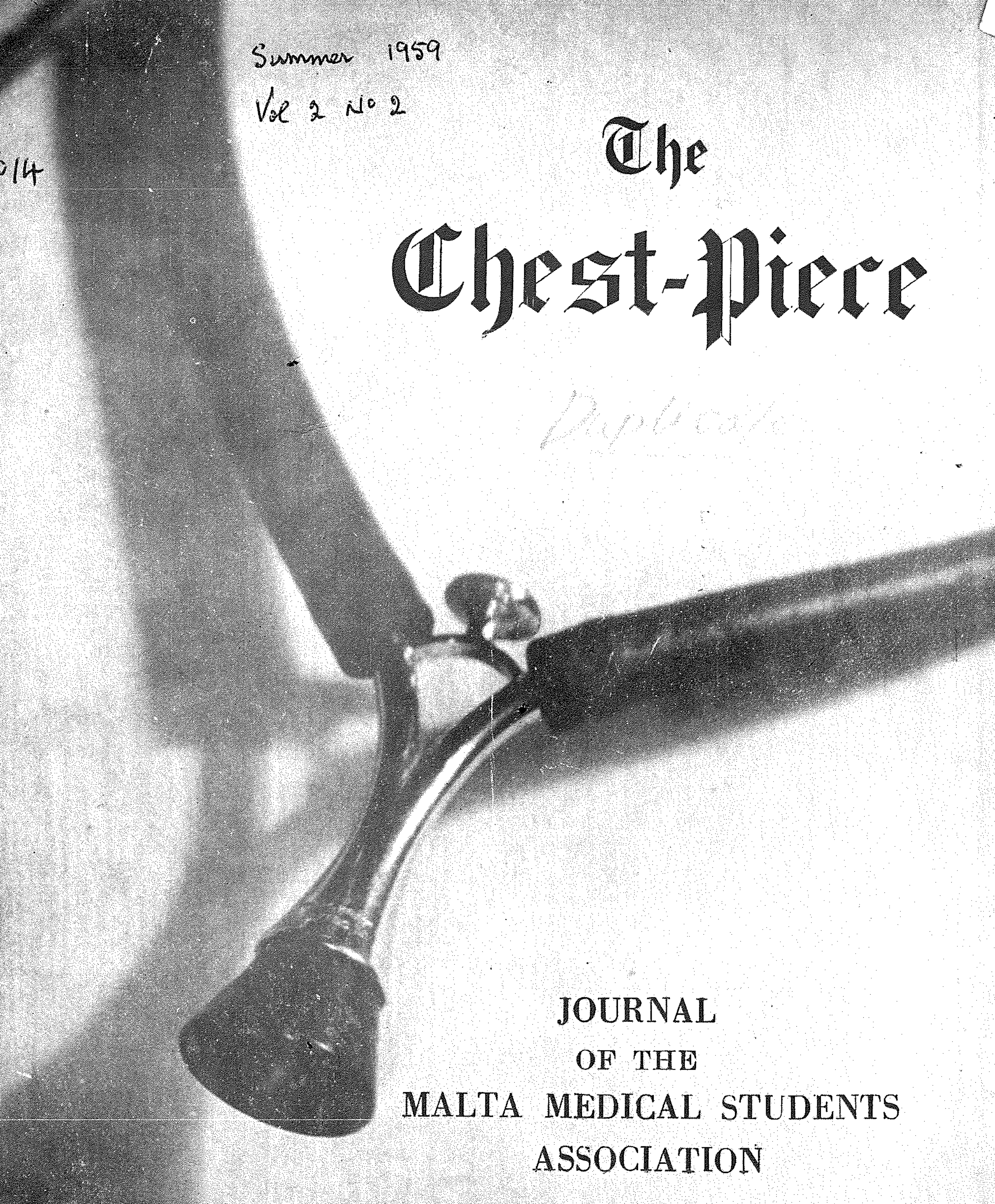

The Chest-Piece

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The Chest-Piece

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Editorial

THE MEDICAL SCHOOL

The need for a medical school building in Malta has been a long-felt one. In order to appreciate how very urgent is this need, one has but to mention that the only facilities available for an average number of fifty students are the very limited ones generously made available to the University by the Medical and Health authorities. These include a lecture hall, limited library accommodation, Students' laboratories within the Pathology Unit and resident accommodation for students doing obstetric firms and causualty work.

Agreement on the site for the building of the proposed Medical School has now been reached between the Government of Malta and the Royal University. The Malta Government has most generously granted the site, and the University now awaits the drawing up of the deed for transfer of these lands. Moreover, the construction of the Medical School will be financed by grants from Colonial Development and Welfare Funds. A provision of £66,000 has been made for this purpose and the money has to be made use of by April 1960.

The Malta Government must, however, help further if this scheme is to materialise within the relatively short time that remains. The administrators of the Colonial Development and Welfare Fund require assurances that recurrent expenditure be shouldered by the Government before they release the money for capital expenditure. The Council of the University has given the assurances that the Medical School will be given priority in the University budget as from 1960. But these assurances can only take the form of guarantees when Government increases the yearly grant to the University by £7.000; this is the estimated figure for maintenance of the Medical School and its services. We have only to think of the recent past to appreciate how important is the question of guaranteeing recurrent expenditure. The Evans laboratories in Valletta have had to remain closed for the long period of eight years as no grants for recurrent expenditure were made by the Government until February 1959. These spacious laboratories for the Science and Engineering Faculties have for years remained unused; a silent indictment of the lack of understanding of the University's role in higher education.

The requirements of the Medical School have been planned over the past year; the planning has now reached an advanced stage and is under the direction of Mr. England Sant Fournier. The Medical School is visualised as an imposing building overlooking the Pieta' sea front and in architectural harmony with the dominating building of St Luke's Hospital. All student amenities will be grouped in the ground floor. Provision has been made for common rooms, games rooms, cafeteria, committee room and changing rooms. The Maltese medical student will at last be able to pursue his studies, as is done by his colleagues all over the world, in a University environment with facilities for study and amenities necessary to lighten the full time burden of medical education.

A department of Dental Surgery will be also housed in the ground floor. The Administrative Services and the Research departments will be grouped in the first floor, and the Library, Medical Museum and the Department of Pathology will be housed in the second floor.

The third floor will include a lecture theatre and two lecture rooms to seat 60 and 40 students respectively. It will perhaps interest the reader to know that examinations will be held in these lecture halls: it will have to be a "regretful farewell" to the dear old Aula Magna. A number of demonstration rooms will also be available in the third floor as well as a well-equipped medical photography unit. From the third floor the Medical School will be connected to St. Luke's Hospital by a bridge to be used for bringing patients for lecture demonstations and to provide an easy access to the hospital wards.

The Medical School will be built in the low-lying green belt along the Pieta' side of St. Luke hospital. The site is a well-chosen one for it combines seclusion with close proximity to the teaching hospital. The main entrance to the Medical School will be reached from the Pieta' main road; this factor is another of the advantages of the site, for a few minutes walk will make it possible to utilise one of the Island's main thoroughfares along which run several bus routes. Built on sloping ground, the Medical School will look out on the impressive panorama of the Valletta and Floriana bastions rising upward from the seas of Pietà creek and Sliema Harbour. These are some of the factors among many others that make us eager to see this project speedily completed.

With the construction of the Medical School, and with the various facilities which shall be available because of its proximity to the hospital, it will be possible, one hopes to hold conferences and international gatherings and organise activities both at graduate and undergraduate level. Last but not least, we shall expect to see considerable increase in the research programmes of the various departments, and we also hope that the Medical School will serve to focus the attention of many outside medicine on the needs of encouraging and subsidising these research programmes.

JEREMIAH QUOTES

DID YOU KNOW IT?

Medicine, the only profession that labours incessantly to destroy the reason for its own existence.

JAMES BRYCE.

ENVIRONMENT IN TREATMENT

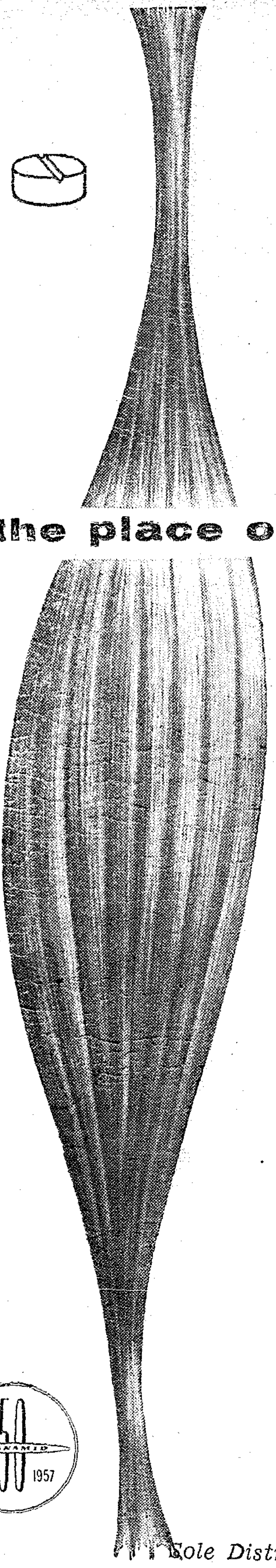
Once Antigonus was told his son was ill, and went to see him. At the door he met some young beauty. Going in, he sat down by the bed and took his pulse. "The fever," said Demetrius, "has just left me." "Oh yes," replied the father, "I met it going out at the door."

