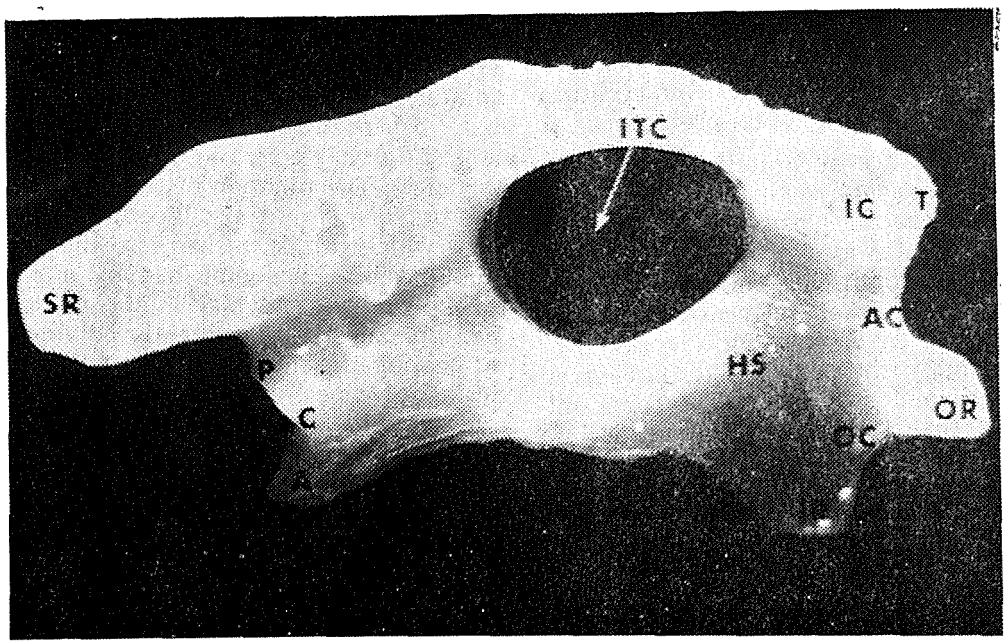


Figure 3: Lateral view of third ventricle with suprapineal (SR), pineal (P), triangular (T), optic (OR) and infundibular (IR) recesses, impressions for anterior (AC) and posterior (C) commissures and optic chiasma (OC). A indicates the aqueduct; HS, the hypothalamic sulcus; IC, the interventricular connection, and ITC, the interthalamic connexus.

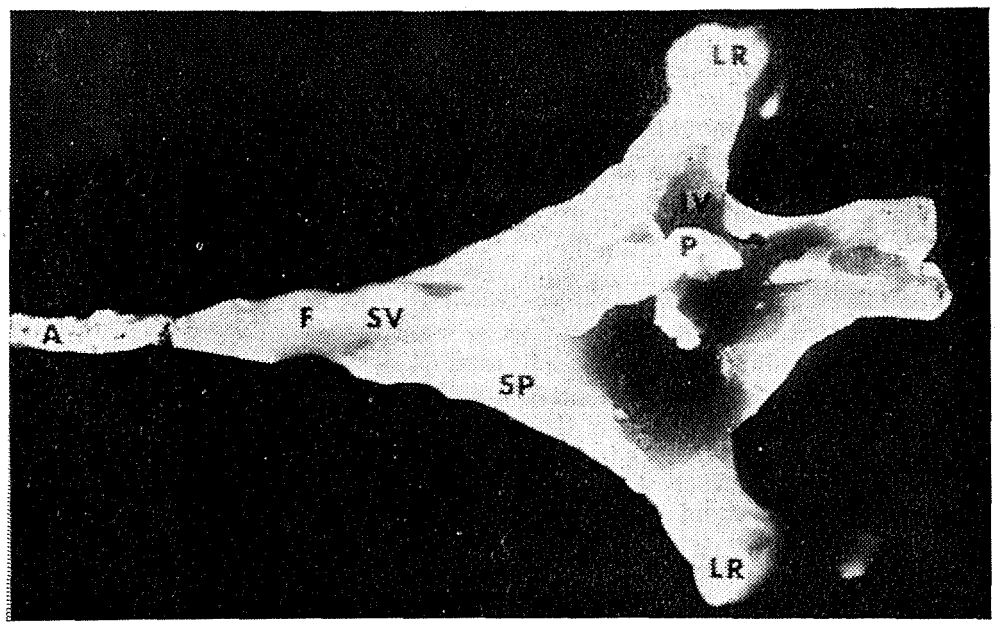


Figure 4: Dorsal view of fourth ventricle with its peak (P) and lateral recesses (LR). A indicates aqueduct; F, the impression of the frenulum veli; IV, that of the inferior and SV, that of the superior medullary velum; and SP the impression of the superior peduncle.

