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RENAL FAILURE AND THE REQUIREMENTS FOR MAINTENANCE HAEMODIALYSIS IN MALTA

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In order to estimate the demands for prolonged management of chronic failure by maintenance haemodialysis, one has to consider the number of patients in the community who are likely to benefit from such treatment. Malta, with its small size and a stable population of just under 300,000, is eminently suited for a survey of the incidence of disease in a community. The purpose of the present study is to find the incidence of renal failure in Malta as well as to assess the number of patients who would be suitable for treatment by long term haemodialysis. St. Luke's Hospital is the only general hospital in Malta and uraemic patients are at one time or other during their illness investigated in this hospital. For the purpose of this study, renal failure was defined as a blood urea value of 100 mg per 100 ml or more (Branch *et al.*, 1971). All patients, who during some stage of their stay in hospital had a blood urea level of 100 mg per 100 ml or more were studied.

Methods

Data were collected in three ways:

1. *Laboratory Records:* A list of patients with blood urea values of 100 mg per 100 ml or more detected during 1968 was compiled from the biochemistry laboratory records.
2. *Clinical Notes:* As potential candidates for treatment by haemodialysis would probably have been admitted to the medical divisions, the case histories of outpatients and inpatients in these di-

visions were reviewed in order to trace uraemic patients who could have possibly been omitted from the biochemistry laboratory records list.

3. *Death Certificates:* The death certificates of patients dying in hospital in 1968 were reviewed and a list was made of the certificates in which uraemia figured as a cause of death.

TABLE 1

Age in Years	No. of Patients			% of total
	Male	Female	Total	
0 - 9	4	3	7	4.3
10 - 19	1	2	3	1.8
20 - 29	1	2	3	1.8
30 - 39	3	2	5	3.1
40 - 49	10	7	17	10.4
50 - 59	14	9	23	14.1
60 - 69	10	27	37	22.7
70 - 79	27	22	49	30.0
80 -	14	5	19	11.8

Age and Sex Distribution of 163
Patients with Blood Urea of 100mg/100ml
or more.

Results

The biochemistry laboratory records at St. Luke's Hospital showed that 185 patients had a blood urea value of 100 mg per 100 ml or more during some stage of their stay in hospital. We were unable to trace the case notes of 35 (19%) of these patients, but none of these were below the age of 60, and only 5 between 60 and 70 years. Six patients were traced on reviewing all the case notes in the medical division and 7 hitherto undetected uraemic patients were traced back from their death certificates. The total number of cases available for study was therefore 163. An attempt was made to determine the predominant cause of uraemia in each instance.

Analysis of the age and sex distribution of patients with uraemia shows a preponderance of elderly patients (Table 1). Seventy-eight per cent of patients were over 50 years and 42% were over 70 years. Eleven per cent were, however, under 40. There was no substantial sex difference, though there was a predominance of female patients in the 60-69 age group, and a predominance of male patients in the over-eighty age group.

TABLE 2

SPECIALITY	No. of Admissions	% of Total
General Surgery	3473	28.6
General Medicine	1789	14.8
Maternity	2073	17.1
Gynaecology	951	7.0
Orthopaedics	1386	11.4
Paediatrics	979	8.1
Otolaryngology	1119	9.9
Ophthalmic	366	3.1
	12,136	100.0
Total Number of Admissions during 1969		

The number of patients admitted under the various specialities is shown in Table 2. General Surgery and Medicine accounted for 43% of all hospital admissions, but for 86% of the patients with the elevated blood urea (Table 3). Most of the patients under the care of the general surgeons were suffering from obstructive uropathy or dehydration secondary to acute abdominal crises, whilst all the patients who were subsequently found to be suitable for maintenance haemodialysis were under the care of physicians.