PLUTARCH.

THE VALUE OF DIETS

Like the diet prescribed by doctors, which neither restores the strength of the patient, nor allows him to succumb, so these doles that you are now distributing neither suffice to ensure your safety nor allow you to renounce them and try something else.

DEMOSTHENES.



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The value of MILTOWN in the relief of common rheumatic diseases is becoming more evident as results of clinical work are published. Satisfactory relief of muscle stiffness and pain has been observed in a high proportion of patients with various rheumatic conditions with a predominance of fibrositic symptoms. Impressive results have also been achieved in rheumatoid spondylitis, cervical root syndrome and mild rheumatoid arthritis. The promptness of relief following MILTOWN in these conditions has been particularly notable. MILTOWN is effective orally—typical dosage in rheumatic conditions being one tablet (400 mg.) three or four times daily.

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THE ROYAL UNIVERSITY OF MALTA

A "Fund for Medical Research"

MR. C. DE GIORGIO'S CONTRIBUTION

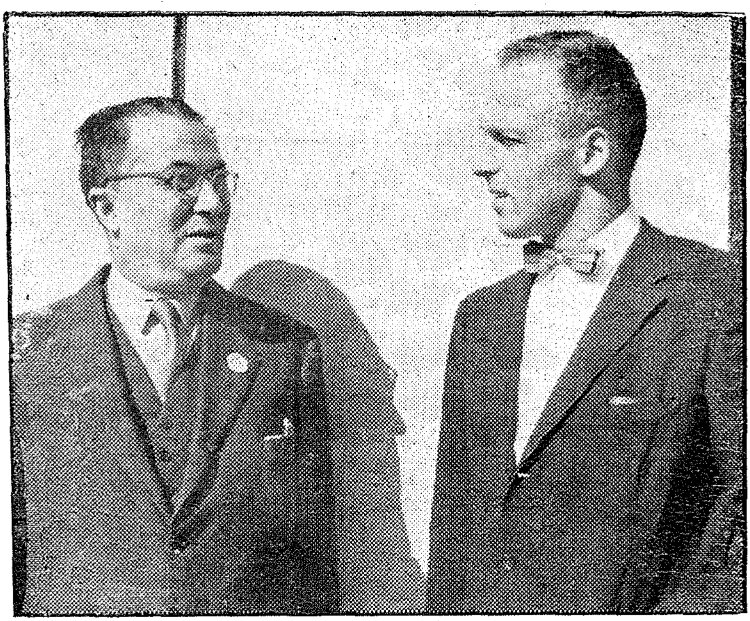
Speech delivered by the Vice-Chancellor and Rector Magnificus during the ceremony of the handing over of a cheque of £300 by Mr. De Giorgio towards the Medical Research Fund

Research work in the Faculty of Medicine and Surgery is bound to receive an added stimulus by the decision of the Council of the University to set up a Fund for the purpose of financing research projects in Medicine. The University has received in the past small grants to support some specific line of enquiry but this form of aid has not been regular and the work published by members of the Faculty of Medicine has largely been carried out without financial assistance. Within the past months papers on Myasthenia Gravis Brucellosis, Spondylitis, Brucellosis Myelopathy and Acute Haemolytic Anaemia have been contributed by the teaching staff to medical journals of the United Kingdom and America. Analysis of these publications shows that the topics chosen for investigation are primarily those that require only time, thought and energy for this pursuit. Research work has been confined to the limited fields where conclusions can be reached without the necessity of providing research assistants and special equipment.

The University has now decided to set up a fund which will be devoted to the fostering of thought and enquiry in the numerous medical and health problems that are awaiting study. The Fund will make it possible for the University to provide research assistantships to be held for a minimum period of one year and to aid the efforts of the individual members of the staff by voting grants to cover research expenses. This Fund for Medical Research will lend coherence and a sense of direction to the dispersed efforts that are now being made. It now rests with the members of the Faculty, graduates and under graduates to bring the existence and objects of this Fund to the knowledge of the people of these Islands and outside it. The University is fully conscious of its mission of advancing knowledge as well as of imparting it: it is with the object of stressing the need for research work that the University has set up this particular Fund.

The Council has been much encouraged by the ready response made by Mr. Carlo de Giorgio who contributed £300 to the recently set up Fund. The promptitude and the extent of this first donation go to show how generous a well-wisher the University, and particularly the Faculty of Medicine, has in the person of Mr. de Giorgio. It must be recalled that Mr. de Giorgio's helpful cooperation extends back into the past. Amongst the limited number of private scholarships and prizes which the University enjoys there is the 'de Giorgio Prize' in Therapeutics; this prize of £25 is awarded every third year to the student who submits the best essay on a subject of therapeutic interest and the first award was made in 1956 to' Dr. W. Bannister Mr. de Giorgio has, in addition, secured the interest of medical firms which he very energetically represents in Malta; it is largely through his efforts and thoughtfulness that the Lederle International Fellowship Committee awards to a graduate of this University a scholarship for advanced research work in their laboratories or other Research Institution in the U.S.A. The first beneficiary of this Lederle philantropic gessture was Professor W Ganado who carried out neurological investigations at Ann Arbor, Michigan in 1957.

Mr. de Giorgio now supports a project which will enhance the pursuit of knowledge within the precincts of our Teaching Hospital. His generous provision, his sustained interest and his willingness to help in every way raise the hopes that other well-wishers of the University, individuals as well as corporate bodies, will see in the Fund an outlet for their public spirit and a worthy object for their support and beneficence. It is hoped that this Fund will provide many with the oportunity to promote this aspect of University life and that, by providing unity of purpose, it will soon lead to visible and tangible results



Prof. Walter Ganado is seen here discussing research plans with Dr. H. J. Sturz, Assistant Director, Foreign Chemical Research, Lederle Laboratories. Professor Ganado was the first Maltese to receive a Lederle International Fellowship for Research Work in the United States. He was sponsored for the Lederle Fellowship by Prof. George P. Xuereb, Dean of the Faculty of Medicine and Surgery at the Royal University of Malta.

THE ORAL GLUCOSE TOLERANCE TEST

J.L. GRECH M.D.

From the Department of Pathology, St. Luke's Hospital, and the Royal University of Malta

Blood contains reducing substances other than glucose. These non-sugar reducing substances, mainly gluthathione and thionine, are present in the corpuscles and therefore "sugar" values do not actually represent the level of glucose. Thus the generally accepted fasting blood sugar level in normal subjects, 80 — 120mg. per 100ml. of blood (Lovatt Evans, 1947; Conybeare, 1949; Bayliss, 1950; Price, 1950; Harrison, 1957), is not the 'true glucose' value. 'True glucose' values may be obtained by deducting 20mg. (Harrison, 1957; Baron, 1957) from this total 'apparent glucose' value when the Shaffer-Hartman method is employed. It is now possible however, to estimate directly the 'true glucose' value by a modification of the Shaffer-Hartman technique as proposed by Asatoor and King (King and Wootton, 1956). The fasting 'true glucose' values in capillary blood of healthy individuals at rest obtained by this method range from 68mg. to 96mg per 100 ml of blood. Other workers give slightly lower values, 53 — 93 mg. per 100ml. (Lovatt Evans, 1947), or even slightly higher values, 70-100mg. (Harper, 1957) and 70-110mg. (Baron, 1957), but the technique used is not stated. The normal 'renal threshold' value for glucose is generally accepted to be 175-180mg. per 100 ml. of capillary blood. In normal persons the blood sugar does not usually rise above 160 mg. per 100ml after the ingestion of carbohydrate (King and Wootton, 1956; Baron, 1957; Harper, 1957).

The object of this investigation is to find out whether the accepted normal 'renal threshold' value, 175-180mg. per 100ml. is altered when the technique for estimating 'true glucose' (King and Wootton, 1956) is used. Furthermore, blood glucose estimations were extended over a period of 3 hours after the ingestion of glucose in order to see whether any additional information on glucose tolerance would be forthcoming.