(c) a very well fixed brain specimen is required in order to withstand, without rupture or distortion, the temperature variations and the injection pressure;

(d) holes are accurately drilled from the external aspect of the cerebral cortex on the precentral gyrus of each hemisphere, 1.5 cm. away from the longitudinal fissure for a depth of 5 cms to produce a communication from the ventricles to the outside. This is done using a cork borer with a highly sharpened edge, having an internal diameter of 5 mm. The communication is then tested by pumping air into one hole with the brain submerged in water when air will bubble out from the other.

The brain specimen is kept for two days in cold water and then dissected to get the wax cast out. Alternatively one could use acid corrosion to remove the tissue; this is however a longer process and furthermore dissection ensures that the resultant model is a more exact replica.

Phase B: Plaster of Paris is mixed and poured into a strong metal mould, previously smeared with vaseline to help the later removal of the solid plaster. The wax cast is then gently placed in the plaster while this is still soft. The mould is closed and pressure applied to squeeze out the excess; this ensures an exact plaster negative. The metal mould, still tightly closed, is placed for an hour in boiling water so that the wax melts and floats out leaving the empty plaster. After cooling the plaster spaces are rinsed by semi-viscous separating medium which prevents the resin from sticking permanently to the plaster; it also keeps water from the plaster from becoming incorporated into the resin as this would affect the polymerization rate and colour of the resin. The resin mixture is then prepared and while still semi-fluid is forcibly pushed into the ventricular plaster spaces, the lid placed on, and great pressure applied.

The greatest advantage of methyl methacrylate is the ease with which it can be processed: the liquid monomer, consisting of pure methyl methacrylate with a small amount of hydroquinone which aids in the inhibition of polymerization during storage, is mixed wth the polymer (dispensed in the form of a powder consisting of coloured small spherical particles). The function of the monomer in the polymer is to produce a semi-fluid mass which can be pushed into the plaster mould; this is accomplished by a partial solution of the polymer in the monomer. The monomer is subsequently polymerized by heating the mixture. Although not critical, the proper ratio of monomer to polymer may be of considerable importance to the structure of the final resin; also, the resin will tend to shrink less during processing if less monomer is used (Skinner and Phillips, 1960). The approximate proportions of polymer to monomer are three to two by volume or two to one by weight.

After half an hour the mould, still under pressure and containing the resin which has started to solidify, is placed in a water bath and the water gradually heated to boiling; the mould is then left in boiling water for another two hours. After cooling, the metal mould is opened and the solid plates block with the resin cast gently eased out of one end. The resin cast is then freed by cutting off the plaster. The covering of separating medium is finally peeled off the resin cast.

Phase C: Pruning and filing off extra bits was found unnecessary; a very thin laver of Humbrol red spray paint was applied at a distance of ten inches. A mounting stand was finally designed to incorporate: (a) greatest safety during handling: this includes shock absorbers in the form of rubber foam rests, a specially arranged wire suspension and a thick perspex cover screwed down to a wooden base;

(b) simplicity in design; and

(c) a mirror affording a better view of the undersurface of the cast.

Labelled photographs of each part of the cast, maagnified to show the impressions left on it by the immediate relations, were then added. Some of these are shown below.

Conclusion

A technique is described for the use of methyl methacrylate as a resin for the preparation of casts of the cerebral ventricles. Its advantages and disadvantages are discussed. It is hoped that in future this resin will be used more for this purpose.

Acknowledgements

My thanks are due to Professor J.L. Pace for valuable advice and criticism of this work. I am grateful for the help received from Mr. J. Zarb of the Department of Dentistry, Mr. J. Spiteri of the Department of Anatomy and to my colleague Mr. J. Pace.

References

HEALEY, J. E. (1960) Tenth Annual Clinical Conference: Segmental Anatomy of the liver with special Reference to the Blood Supply of Liver Tumours.

NARAT, J. K., LOEF, J. A. and NARAT, M. (1936) On the Preparation of Multicoloured Corrosion Specimens. *Anat. Rec.* 64:155.

ROFF, W. J. (1956) Fibres, Plastics and Rubbers — A Handbook of Common Polymers. Butterworths.

SKINNERS, E. and PHILLIPS, R. W. (1960) The Science of Dental Materials. Saunders.

TOMPSETT, D. H. (1956) Anatomica lTechniques. Edinburgh: Livingstone.