TABLE 3

SPECIALITY	No. of Patients with Bl.Urea 100	% of Total
General Medicine	107	65.6
General Surgery	37	22.7
Paediatrics	8	4.9
Orthopaedics	5	3.1
Others	6	3.7
	163	100.0

Speciality under which the 163 patients were admitted

Pre-renal uraemia

The raised blood urea was due to pre-renal factors in 55 out of the 163 patients (34%). These patients have been subdivided into 7 main groups according to the predominant cause of the uraemia and their distribution by age and sex is shown in Table 4.

1. *Cardiac:* Most of the 19 patients (34%) in this subgroup were suffering from ischaemic heart disease and congestive failure. Uraemia was a terminal manifestation in the majority.
2. *Gastro-intestinal:* The 12 patients in this subgroup include 5 cases each of acute intestinal obstruction and gastro-intestinal haemorrhages as well as 2 cases of acute gastro-enteritis. The blood urea returned to normal values

TABLE 4

Causes of Prerenal Uraemia	Age-Groups (yr.)										Grand Total		
	0-9		10-49		50-59		60-69		70+		Total		
	M	F	M	F	M	F	M	F	M	F	M	F	
Cardiac	—	—	1	1	2	1	1	1	7	5	11	8	19
Gastro-Intestinal	—	2	3	—	—	1	1	—	2	3	6	6	12
Hepato-Biliary	—	—	1	—	—	1	—	1	1	1	2	3	5
Malignancy	—	—	—	—	—	—	1	2	2	1	3	3	6
Cerebral	—	—	—	—	2	—	—	—	1	2	3	2	5
Respiratory	2	—	1	—	—	—	—	—	1	1	4	1	5
Miscellaneous	—	—	—	—	1	—	1	—	1	—	3	—	3
Total	—	2	6	1	5	3	4	4	15	13	32	23	55

Causes of Prerenal Uraemia by Age and Sex

after adequate hydration in the 5 patients who survived.

3. *Hepatobiliary*: 3 of the 5 patients (9%) in this subgroup were in terminal hepatic failure. The other two patients had acute cholecystitis and empyema of the gall-bladder.
4. *Malignancy*: 6 patients with prerenal uraemia (11%) had malignant disease. The site of the primary tumour was prostate in two and breast, stomach, caecum and bladder in the other four. All 6 patients died in hospital.
5. *Cerebral*: The 5 patients (9%) in this subgroup include 3 old patients dying in hospital from cerebral thrombosis. The other two patients were admitted for hypertensive encephalopathy and were probably suffering from concomitant hypertensive reno-vascular disease.
6. *Respiratory*: 4 of the 5 patients (9%) were suffering from acute bronchopneumonia and the blood urea was only transiently raised. The other patient

died of pulmonary embolism 4 days following prostatectomy.

7. *Miscellaneous*: The 3 patients in this subgroup (6%) died in hospital from pemphigus, septicaemia and haemorrhage following a severe injury.

Renal and Post-renal Uraemia

Primary renal disease and obstructive nephropathy accounted for the raised blood urea in 108 out of the 163 patients studied. These patients were subdivided into 8 main groups according to diagnosis and their age and sex distribution is shown in Table 5. As expected, pyelonephritis and glomerulonephritis were the main causes of renal failure accounting for nearly half of the 108 patients in this category. Pyelonephritis was commoner in females especially in the 60 to 69 age group. Sixteen out of the 20 patients in the obstructive nephropathy group (80%) were males over 70 years and in nearly all these cases, the obstruction was secondary to prostatic disease.

Diabetic nephropathy was the major

TABLE 5

Disorder	Age - Groups (yr.)										Grand Total			
	0-9		10-49		50-59		60-69		70+		Total		% Grand Total	
	M	F	M	F	M	F	M	F	M	F	M	F		
Pyelonephritis	-	-	2	-	3	2	3	10	4	5	12	17	29	16.8
Glomerulonephritis	1	-	4	5	2	1	3	5	-	1	10	12	22	20.5
Obstructive nephropathy	-	-	-	-	2	-	-	1	16	1	18	2	20	18.5
Diabetic nephropathy	-	-	1	1	1	2	-	4	2	5	4	12	16	14.8
Hypertensive renal vascular disease	-	-	-	-	-	-	-	3	4	-	4	3	7	6.5
“Nephrotic Syndrome”	-	-	1	4	-	-	-	-	-	-	1	4	5	4.6
Acute Tubular Necrosis	-	-	-	2	-	-	-	-	1	-	1	2	3	2.9
Miscellaneous	1	1	1	-	1	1	-	-	-	1	3	3	6	5.4
Total	2	1	9	12	9	6	6	23	27	13	53	55	108	100%