Material and Methods

An oral glucose tolerance test was carried out on 56 patients referred for investigation from various departments of the hospital; in the majority of these cases reducing substances had been detected in the urine at one time or another. No attempt was made to select the material; all cases of pregnant women were, however, not included in the series. A clinical history of the patient was taken on the day of the test. The age-groups, sex-distribution and the incidence of diabetes mellitus in these cases is shown in the accompanying histogram (Fig. 1).

Fig. 1. — Age-groups, sex-distribution and incidence of cases of diabetes mellitus in the series.

All tests were carried out in the morning after an overnight fast, only a cup of tea or coffee with no added sugar or milk being allowed on rising. A fasting capillary blood specimen was taken and glucose was administered. Fifty grams of glucose was given in 170 ml. of weak coffee in each case. Capillary blood was taken and urine specimens were collected at half-hourly intervals for three hours after administering the glucose.

Blood sugar estimations were carried out on the same day of the test by the Shaffer — Hartman method as modified by Asatoor and King (King and Wootton, 1956). The amount of glucose present in the urine specimens giving a positive reaction to Benedict's qualitative reagent, was estimated by Meyer's modification of Benedict's quantitative technique (King and Wootton, 1956).

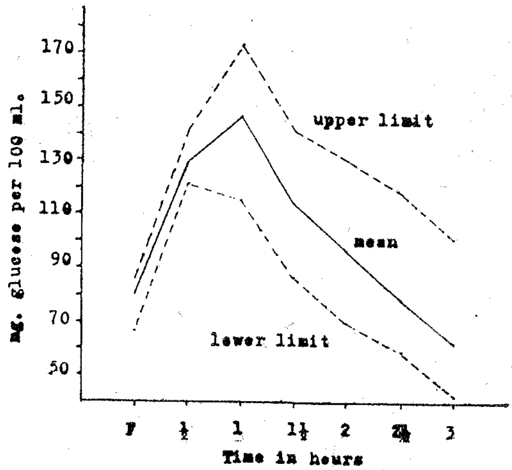


Fig. 2 — Showing the upper and lower limits of normality and the mean curve resulting from the values in Table I.

Results

In six cases no reducing substances were present in the urine specimens collected during the test, and in no instance does the peak of the curve exceed the value of 173 mg. per 100ml . Table I shows the values obtained in each case as well as their mean. Fig 2. represents the upper and lower limits of normality and a mean curve derived from the values in these six cases.

The blood glucose fasting level in these cases ranges from 66 mg. to 86 mg. per 100 ml.; and the highest value is reached within one hour in all cases. Return to the normal fasting level occurs within 2½ hours except in case No. 20. The mean of these values yields a curve with a fasting level of 80 mg. per 100 ml., a peak value at one hour and a return to normal fasting level within two hours.

In the remaining 50 cases, glucose was present in the urine in measureable quantities at some time during the test. These cases have been subdivided according to whether the resulting curve is of the diabetic or non-diabetic type. In four cases the curve is not of a diabetic type: the blood and urine glucose values (Table II) in these cases support the diagnosis of a 'renal' or an 'alimentary' type of glycosuria.

Table I. — Normal Glucose Tolerance Tests in Six Subjects and their Mean Values.

Case No.	F.	½hr.	Blood Glucose (mg./100ml.). 1hr.	1½hr.	2hr.	2½hr.	3hr.
2	66	121	14[illegible]	141	123	83	49
3	77	126	141	86	69	63	55
20	86	127	158	141	130	118	101
44	86	130	144	115	86	72	57
45	78	141	173	101	81	58	52
54	86	130	115	101	86	72	58
Mean	80	129	146	114	96	78	62

Table II. — Results of Glucose Tolerance Tests in Four Cases of Non-diabetic Glycosuria.

Case No.		Time in Hours F.	½	1	1½	2	2½	3	Type of Curve *
22	Blood (mg./100 ml.)	84	127	141	121	107	84	72	R
	Urine (G.)	—	—	0.06	0.08	—	—	—	
28	Blood (mg./100 ml.)	80	144	172	109	89	74	66	R
	Urine (G.)	—	1.06	2.04	0.42	0.04	—	—	
37	Blood (mg./100 ml.)	109	150	193	147	86	78	58	A
	Urine (G.)	—	0.19	1.20	1.15	0.10	—	—	
56	Blood (mg./100 ml.)	86	115	130	115	86	75	72	R
	Urine (G.)	—	—	0.65	1.21	—	—	—	

*R = 'renal'; A = 'alimentary'

Cases 22, 28 and 56 are typical examples of a 'renal' or 'low threshold' type of curve: glycosuria is present, but there is no hyperglycaemia. Case 37 is an example of an 'alimentary' or 'lag' type of curve. Hyperglycaemia and glycosuria are present but the blood glucose falls to normal limits within 2 hours. Moreover, the symptoms complained of by the patient were not typical of diabetes, and no family history of this condition was forthcoming.

In the remaining 46 cases the findings of the glucose tolerance test establish the presence of diabetes mellitus. In these cases there were no complications directly attributable to the diabetic state. One of these patients gave a history of repeated episodes of diabetic coma: ketone bodies were however absent in the urine at the time of the test.

The fasting blood glucose level falls within the range 58-98 mg. per 100 ml in only 6 of these cases (13 per cent); the values obtained after glucose ingestion show the presence of a mild or moderate degree of diabetes. Cases of severe diabetes show a fasting glucose level either above or just below 200 mg. per 100 ml. In 31 cases (67.4 per cent) the peak of the curve is reached 1 hour after glucose administration; the values recorded fall within the range 179-400 mg. per 100 ml. with a mean value of 287 mg. per 100 ml. The blood glucose reaches its highest level 1½ hours after glucose ingestion in 14 of these cases (30.4 per cent). In this group of cases the values recorded range between 201 and 414 mg. per 100 ml. with a mean value of 270 mg. per 100 ml. In only 1 case is the peak reached at the first ½ hour of the test with a blood glucose level of 244 mg. per 100 ml.

In these cases of diabetes mellitus the 3 hour glucose level in the blood is found to be significantly lower than the 2½ hour level. In 30 of these cases (65.2 per cent) there is a fall ranging between 10 mg. and 30 mg. per 100 ml.; in 13 cases (28.3 per cent) the difference is greater, and the values obtained range from 30 mg. to 64 mg. per 100 ml. Only in one instance does the 3 hour level exceed the 2½ hour one, and that by only 7 mg. This variation cannot be correlated either with the height of the curve or with the urinary glucose output during the period of the test. Moreover, 3 hour blood glucose values exceed the level of 145 mg. per 100 ml. in 34 of these patients (74 per cent); in 8 other cases (17 per cent) the levels recorded fall within the range 65-110mg. It has also been observed that in 7 cases (15.2 per cent) a return to the original fasting level occurs within 2½ hours, and in yet another 7 cases (15.2 per cent) within 3 hours.

Discussion

Though the number of tests yielding a normal response is undoubtedly limited, yet the resulting mean curve is considered to be representative of the normal. A fasting glucose value above 96 mg. per 100 ml. is strong evidence in favour of diabetes mellitus, and little additional information of signfiicance may be derived from an oral glucose tolerance test. It is only when the fasting glucose level in the blood is normal and reducing substances have been repeatedly detected in the urine, possibly in variable amounts, that a glucose tolerance test is necessary for diagnosis.

Analysis of the findings recorded shows that there is no scope in prolonging the test to 3 hours. It may even be suggested that for the purpose of establishing a diagnosis of diabetes mellitus, the customary 2½ hour oral glucose tolerance test may very well be simplified. Instead of taking the usual six half-hourly samples of blood, only three are really essential to complete the test: a fasting specimen, a second specimen 1 hour after administering the dose of glucose and a third after 2½ hours. Baron (1957) maintains that a blood glucose level above 145 mg. 3 hours after the ingestion of 50 G. of glucose indicates impaired tolerance; while a value between 65 mg. and 110 mg. points to normal tolerance. Analysis of the 46 curves classified as diabetic shows that the 3 hour level exceeds 145 mg. per 100 ml. in 73.9 per cent of cases. However, in 17 per cent of these diabetic patients the 3 hour glucose values fall within the normal fasting range of 68-96 mg. per 100 ml. (King and Wootton, 1956). This latter finding indicates that the 2½ hour level of blood glucose is a more reliable indication of diabetes mellitus than the 3 hour level suggested by Baron (1957).

The simplified oral glucose tolerance test proposed above has some practical advantages. It reduces considerably the number of technical procedures, and in those cases where venous blood is collected it limits the number of venepunctures to three. This simplified test makes possible more frequent studies of glucose tolerance in diabetic patients under treatment. This is an important consideration now more than ever for in addition to Insulin, BZ 55 and D 860, aspirin is also known to lower the blood glucose in diabetics (Reid, Macdougall and Andrews, 1957; Reid and Lightbody, 1959). The modified glucose tolerance test is not recommended in those cases where 'renal' glycosuria is suspected, and in endocrine disorders other than diabetes mellitus.