MEDICAL NEWS

In July 1969, Professor Joseph J. Mangion retired from his post of Senior Dental Surgeon and professor of Dental Surgery on reaching the age of 60, staying on for some months afterwards unofficially. His first love had been medicine, having graduated M.D. in 1934, but as he often remarked "after flirting with medicine he married dentistry" and qualified Dip. D.S. in 1940. His medical background, which included being medical superintendent and anesthetist at the Central Hospital during the war, gave him a broad medical approach to dentistry. As a result, a strong medical grounding is likewise one of the features of Maltese dental graduates. Besides his undoubted ability as an oral surgeon, he has a quiet determination and a flair for far-sighted planning which have borne ample friut in the expansion of the government and university dental clinics.

In 1954 he filled the newly created post of junior dental surgeon and on Professor Lapira's retirement that year he was appointed senior dental surgeon and professor of dental surgery. During his headship the dental clinic was transferred to its present place in the Out-patients' Block at St. Luke's where the University clinic was also set up. His quiet manner can be deceptive and his ability in the committee room has helped to lay down the foundations of many new advances in dentistry in Malta.

In the span of 16 years as professor many of Malta's present dental surgeons were taught mainly by him; there were also students from far away countries such as Australia, Holland, Nigeria, Wales and Malaya but, surprisingly enough, so far, none from Gozo. A Fellow in Dental Surgery of the Royal College of Surgeons of England since 1948, he has always encouraged his students to further their studies abroad.

His many interests outside dentistry range from cinephotography and travel to bowls and included the presidency of Floriana F.C. during the team's heyday in the fifties. This attitude of Prof. Mangion is reflected in the newly instituted Mangion Prize at the University, which will be awarded to students for interest and ability in some extra-curricular activity.

We wish Professor and Mrs. Mangion a long and happy retirement, knowing full well that they will continue to play an active role in medical and dental social and academic circles in Malta.

We congratulate:

Mr. George Camilleri, of the editorial board of this periodical, on his appointment to the whole-time post of Professor of Dental Surgery and Senior Dental Surgeon.

Dr. Alfred Grech on attaining the rank of Principal Medical Officer in the Health Department;

Dr. Angelo Psaila ('61) on qualifying as M.R.C.P. (Edin.) in July and M.R.C.P. (U.K.) in October 1969;

Dr. Norman Griscti ('64) on getting his M.R.C.P. (Eng.) last August, whilst studying at Birmingham;

Dr. Vanni Cremona ('64) on his qualifying as M.R.C.O.G. last January;

Professor Herbert M. Gilles ('46) on his long and brilliant career in the study and teaching of Tropical Medicine being crowned by his appointment to a personal chair in that subject at the University of Liverpool;

the following on their appointments as university demonstrators: Mrs. C. Olivieri Munroe and Mr. H. Galea (Dental Surgery), Dr. A.V. Portelli ('61) (Microbiology), Dr. A.J. Psaila (Physiology).

Miss Mary Anne Borg, on being awarded the B.M.A. medal for nurses for 1970.

This year the president of the B.M.A. (Malta Branch) is the editor of this periodical. Mr. J.B. Pace ('55), surgeon, is the new Honorary Secretary and Treasurer. His home address is 50, St. Francis Street, Balzan. Dr. John Rizzo Naudi, now on the B.M.A. Council, has retired from the secretaryship after serving for quite a few years. The highlight of his work was that in connection with the holding of the 12th. Annual Clinical Meeting of the B.M.A. in Malta in 1969. Incidentally it was only the accident of our sitting next to him at the

banquet on that occasion that revealed to us the unsuspected fact that John is a keen golfer. One never knows! The success of that meeting was such that even now we keep on having pleasant reminders of it. On the 12th January last the Branch had a small party at which a film, nearly an hour long, depicting almost all the phases of it, was shown. Mr. Maurice Micallef, who did the filming with professional perfection, is evidently also a good psychologist, knowing that everybody, however blasè he may appear to be, cannot resist being pleased at seeing himself in a film, so there were plenty of personal close-ups. What is more, at this party the Branch showed it's appreciation of the help it had received in many ways from the Malta College of Arts, Science and Technology by presenting to its Principal a cheque for £120 for the purchase of books. Even this is not all. Indeed the best (which we hope to announce in our next issue) is yet to come. They do say that nothing succeeds like success.