Main renal disorders by age and sex

cause of renal failure in 12 female and 4 male patients. Ten other patients with renal or postrenal uraemia were found to be suffering from diabetes mellitus, bringing the total number of diabetic patients in this category to 26 (24%).

All the 7 patients with hypertensive renal vascular disease were over 60 years old. The diagnosis was uncertain in 2 out of the 5 patients suffering from the nephrotic syndrome. The other 3 patients had systemic lupus erythematosus, polyarteritis nodosa and congenital nephrosis. Two out of the three patients with acute tubular necrosis were females with severe bleeding in relation to pregnancy. The miscellaneous subgroup was made up of 2 cases of nephrolithiasis and one each of renal hypoplasia, renal tuberculosis, perinephric

abscess and renal amyloidosis. No cases of renal failure secondary to analgesic nephropathy were found.

Discussion

There were 36 patients with uraemia secondary to renal disorders which fell in the age group 10 to 60 years (Table 5). This is the age group where potential patients suitable for long-term haemodialysis are likely to be found. Conservative treatment resulted in clinical remission or cure in 7 patients. Maintenance haemodialysis was thought to be contra-indicated in another 15; this latter group includes 7 patients with diabetes mellitus, 2 suffering from malignant disease and 6 others with severe co-existing extra-renal disease.

Out of the remaining 14 patients, 12

TABLE 6

	10-55		56-60		10-55	56-60
	M	F	M	F	M+F	M+F
Glomerulonephritis	3	2	1	1	5	2
Pyelonephritis	1	1	-	-	2	-
Nephrolithiasis	-	-	1	1	-	2
Congenital Nephrosis	1	-	-	-	1	-

Diagnosis, age and sex in patients requiring Haemodialysis

died from uraemia during 1968 and would have been suitable for immediate haemodialysis. The diagnosis in these 12 patients and their age and sex distribution is shown in Table 6. The other 2 patients were discharged with fairly good renal function but would have probably been accepted for treatment within a year.

Various retrospective surveys (Branch *et al.*, 1971; De Wardener, 1966; Department of Health and Social Security Annual Reports 1968-70) have shown that the incidence of patients requiring maintenance haemodialysis varied from 22 to 75 per million population; however both the sources of information as well as the age group considered varied from one study to the other. In two prospective studies (Pendreigh *et al.*, 1972; McGeown, 1972) in Scotland and Belfast, the incidence for patients under 55 years was 38 and 33 per million population per year respectively.

In this study, 12 patients would have benefited from dialysis giving an incidence of 27.2 per million population per year for patients under 55 years and 40.8 per million per year for patients under 60.

The incidence of chronic renal failure secondary to diabetes mellitus was 14.8% (Table 5). This is consistent with the high incidence of the disease in the Maltese is-

lands (Zammit Maempel, 1968). If the more liberal view for the selection of patients for chronic haemodialysis becomes prevalent making diabetic patients acceptable for such treatment, then the local incidence of patients who would benefit from such treatment would increase to 40.8 per million per year for patients under 55 years and 57.8 per million per year for patients under 60.

We wish to thank the Consultant Staff at St. Luke's Hospital for allowing us to study the case notes of patients under their care.

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LAPAROTOMY FOR FEVER

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The problems involved in the diagnosis of fever of uncertain or unknown origin are well known. In the majority of these patients, the diagnosis becomes established after a full investigation. Others no doubt are treated empirically and are considered to be cured because of the subsidence of the pyrexia. There are, however, cases where the most careful investigation fails to discover the cause even though the fever may have lasted months. It is indeed some of these patients who may benefit by a laparotomy not only because a definite diagnosis may result but also because a definitive cure becomes possible. The following two cases will illustrate this fact.