No convincing evidence can be adduced from the findings presented in this paper that the normal 'renal threshold' for glucose is set at a lower level than 175-180 mg. per 100 ml. of blood In the normal cases a level of 173 mg. per 100 ml. is recorded in 1 case.

Summary

Fifty-six oral glucose tolerance tests were carried out on different subjects; of these 46 showed a diabetic type of response.

Fasting glucose values ranging from 66 mg. to 86 mg. per 100 ml. of blood have been obtained in normal individuals, in diabetics and in cases of non-diabetic glycosuria.

In the great majority of cases, whether diabetic (69.6 per cent of diabetic cases) or non-diabetic (90 per cent of

non-diabetic cases) the peak of the curve is reached at 1 hour. It is observed that in cases of diabetes mellitus the 3 hour glucose level in the blood is significantly lower than the 2½ hour one.

No information of value is derived by prolonging the test to 3 hours instead of the usual 2½ hours.

It is proposed that the test be carried out employing only three blood specimens: a fasting, a 1 hour and a 2½ hour blood specimen. This modification satisfies all requirements for the diagnosis of diabetes mellitus.

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Mr. Carlo de Giorgio is seen here presenting the cheque of £300 to Prof. J. A. Manchè, Vice-Chancellor and Rector Magnificus of the Royal University of Malta, as the first donator to the "Fund for Medical Research".

Prior to the presentation of the cheque, Mr. de Giorgio said he had been in the drugs business for the last 39 years and it had always been his wish to be helpful to the local medical profession. The Medical Fund will be of great benefit to the Faculty of Medicine and Surgery and will help to continue to raise the level of the profession.

In his reply, Prof. Manchè paid tribute to Mr. de Giorgio for his continued help to the University and recalled that he annually presents the University with £100 out of his own pocket, besides the 'de Giorgio Prize' in therapeutics awarded to the student who submits the best essay on the subject.

The Influence Of Bacteriology And Parasitology On Civilisation

By Dr. E. AGIUS B.Sc., M.D., D.P.H., D. Bact. (London).

The study of history and of the rise and fall of civilisations is simple enough if one limits himself to a mere chronicle of occurrences, but as soon as one attempts to detect and trace any specific factor which has initiated events and determined their cause, then, unless one is on his guard, one may be opening the door to the personal factor, inseparable from judgement, and, possibly, to a multitude of errors. Still this is a risk which like so many in life has to be taken. One wonders what would have happened, if anything, if in the beginning Adam had decided it would be too risky to marry Eve. History would lose most of its value if we fail to discover the motive forces which brought about important events. If it is true (and I think it is), that history is the teacher in life this is only so because through seeing what has caused certain events in the past, we can avoid or foster those consequences in the future.

One of the dangers one must guard against in interpreting history is that of reading more into it than it actually contains—in other words that of tracing a logical pattern where there is no pattern at all. There have been wars fought about dynastic successions in which it is difficult to see any logic. Often—far too often in fact—the course of human affairs has been deflected by trifling accidents, even more trivial than the fact that a queen was childless or that a king fell in love with the wrong lady. But there are many cases where the course of history has certainly been determined by certain definite factors whose effect can be traced throughout the fabric for a very long distance. These causes are generally the fundamentals of life, those concerned with food and health and the basic facts of geography. I believe that one of the most important factors which have influenced and still influence civilisation are the series of discoveries of the causes of epidemic disease which form the subject matter of the twin sciences of bacteriology and parasitology. Some cynic has said that it is safer to read history written by somebody with a known bias, for which one can allow, rather than that by an allegedly impartial author. Therefore I must tell you that I am myself a bacteriologist, but having made that admission I must say I am really convinced of my thesis.

Look at it this way. Up till about the middle of the nineteenth century, humanity had no real inkling of the causes of infectious disease. People knew, of course, that certain diseases were catching, but they did not know exactly why. The operative word there is, "exactly". The knowledge in question is only of value if we can use it to stop disease and to do that it must be detailed, completely accurate and true. Vague knowledge is little better than ignorance Now since the latter half of the wonderful nineteenth century, thanks to the work of Pasteur, Koch, Roux, Manson, Ross and so many others the causes of disease were discovered and made to yield all their complex secrets. The practical result was that the science of hygiene was born, and we could not only treat disease, which is only important up to a point, but we could prevent disease which is the most important thing in the material world. These were the facts which came to have a most vital bearing on the course of civilisation, for men feel instinctively, and quite rightly, that they have a right to health. Only a potential suicide can feel differently and the potential suicide is, thank God, only a pathological exception. So long as a minimal standard of living had not been proven to be indispensable to prevent men laying themselves open to disease, the people could not demand it as a right and governments could conscientiously refrain from providing it. So long as the unhealthiness of marshlands was still debatable, one could ignore the necessity of draining them, but it became nothing less than mass murder not to do so after marshland had been proven to be so completely responsible for malaria. Now it is a matter of history that there were a series of such discoveries which made bad housing, badly built towns, deficient feeding, bad industrial conditions stand out clearly as causes which fostered disease which could in the light of the new knowledge be prevented and which therefore had to be prevented. And hence it followed that politicians with any pretence to honesty had to make the health of the people an important part of their platform. Hence the beginnings of modern social reform, the attack on the slums, the factory acts, the health acts, and, in the last conclusion, the whole paraphernalia which we now know as the welfare state—a complex result which Koch and Pasteur could have imagined to follow their often academical investigations only in their more imaginative moments.

Apart from the political application, and perhaps more important than that was the result in the practical and more strictly medical applications. In this sphere bacteriological and parasitological discoveries have been so successful that we do not even realise their astonishing effectiveness. It is difficult for people of the present time, especially those under fifty, to visualise what life was like before the age of the great discoveries. There has been recently—a few years ago — a small outbreak of cholera in Egypt. That country itself and the world in general dashed so sharply to attack and confine the terrible illness, by isolation, treatment and vaccination, that in a matter of days rather than weeks the epidemic was brought under control and eliminated. In the past it would have had to kill thousands before it would eventually have burned itself out. Now this knowledge of how to deal with an illness has made widespread epidemics things of almost purely historical interest. We did have a most forcible and painful reminder of what things could be like when in 1918 there was an epidemic of an illness — influenza — about which our knowledge then was very scanty. Influenza went right across the world, attacked widely, seeming to chose its victims with a special malevolence amongst the young and healthy, and in a few months made more victims than men had made in the terrible war of 1914-1918. We now know far more about 'flu than we did then but that does not mean that in this case we know enough.

A similar situation prevails with regard to poliomyelitis and a few other illnesses. We should also not forget that there are bacteria and viruses at the moment of little or no importance which can throw variants which would be capable of causing serious outbreaks. But, on the whole, it is safe to say that the great pestilential diseases of the past — plague, cholera, smallpox, yellow fever, typhoid, typhus, the dysenteries, the enteric diseases of childhood, malaria, etc. are greatly curbed as causes of mass depletions of the population. We have been least successful, perhaps, with malaria, but still the improvement has been so extensive that it is now a fact that human life has on the average been lengthened by at least 20 years in the last hundred years.

It is also a fact that whereas up to 1850 3 out of every 4 children died before reaching the age of 5, only 1 out of every 8 did so in 1939, since then I have no doubt there has been further improvement. People are living longer and fuller lives and the effect of applied becteriology makes itself manifest in rising populations. It is also true that applied bacteriology has vastly improved living conditions amongst plants and animals, in other words among the sources of our food supplies. To give an example, tuberculosis as a disease of cattle has been eliminated in many countries. A curious application of antibiotics has brought about great improvements in the breeding of animals for food. These facts are extremely important — vital in the literal sense of the word.

There are also disturbing facts. If you are going to stop people from dying then a population pressure is going to be set up as in fact it has been. This, of course, is why it is so fortunate that improvement has also occurred in our sources of food. One needs a powerful imagination to trace in all their ramifications the consequences of the new standards of health. We have more people capable of working, and being less harassed by disease they can devote more of their time to the better things in life. We have more old people in the population, but through medical progress old age is becoming less and less of a burden. More and more of the population are in a better state of health. The times are gone for ever when it was expected that every village should have its quota of the halt and the lame and the hunchbacked — many of these conditions probably the result of tuberculosis and poliomyelitis.