The following B.M.A. meetings have been held:

On the 11th. December, Mr. Roger Parnis lectured on "Unusual Surgical Conditions in Nigeria";

On the 30th. December, Mrs. Winifred Raphael, until recently a Deputy Director of the National Institute of Industrial Psychology, spoke on "Patients and their Hospitals";

On the 13th. February, through the interest of Dr. F. Damato, a Parke, Davis film called "An Introduction to Ophthalmology" was shown;

On the 19th. March, Mr. L. L. Bromley and Dr. E. M. M. Besterman, both of St. Mary's Hospital, London, here on one of their consultant work visits, lectured on "Cardiac Surgery in Maltese Patients" and on "Some lessons in Coronary Intensive Care". The meeting was very well attended, even though it was on a holiday; Also on a holiday — in the midst, in fact, of the Easter period — a very successful meeting was held on the 28th. March when Dr. Alan S. Curry, director of the Home Office Central Research Establishment and an authority on toxicology, spoke on "Poisoning. Accident, suicide, or murder?".

On the 8th April, Dr. V. Captur, Dr. J. Rizzo Naudi and professor Leslie Pace spoke on the anatomy and physiology of the thymus and on the clinical aspects of its enlargement in children. The meeting included an interesting and lively discussion.

When Dr. Paul Crossfield ('46) came to Malta last year, on a holiday from Canada which is now his home, he said he had come on a sentimental journey to the place where he had got his degree. But evidently Paul does not waste his time in pure sentimentalism. He presented the Medical School with a hundred pounds to spend on books. We had a very welcome visit from Dr. P. Demanuele last May. He is now flourishing in private practice in Toronto, Canada. As welcome as it was unexpected was a visit from courteous and accurate Dr. Anthony Buhagiar ('61). He has very recently been appointed Consultant Obstetrician-Gynaecologist with the Birmingham Regional Hospital Board, with duties in the mid-Staffordshire region where the old hospital is being replaced with a brand new building. Some of these new buildings, such as one we saw in Swindon not so long ago, make one green with envy. There is about them so much of what the French call *les douceurs de la vie* (and we don't mean *"dolce vita"*), and which, in our harsh environment, we lack so badly. We always feel this could be partly attributed to the fact we do not use wood in building.

The International Association of Dental Students will be holding its Annual Congress for 1971 in Malta.

Father Andrew Cuschieri O.F.M. has written an interesting paper on "Paranoia: partial or integral insanity". This has appeared in "The Jurist" (Vol. XXIX, No. 4, October 1969) which is published by the School of Canon Law of the Catholic University of America, in Washington, D.C.

From the 28th. to the 30th. May about 200 doctors, including some very eminent ones, mainly from Italy met (through the sponsorship of a pharmaceuticals firm) in Malta for what were

called *'Incontri di Medicina Mediterranea'*. These meetings were held in the Chameleon suite of the Corinthia Hotel under the chairmanship of professor Sergio Cerquiglini, the director of the Institute for Human Physiology of the University of Rome. Local doctors were invited and some took an active part. It was a pleasant gathering. Amongst other, probably more important things, it showed us the continued and perhaps increasing appreciation of Malta as a "convention centre".

The First International Congress on Dentistry for the Handicapped will be held, under the sponsorship of "The Academy of Dentistry for the Handicapped" in Atlantic City, New Jersey, U.S.A., on October 7-8, 1971 just prior to the annual meetings of the American Society of Dentistry for Children and the American Dental Association. Anybody interested in attending or in presenting papers should communicate with the convention chairman, Dr. Maauel M. Album, Medical Arts Building, Jenkintown, Pennsylvania, 19046, U.S.A.

PUBLICATIONS LIST

Recent publications by graduates of our medical school include:

GRECH J.L., SPITERI L., VASSALLO L. (With CURRY A.S.): 1969. Death from thallium poisoning — a case report. Europ. J. Toxicol., *No. 5*, 260.

GRIFFITHS V.G. 1968, Observations on Biliary Surgery. Royal University of Malta.

VELLA F. (With GRAHAM B.) 1969. A variant of Haemoglobin A_2 in Alberta Indians. Clin. Biochem., *2*, 455.

VELLA F. (With ENG, A.C. and MERRY, C.C.) 1970. Two possible instances of haemoglobin E Saskatoon in Manitoba. Canadian J. Biochem., *48*, 45.

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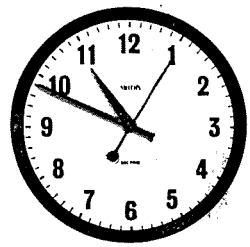

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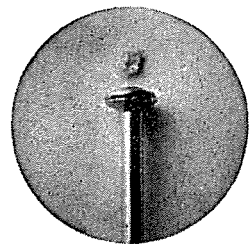

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