CASE 1

A.S. a 58 year old male from Valletta, was first seen by one of us (F.F.F.) on 1st April 1971 for recurrent fever of unknown origin. He gave a two to three years history of recurrent episodes of rigors with fever up to 101°F and on occasion up to 103°F lasting two or three days. These episodes were becoming more frequent. He had been given several courses of penicillin by his doctor. A careful history elicited a few other symptoms, namely early morning cough with some whitish expectoration, which was occasionally purulent and mild exertional dyspnoea on moderate effort with occasional substernal discomfort. There was no loss of appetite or weight. Over the past year or two, he passed frank red blood per rectum with his stools at times — ascribed to piles —

but his bowels were open normally otherwise. There was no disturbance of micturition apart from nocturia x 1. He had lately become somewhat hard of hearing. He smoked 20 cigarettes daily and drank moderately. He was stated to have had hereditary spirochaetal infection and had also had some treatment for hiatus hernia in the past. He had suffered from sciatica.

Clinical examination revealed a somewhat obese but otherwise healthy middle aged man. There was no abnormality whatever in any system. His temperature was 100.8°F and his blood pressure was 130/80. The investigations carried out included:- full blood counts, serum electrolytes, blood urea, blood cultures, agglutinins titration: all negative or within normal limits. RPCF, Kahn's and VDRL tests were negative, so were urine analysis and culture. ESR was 30 mm/hr. Culture of the sputum elicited some mixed flora; while cytology showed squamous metaplastic changes but no evidence of malignancy. Test for occult blood in the faeces was positive. An X-Ray Chest and E.C.G. were within the normal. A barium meal and follow through simply confirmed the presence of hiatus hernia.

The patient had been admitted on two occasions for a few days but was being investigated mainly as an out patient. By now it was late June 1971. As he still had slight bleeding per rectum off and on, a barium enema was carried out and it showed a polypoidal filling defect in the sigmoid region with irregular margins suggesting possible malignancy. Rectal examination of the patient yielded blood stained faeces at this stage. Finally, an IVP was carried out but the only abnormality here was slight prostatic indentation in base of bladder. It was decided to

deal with the lesion in the colon and of course at the same time thoroughly explore the abdominal cavity.

At laparotomy (R.A.) on 26th July 1971, thorough exploration revealed only a growth of the sigmoid colon with no obvious extension beyond the organ. A pelvic colectomy was carried out with end to end anastomosis and a rectal tube was used for decompression as described elsewhere (Attard R. 1972). No other cause for the recurrent fever was found anywhere in the abdomen. The histology report relates that sections showed proliferative pinkish grey tumour tissue in the lumen over a length of 13 cms. The lymph nodes were not enlarged. Microscopical examination showed adenocarcinoma with little mucus formation. Mitotic activity was marked but there was no muscle infiltration. The patient was somewhat chesty postoperatively but he made an excellent recovery and was discharged on 10th August 1971. He has remained very well since then and when seen last week stated he had not had fever since the operation.

CASE 2

J.V., a 51 year old man from Naxxar, was first admitted under the care of one of us (F.F.F.) on 20th August 1970 for "orchitis". He had had three episodes of fever up to 101°F and pain over the lumbar spine in the previous six months accompanied by profuse night sweating. He also complained of loss of appetite and weight as well as bilateral somewhat painful testicular swellings. Further questioning elicited the presence of a non-productive hacking cough over some months possibly years, and also nausea and vomiting on occasion. There was slight dysuria. His bowels were open regularly. He did not smoke or drink. The patient stated he had had some rheumatic joint pains four years prior to the present condition.