One by-product of bacteriological progress has been the effect on war. In the past disease played a vast part in military compaigns. In the Crimean War typhus and cholera played an enormous part. In the Boer War it was typhoid. In the 1914-18 war it was dysentery, malaria, gas gangrene and typhus especially in the Eastern front.; not because there was not some bacteriological knowledge but because it was incomplete and only half-heartedly applied and also owing to the great difficulties inseparable from warfare. In the last war — 1939-45 — science was put to use by both sides and everybody was fully alive to the dangers and specific prevention, including new practicable measures for stopping malaria, were most effectively taken. It follows that bacteriology at least saved — thousands of lives. Perhaps it lenghtened the war — who can tell? But except in prisoners-of-war camps, the expected epidemics did not materialize. A great part of that war was fought in the steaming jungles of South-East Asia, a country in which malaria, yellow fever and exotic types of typhus abound, besides who knows how many diseases as yet unknown. All these could be avoided or have their effects minimised through the newer knowledge of the ways in which disease is spread.

In other parts of the world and under other circumstances we have been less fortunate. In the equatorial regions of Africa and South America the insects have so far successfully contested man's supremacy, through their strange association with some agents of disease, such as the Trypanosome of Sleeping Sickness and the virus of Yellow Fever. Insects live on big game and parasites often live on both, passing part of their life in an insect and part in a vertebrate. It is a curious cycle which seems to work mainly to the parasite's advantage. The net result is that vast tracts of the world's surface are rendered uninhabitable to man or habitable to a very low degree. Life is also made very difficult for the larger vertebrates: Africa could have become another Australia or New Zealand, a rich source of meats, had it not been occupied by disease-bearing insects. So far we have lost this battle, but at least we now know who is the enemy and can trace him to his unsuspected lurking places — the salivary glands of a fly or the stomach wall of a mosquito. Some day we may triumph in these areas too.

A less serious but interesting result of bacteriological knowledge has been the effect on manners and behaviour. Man has always had an instinct for cleanliness, but it was the discovery that bacteria can be spread through coughing and spitting that have curbed these habits in civilized societies. Hence also the emphasis on cleanliness of hands, cooking utensils, dishes etc., which has finished by turning kitchens into places very reminiscent of operating theatres. And also certain changes in costume, such as the abandonment of headgear amongst school children, whereever the climate allows it. It is also bacteriological knowledge which has taught us why foods decay and how this can be prevented. And from this followed the methods of canning food of all sorts, and the techniques of refrigeration which has put Europe within reach of distant sources of food. Even as it is meat is still one of the most desired and the most expensive sort of foodstuffs. Without refrigeration supplies of meat for Europe would be almost unprocurable for a very large proportion of the population. Even the pattern of domestic cookery has changed and many families now keep their food supply fresher by stopping the propagation of bacteria through the use of refrigerators. Milk is another food the supplies of which have been much influenced. Our ancestors who knew no better hankered for milk straight from the cow, or the goat, as the case may be. Now in countries where these animals are known to be diseased only a lunatic drinks milk raw or untreated.

Bacteriology and its ancillary science mycology have also been responsible for the development of the antibiotic drugs. The effects of those on civilisation must in the long run be found to be enormous, but perhaps that is another story.

MEDICAL STUDENTS?

"'In other words they're Medical Students, I suppose? said Mr. Pickwick. Sam Weller nodded assent.

'I am glad of it', said Mr. Pickwick, casting his nightcap energetically on the counterpane. 'They are fine fellows; very fine fellows, with judgments matured by observation and reflection; and tastes refined by reading and study. I am very glad of it.'

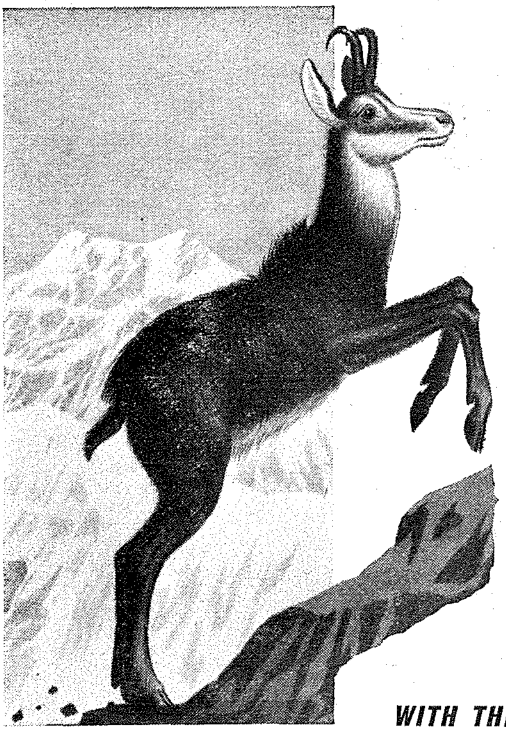
'They're a smokin' cigars by the kitchen fire', said Sam.

'Ah!' observed Mr. Pickwick, rubbing his hands. 'Overflowing with kindly feelings and animal spirits. Just what I like to see!'

'And one of 'em', said Sam, not noticing his master's interruption, 'one on 'em's got his legs on the table, and is drinkin' brandy neat, vile the t'other one—him in the barnacles—has got a barrel o' oysters atween his knees, vich he's a openin' like steam, and as fast as he eats 'em, he takes a aim vith the shells at young dropsy, who's a sittin' down fast asleep, in the chimbley corner.'

'Eccentricities of genius, Sam', said Mr. Pickwick. 'You may retire.'"

—CHARLES DICKENS (1812-1870).



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The Influence of the Nervous System on the Endocrine Glands

By Mr. A. CUSCHIERI

The human body is a marvellous living example of a philosophical entity — all parts for the whole and the whole for the parts. This extreme integration of bodily functions, which becomes more prominent the upper we go the evotionary scale is brought about by two mechanisms; the nervous system and the endocrine glands and their hormones. As such it is but natural for us to inquire into the relation that exists between these two intricate mechanisms.

The endocrine glands number eleven: thyroid, parathyroid, pituitary, the pancreatic islet tissue, suprarenal cortex and medulla (two distinct glands, phylogenetically, ontogenetically and functionally), gonads, liver, kidneys, pineal and thymus. We shall not discuss the last two, as evidence of their secretory powers is doubtful.

The liver is not usually classified as an endocrine gland. That it is a gland there is no doubt; it too, however, agrees perfectly with the definition of an endocrine gland — glands which elaborate chemical substances and secrete them directly into the blood stream. The liver builds up glucose and secretes it into the blood. Its internal secretion is in fact none other than glucose. An objection might be made on the nature of the internal secretion — glucose is not a hormone. Well, exactly what is a hormone we do not know except for the general concept of a substance that is carried by the blood stream and affects other tissues, distant from the gland that secreted it. Glucose is carried by the blood, glucose is needed everywhere in the body, and consequently hypo — and hyper glycaemia bring about disturbances of the nature of hormonal dyscrasias.

These observations led the French physiologist Claude Bernard to definitely state "The liver is an organ of internal secretion." Claude Bernard named it "the blood glucostat", reacting to maintain the blood glucose within the normal range. As to the kidney, the cortex of this organ produces a chemical substance, the hormone Renin, which enters the circulation, acts on hypertensinogen (a globulin) and produces hypertensin which raises the blood pressure by constricting the arteries, especially those of the kidney. The kidney, by this mechanism, thus shares in the normal physiological control of blood pressure. It is true that the main function of the kidney is to elaborate and secrete urine, but as we have seen, if we may not call the kidan endocrine gland, we are certainly justified in stating that it has endocrine functions.

It may be surmised that, in the early evolutionary history, endocrine glands were developed as an extension of the essential basic mechanisms responsible for maintaining the existence and growth of the individual and for promoting the continuance of the species. These basic mechanisms are the glandular epithelial structures, concerned with the absorption and assimilation of food, the primitive neural apparatus, controlling the vegetative functions of the body, and the reproductive organs. With the progressive elaboration of the metabolic processes and differentiation of the neural apparatus the latter came to be the dominating controlling influence in the body; in many instances, however, it acted through the endocrine glands. Thus the endocrine glands have been relegated to a position of less importance, but they still continued to affect tissues under the dominating control of the central nervous system.

The central nervous system affects certain endocrine glands directly by nervous connections with them; it affects others indirectly through the pituitary, the latter having such endocrines as thyroid, adrenal cortex, and gonads under its direct influence. In discussing the relation between the C.N.S. and the endocrine system, we must therefore first and foremost inquire into the relation that exists between the nervous system and the pituitary.

The pituitary consists essentially of two parts, anterior or adenohypophysis and posterior neurohypophysis which differ in their embryological development, in their secretory powers, and in their relation to the central nervous system. We shall thus deal with the two parts separately.

The anterior lobe, derived from Rathke's pouch, is the glandular part containing cells which secrete hormones controlling the suprarenal cortex, thyroid, and the gonads. Postganglionic sympathetic fibres from the superior cervical ganglion reach it by way of nerve plexus around the internal carotid artery and its branches. Parasympathetic fibres may also reach it through this plexus from the petrosal nerves but these are few in number and unimportant The sympathetic postganglionic fibres are definitely vasomotor in function. Very few, if any nerve fibres have been traced from the hypothalamus and even these probably supply the blood vessels. Stimulation of the hypothalamus, however, readily evokes the secretion of such hormones as TSH, ACTH, etc... "We have therefore, the paradoxical situation of the nervous control of a gland which has no significant nerve supply.' The paradox is however easily done away with when we consider the anatomical disposition of the blood vessels of this region. Blood is conveyed by small arterial twigs from the internal carotids to a vascular plexus between the median eminence and the pars tuberalis. From this, straight vessels draining blood travel along the stalk of the hypophysis to the anterior lobe, where they again break up into sinusoids. In this way, products of "hypothalamic activity" could readily reach the anterior lobe; in fact it has been suggested that the hypothalamus elaborates certain chemical agents which travel in the portal vessels to the anterior lobe exciting it to secrete Evidence of this hypothesis is now available: (i) If the described portal vessels are ligated the nervous control of the anterior lobe is abolished. (2) If the hypophysis is grafted on to a hypophysectomised rat, gets vascularised and remains alive, it will only function if placed under the median eminence. Some authorities, however, claim that secretion follows stimulation of cervical sympathetic. Anterior pituitary function has been shown to be regulated, in part, by the level of the hormones secreted by glands that are under pituitary control: this mechanism is involved in the secretion of thyrotrophin, gonadotrophins and ACTH.

The significant point about the anatomy of the neurohypophysis is the complete absence of glandular-looking cells in an organ of proved endocrine function. Another noteworthy fact is the large number of what simulates nonmedullated nerve fibres, all 100,000 of them in man, which stream down to it from the hypothalamus — known as the hypothalamo — hypophyseal tract, the cells of which are in the paraventricular, supraoptic and tuberal nuclei of the hypothalamus. Hence the tract is subdivided into supraoptico-hypophyseal, tubero- hypophyseal tracts etc. It is definitely certain that the neurohypophysis is under nervous control. However, there is considerable controversy as to how this is brought about and as to the actual site of secretion of the so called posterior pituitary hormones. The latter have no influence on other endocrine glands. One view holds that the pituicytes (modified neuroglial cells) secrete the hormones and that the activity of the pituicytes of the posterior pituitary is governed by hypothalamic nuclei via the hypothalamo-hypophyseal tract; the latter when severed is accompanied by a loss of secretory powers on the part of the neurohypophysis. It seems strange, however, that a tissue completely devoid of glandular cells should be capable of forming several hormones. In fact, the modern consensus of opinion is tending to the view that the secretion of the hormones occurs in the hypothalamus, probably by the cells of the supraoptic and paraventricular nuclei, and that the secretion travels down in fine tubes (mistaken for nerve fibres) to the posterior lobe. This bundle of fine ducts has been erroneously called the hypothalamo-hypophyseal tract. The whole process is technically known as neuro-secretion or neurocrinic. Let me quote Le Gros Clarke, "The presence of inclusions of a colloid material in certain nerve cells has assumed some importance recently, since it forms the basis of the conception that these cells, besides their purely neutral functions are capable of an endocrine secretory activity. This process has been termed neurocrinic and has been described as occuring in certain groups of cells in the hypothalamus."

The anterior pituitary, besides elaborating hormones having a specific direct action on tissues such as the growth hormone and prolactin elaborates too trophic hormones that regulate the secretory activity of what are termed target organs, viz., thyroid, adrenal cortex and gonads. The hormones in question are ACTH, TSH, and GH respectively. The anterior pituitary acts on tissues indirectly by activating these organs. Nevertheless, everything ultimately centres on the hypothalamus because the anterior pituitary itself is dominated by the latter. The activity of the hypothalamus is, to a greater or lesser extent determined by stimuli of every possible nature and intensity which reach via efferent tracts, modified perhaps, due to passage through intricate pathways and synapses. A logical conclusion would be that the central nervous system acts on the target organ via the anterior pituitary. As such, there is no need of any nervous connections and, in fact, all these target organs. thyroid, adrenal cortex and gonad have a very poor supply and what fibres there are, are possibly vasomotor in function. In any case, secretomotor fibres have never been detected.

The adrenal medulla, liver, kidney, pancreatic islet tissue all have a rich nerve supply in view of the fact that the activity of these is under direct control of the sympathetic and parasympathetic centres in the hypothalamus.

To the adrenal medulla streams a plexus of nerve fibres derived mainly from the greater splanchnic nerves. The significance about all this is (1) that none of the fibres end in the cortex which they penetrate and (2) the fibres are all preganglionic sympathetic secreting acetyl choline at their terminals thereby exceiting the cells of the medulla. The latter stands in the same position as that of the postganglionic sympathetic neurones and is on phylogenetic, ontogenetic, and functional grounds, a collection of such cells. The suprarenal medulla is an enormous autonomic ganglion secreting adrenalin and noradrenalin (in varying proportions) in the blood, thus reinforcing the activity of the sympathetic nervous system.

Filaments from the vagus innervate the pancreatic islet tissue and that these are secretomotor is proved very easily by the fact that stimulation via such pathways readily evokes secretion. However, it has been proved that the pancreatic islets secrete continuously and furthermore, section of the nerve supply does not influence very much the secretion Fundamentally then, the regulation of carohydrate metabolism does not depend on the integrity of the nerve supply to the pancreatic islets. It is definitely certain that insulin secretion is regulated by the concentration of glucuse in the blood reaching the pancreas but it is possible that changes in the level of blood glucose may act centrally — "Cross-circulation experiments indicate that changes in the blood glucose act on the central nervous system and modify the insulin secretion appropriately via the vagi." The vagus innervation is thus a finely adjusting mechanism.

The liver and the kidneys, each has a plexus of nerves of its own: the hepatic and renal plexuses of nerves. As to the plexus of the kidney, this is made of about fourteen nerves; it is only rational to assume, therefore, that some twigs could reach the secretory cells of the renal cortex.

The parathyroid remains to be an enigma in the sense that both the mode of action of its hormone and the control of its secretion are still disputed. It certainly has a poor nerve supply, and, in all probability, this influences the vasomotor tone. Secretory nerve fibres have never been demonstrated. A suggestion has been made that the activity of the parathyroids is determined by a trophic hormone from the anterior pituitary but no sufficient proof has been forwarded. The only plausible explanation is that the secretion of this endocrine gland is influenced by local factors such as the calcium concentration of the blood reaching it.

The relation between the nervous system and the endocrine system, as has been shown, is an intricate. . . and an improtant one too. To put things in a nut-shell we can say that the hypothalamus is the main controlling centre, and that it acts on certain glands directly via nervous connections with them, on others it exerts its influence via the anterior pituitary. The relation between the hypothalamic nuclei and the hypophysis is very intimate and the whole hypothalamus (including pituitary) is now generally regarded as a complex neuroglandular mechanism which is concerned with the regulation and coordination of visceral and vasomotor activities.

ODD QUOTES

SECTION ONE BIT, SPECIMEN PRESERVED

"Here is a slide of a young girl who has just been to circumcision." — Professor Bull, B.M.S.A. lecture.

HISTORY-TAKING AND DIAGNOSIS

Adult rickets is a rare disease practically confined to women who seldom see the sun, live principally on cereals, drink no milk and have repeated pregnancies.— Davidson's Textbook of Medicine.

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GUIDING PRINCIPLES FOR THE MANAGEMENT OF ST. LUKE HOSPITAL

By Prof. WALTER GANADO M D., B.Sc., (Lond), M.R.C.P. (Lond.)
Member of the St. Luke's Hospital Management Committee

The Council of Nicea declared compulsory the opening of hospitals as a Christian duty (1). Christ was called "iatròs" because he healed the sick. The Saints followed in Christ's footsteps. Nineteen centuries ago Paul the Apostle was shipwrecked at Malta, and healed the aged father of Publius. This event has been recorded in the Acts of the Apostles by Luke the Evangelist, who had studied medicine and was with Paul at Malta. To Luke is dedicated Malta's main hospital. As a teaching hospital, St Luke Hospital is the continuation of the Sacra Infermeria, which was founded in Valletta by the Knights Hospitallers of St. John of Jerusalem, successors to the Crusaders. The Island's most ancient hospital is Santo Spirto, continuation of the Ospedale San Francesco, which, tradition says, was founded by Francis of Assisi when he was on his way to the Near East. (2) Catholic Malta is proud of this Christian heritage. It runs its hospitals on Catholic principles. The spiritual welfare of the patients is cared for as well as their bodily needs. Catholic ethics are observed.

One must not form the impression that in the early centuries hospitals were established only by Christians. Egyptian temples and aesculapian temples in Greece and Rome had much which flavoured of hospital care. Hospitals were established in Buddhist India and Ceylon as well as in China (3) After A.D 750 Islam opened hospitals on a large scale. They admitted every patient who needed hospital care, with no reference to colour, creed, sex, or social status (4). Care of the sick has been practiced wherever humanitarian feelings have developed. Care of the sick is a Christian duty because it is humanitarian. We are bound to help patients irrespective of race, creed, social status, opinions, merits or shortcomings. We are bound to take care of their bodies, their welfare and their comfort and to respect their personality. No one should be allowed to bring pressure on patients to make them change opinion or to force them to act against their opinion. Political factions and political interference should be banned from hospitals. Politics should have no weight in hospital administration or in the selection or promotion of the staff.

For many centuries hospitals were more places of refuge for the needy than centres of skilled medical care. Hospital growth was hampered by improper nursing and poverty of knowledge on the arts of scientific diagnosis and treatment; hospital care provided opportunities for the spread of infection, and hospital fever or gangrene were common Hospitals occupied a low position in public esteem. They were looked down upon as places for the segregation of those that were a danger or an inconvience to others, as lunatics, the sick poor, the infectious. Not until Louis Pasteur, Joseph Lister, Florence Nightingale brought their epoch-making contributions did hospitals begin to come to their own. Increased comfort at hospital, new drugs, modern techniques are attracting the patients to our hospitals in increasing numbers. Deep-rooted prejudice against hospitalisation is rapidly dying down also at Malta, but our public still lacks complete confidence in our hospitals. The growing efficiency of our staff is at times outdone by faulty organisation or by insufficient equipment. This is particularly dangerous because our public is exposed to intensive, at times disloyal, medico-commercial propaganda originating form neighbouring countries. Our doctor-patient relationship is disturbed and at times seriously harmed, with great detriment to patients.

Public confidence in our hospitals cannot be maintained unless the staff is supplied with better means to do the job and is better organised. The problem of equipment is wedded to the economic potentialities of the hospital (and of the Island), as well as to the degree of specialisation wihch these economic potentialities and the size of the Island's population allow. Yet much improvement can take place if there is a rational approach to the problem with a comprehensive and coordinated effort and with care to direct the Hospital's expenses to what is necessary and really useful. There is also urgent need for the establishment or development of services to cover such fields as Biochemistry, Physical Medicine, Dietetics. More liaison between the Hospital's units is necessary. Means must be devised to encourage more members of the nursing staff to reach state Registration Standards. Understaffing will have to be corrected. It produces not only frustration, but often-times it causes unnecessary prolongation of a patient's stay at hospital, with deprivation of the benefits of hospitalisation to others. Efforts are necessary to ensure fairness of terms of appointment, conditions of work and remuneration. No degree of exploitation and no measure of bullying into obedience can ever replace contentment in preserving efficiency, honesty and discipline.

St. Luke Hospital is at the centre of our medical and health services. It absorbs the best brains of the professions and takes a lion's share of effort and expense. As a centre of skilled care the hospital is-self-contained, but cannot close itself within its walls. Hospitalisation should be conceived as a stage of the process of healing, as a temporary step in the rehabilitation of the diseased to a life outside hospital as full as possible. A closer understanding and collaboration must exist between hospital and general practice in the towns and villages. Furthermore hospitalisation should be resorted to only if the patient cannot be treated at home, where environment is generally more congenial to his personality; but the hospital should within limits be ready to supply such services as may be required for domiciliary treatment. The general practitioner, not the skilled specialist, must remain the backbone of the profession; but more collaboration between hospital and general practice is required, especially for the after-treatment and follow up of cases that are discharged from hospital These considerations should apply also to the almoner's service, which is urgently required. The almoner's help should facilitate not only a patient's entry and stay at hospital, but should also extend to the period of convalescence or rehabilitation of the patient, and in collaboration with other social workers should cover the long period of a patient's adaptation in case of incurable disablement.

To St Luke Hospital are attached Medical, Dental and Nursing Schools that train students up to registration standards. Medical students leave the hospital soon after graduation or after a period of internship. Many go abroad and widen their experience in foreign hospitals and schools; but those who remain to practice their profession at Malta very rarely return to St. Luke Hospital for post-graduate experience. Yet the material offered by St. Luke Hospital is as abundant, varied, and interesting as in any foreign hospital. With some effort it could be presented in a most attractive form to post-graduates. One would not envisage refresher courses of dull lecturing, but would suggest part or full-time temporary employment of practitioners with the hospital for periods of, say, two weeks per year to refresh and deepen their knowledge by bringing them in close contact with cases while doing supervised work. During the rest of the year practitioners would be encouraged to follow the treatment of such cases as may be referred to hospital by them. No effort should be spared to recall back to the practitioner's attention that the Hospital is not only a centre of care but a centre of teaching.

Last but certainly not least, is the important fact that the medical school attached to St Luke Hospital forms part of the University of Malta. Hence many members of the medical staff are bound to enrich Academic life by carrying out research projects and supervising research work in their units. For this purpose the University has set-up a Medical Research Fund and has taken steps to facilitate research projects by providing accomodation to research workers in the new building that will soon be constructed for the Medical School on a site close to the Hospital. But frustration is in store unless the hospital is reorganised to support research. First and foremost it is necessary to start urgently a Records Office where case records can be filed and preserved. At present these records are dispersed all over the hospital. Many are not filed, and those that are filed are not classified properly. Some may be lost; others are difficult to trace or to obtain; the majority are not sufficiently informative because housemen are not stimulated to enter detailed and complete notes when they have found from experience that the record would not be serving much use The Registrar service is very limited in number and in scope and is practically restricted to serve only a few wards. Hospital statistical data are impossible or difficult to obtain. Any experienced reader will appreciate that apart from research a reform in this direction is necessary to raise the efficiency of the resident staff, to provide statistical guidance to the consultants and to the management Committeee, to facilitate teaching, and to benefit such patients who need readmission or follow up.

Does this sound utopian to some at Malta? It is a dynamic programme which can and would be made a reality given tentacity, patience, determination and time.

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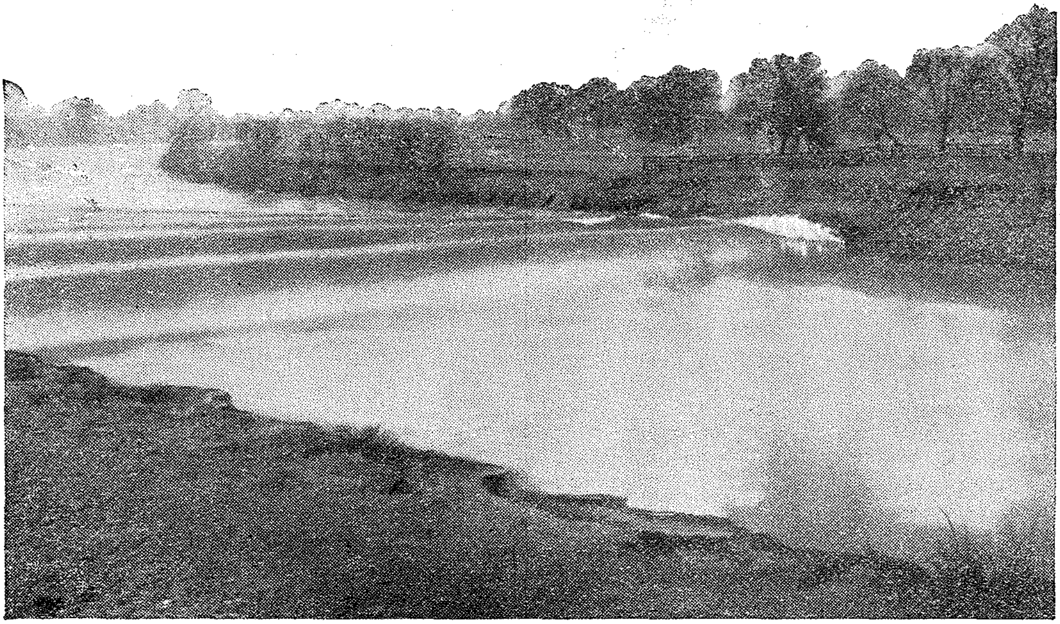

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Some Factors Influencing Pigmentation

By JOHN R. G. AGIUS, B.Sc., M.D., D.C.H.

Pigmentation according to the Oxford dictionary is the presence of a substance giving colour to animal tissue. In one sense the only human beings who are free from pigment are the ALBINOS, so that every human being should have a certain minimum of pigmentation in his body. This is found where melanin formation is active i.e. in the epidermis (not dermis), the uveal tract, meninges and arachnoid and in the intestinal endothelium.

The origin of the pigment cells was for long a debatable point and only recently has it been established to the satisfaction of most dermatologists that the pigment-forming cells are derived from the neural crest.

The amount of pigment in the skin (epidermis) of individuals from different races varies. At one end we have the platinum blond with practically white hair and very little pigment in the epidermis and at the other end we have the negroes — especially those living in the Ghana, Sierra Leone regions of Africa, which are practically on the Equator.

At this stage it might be worth while reviewing the changes in pigment of races living in the region of the Equator. We have negroes in North America (U.S.A. and Canada.) who by living in regions well away from the equator have gradually lost the "black" pigmentation but have acquired a "Chocolate brown" pigmentation, while the race of negroes known to be their ancestors are of a definitely much darker pigmentation. Here therefore we have the tendency of the negro living in temperate climates gradually, over centuries, to lose his pigmentation at least partially. At the other end we have the Central Americans, most of whom are of Spanish Portuguese or Italian stock and who are now of a much darker pigment than the stock from whom they are derived. A third point of some importance is, that some Ceylonese who live at a distance from the Equator are much darker than the Indians who actually live on the equatorial line. If the theory that the Indians were of European stock originally is believed it enhances the above conclusions that after the passage of centuries the amount of pigment found in a race of people will alter with the amount of sun present in the locality.

Whatever the reason for the difference in the pigment of the epidermis in different races, there is no doubt that its presence is protective. The pigment forming cells of the basal cell layer of the epidermis are not very numerous, but each one of them sends out dendritic processes which enter cells in the vicinity of these cells and when the stimulus to pigment formation occurs (e.g. exposure to the sun) they will inject melanin into these recipient cells. This pigment is deposited above the nucleus in much the same way as a cap.

Mary Rolls has set established the neural origin of these melanocytes; the method in which these cells can be stained, e.g. by methylene blue, is a further suggestion of the neural origin, since other cells of neural origin behave similarly. However, the best way to stain these cells is by 3-4-Dihydroxy-phenylalanine or DOPA used in a 1/1000 solution. This substance can be seen to resemble in many ways tyrosine which in its turn is not very different from ascorbic acid. It may be interesting to note en passant that so many diseases of the skin with pigmentation often show a deficiency of suprarenal cortical activity as does for instance Addison's disease. At the same time it is also known that the largest reservoir of Vitamin C in the human body is the suprarenal cortex. Whatever the relationship, however, the skin pigmentation can be rendered of a paler colour, by the simple process of administering Vitamin C (Ascorbic Acid).

The reaction which produces melanin depends on the action of Dopa on tyrosine, the catalyst being tyrosinase, and if irradiation of the skin is applied beforehand this results in pigmentation. Considerable study has been put into this reaction because as time goes on one sees greater needs for protection against irradiation of all sorts, because this type of melanin does not protect solely against the rays of the sun, but also against other electro-magnetic waves, including X-Ray. Other obvious uses come to mind; the finding of oil in Sahara, for example, requires that the Europeans have more pigmented skins in order to be able to resist the intense sun rays. In Northern Australia the settlers of Northern European stock are finding that they are getting skin cancer much more frequently and at an earlier age than those of Southern European Stock. It seems not impossible that the latter have inherited a more facile way of manufacturing pigment and thus of protecting their cells from the ravages of the sun.

It has already been intimated that there is a strong connection between the Central Nervous System and the skin pigment as well as between this and the suprarenal cortex; however the relationship goes further than that as regards hormones. The anterior pituitary is now known to produce M.S.H., the melanocyte stimulating hormone, formerly known as Intermedin. The production of this pigment is one of the important differences between Primary Suprarenal cortical deficiency or Addison's disease in which disease pigment is a most important feature, and Secondary Suprarenal Cortical deficiency as found in Simmond's disease. In the former disease, moreover, the dependence of the pigment on Suprarenal Cortical deficiency is further demonstrated, because of its disappearance during treatment with nothing else but hormones such as Prednisone. The explanation is, that the hormones formed by the suprarenal cortex inhibit the pituitary; in their absence the pituitary is stimulated into action (with the production among other things of an excess of M.S.H.) in an attempt to activate the atrophic or destroyed suprarenal cortex. As this does not — cannot — respond, the anterior pituitary tries harder and harder but the only thing that comes out of this exertion, is more pigment. As soon as treatment with steroids is started the anterior pituitary. is soothed down and no more (excessive) M.S.H. is produced.

In the Nephrotic Syndrome the same thing happens. The child (or adult for that matter) is both producing (and is often receiving) therapeutically large amounts of Coticosteroids — the result is that the epidermis loses most or all of its pigment and assumes a transparent, marble-like, non-pigmented appearance.

Again there is a group of diabetics in whom the skin seems to take on an angelic appearance with smooth shiny skin and rosy cheeks — these patients too show an almost complete absence of pigment.

Another most important relationship between pigment and hormone activity is to be noticed in the following experiments. If oestrogens are painted on one nipple and subsequently both nipples are exposed to the sun, only the painted nipple will darken in colour. While this experiment prima facie seems to imply that oestrogens aid in the production of pigment, yet it seems more likely that such a painting produces a reactive local concentration of androgens to neutralise the effect of the oestrogens. Anyway whatever the explanation not much can be concluded from the experiment. On a different footing is the experiment which was carried out on a eunuch. Half his body was exposed to the sun while the other half was shaded. Two months later, a dose of androgens was given; pigmentation was noticed to appear, soon after, on that side of the body which had been exposed to the sun. This shows not only the effect of androgens on pigmentation but also the fact that the stimulus persists for a long time.

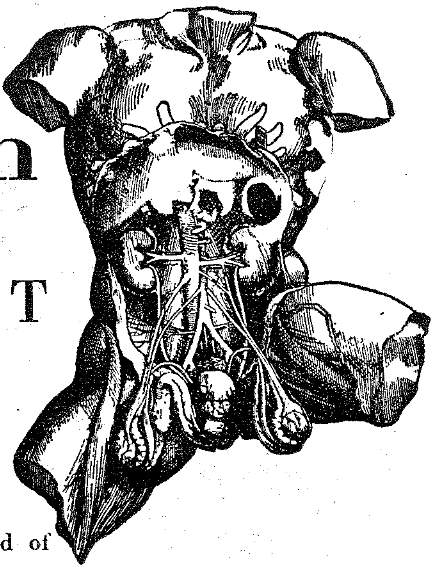
Finally, the hormonal influence on pigmentation can also be seen in pregnacy — not only does the skin become more sensitive to the sun rays and hence pigment formation but even in the absence of exposure to the sun, more pigment is deposited in the basal cells of the epidermis — cfr. the pigmentation of the vulva and nipples and the appearance of the linea nigra.

Up to this point an attempt has been made to tabulate the various substances which have an influence on pigment formation. It will, however, soon become apparent to even the casual observer that there must be other non-local causes, as well as local ones. The presence, for instance, of pigment associated with Chronic Heart, Lungs, Kidneys and Liver disease suggest that many influences have still to be found; for leaving apart the bile pigments as a source of pigmentation as well as haemosiderin or other iron pigments there will still be pigmented cases belonging to the above four groups. At the same time the influence of SH- containing amino acids, copper and the heavy metals on local pigment formation, is well recognised, and in fact the presence of anti-oxidants in rubber has resulted in the development of depigmentation in several individuals, a state which is reversible after a suitable period of time has elapsed since the stopping of exposure. On the other hand, many foods as well as local applications may sensitize the skin to the rays of the sun. Most fruits, for instance, as well as many vegetables seem to have this sensitizing effect; while on the other hand many a woman has come up with a tear drop (or larger) area of pigmentation, which was the result of localised increase in pigmentation, produced by the volatile essential oils in the perfume: this is otherwise known as Berloque Dermatitis Tar is another substance well known as a skin sensitizer and with an increasing number of workers being exposed to it for a greater number of years (in road surfacing) we are likely to meet, more often than formerly, with skin cancer.

The administration of arsenic has been stopped by everybody practically, but there are still a few doctors especially those with the "Italian School Influence" who still tend to use it. Arsenic produces pigmentation too, but apart from that it also produces cancer and hence one should be more reluctant to use it medicinally either for internal or external diseases.

Finally the association of pigment on the skin and on the internal mucosa (cfr. the correlation between these two described earlier) together with the appearance of malignant tumours of the small intestine has been described under the Peutz-Jeghers Syndrome and two cases were demonstrated 2 years ago here in Malta.

Terramycin
in
URINARY TRACT INFECTIONS



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6. Infections due to other Terramycin-sensitive organisms.

Pfizer

Full literature is available and will be supplied on request.

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