On clinical examination, he was found to have only slightly enlarged tender testes. A blood count was within normal limits, urine analysis showed traces of protein and a chest X-ray showed

prominent hilary shadows. The patient was an anxious man who did not like staying in hospital. So he was discharged on 5th September 1970 to be followed up in Out-Patients' Clinic. But he did not turn up till he was readmitted on 17th February 1971. He said the testicular swellings had subsided some three months after he had been previously discharged. However, he was still getting intermittent bouts of fever going up to 101°F in the evenings with malaise, anorexia and night sweats. The dry cough was still present and the right testis was a little painful. On examination, he had a temperature of 99°F, a Blood Pressure of 135/80 and a slightly tender right testis. His liver was just palpable. There were no other positive findings. The investigations were as follows: Hb was in the region of 8 to 9 G. on repeated testis but the differential count was within normal limits and total WBC was in the region of 7000/c.m. Reticulocytes 1.4%; ESR 110mm/hr. Blood urea ranged from 60 to 72mg/100ml. Serum electrolytes were normal. Tests for agglutinins were negative on three occasions. (Serum electrophoresis showed the pattern of an inflammatory process associated with diabetes — though he was not a diabetic). Urinalysis showed no abnormality except for calcium oxalate crystals and urine culture was negative both for the usual pathogens and for mycobacteria. Culture of sputum revealed no particular pathogens and a Chest X-ray was now passed as clean. Tests for occult blood in stools were positive on one and negative on two occasions.

As well as repeating these tests others were carried out. Liver function tests were within the normal. Blood for culture taken during bouts of fever on five different occasions was persistently negative. Coomb's test was negative. About a month after admission, his temperature was fluctuating between 100° and 103°F and his ESR was 130mm/hr., though at times it dropped to 50mm/hr. Haemoglobin electrophoresis was normal. An IVP (11.3.71) showed an enlargement of the spleen in the plain film and malrotation of the left kidney in the urography but no other abnormality. A barium meal (24.3.71) showed a hiatus her-

nia. A bone marrow examination revealed only definite features of an iron deficiency anaemia. During this period, he had had empirical treatment with penicillin and streptomycin (at home), ampicillin, salicylates, iron and folic acid preparations to no avail. The patient was finally persuaded to undergo an exploratory laparotomy after being given two units of blood.

At operation on 26.4.71 (R.A.), the spleen was found to be much enlarged, especially posteriorly and medially, entirely within the deep chested rib cage. It was turgid, smooth, diffusely mottled with small hard yellowish-white nodules. It weighed 1.28 kg (the normal spleen weighs not more than 200 mg.) and measured 18 × 17 × 11cm. Nodules similar to those on the surface were diffusely distributed within the pulp and were variable in size and shape. Microscopy showed malignant lymphoma with Sternberg-Reed cells, binucleated as well as multinucleated. Reticulum, lymphoid, plasma cells were arranged with sarcomatous cells to form a nodular pattern that replaced splenic pulp. Diagnosis:- Hodgkin's Disease. The temperature fell straight after the operation but was up again the following day and continued.

On the 21st May 1971, he was started on monthly courses of the four drugs: endoxan, velbe, prednisone and nitrogen mustard. This controlled the fever and his general state improved. However, 17 months later, in October 1972, he was still having bouts of fever, his ESR was 138mm/hr. and the Haemoglobin 10G., inspite of continued treatment. He died in November 1972.

Discussion

Sheon and Van Ommen (1963) state that the fever of undetermined origin that may well require laparotomy for its elucidation should have three characteristics: that it is over 38°C (100.5°F), lasts longer than three weeks and has remained undiagnosed after extensive investigations. Case 2 above fits these three characteristics completely. While in Case 1 a probable cancer of the sigmoid colon was discovered preoperatively, it was only laparotomy that excluded other causes of fever and in fact helped to cure the patient as well of the cancer. There is no doubt that the carrying

out of laparotomy should be the final court of appeal, the last logical step in the series of investigations for fever of unknown origin, which may be caused by a large range of 'conditions' grouped as: infections, malignant tumours, collagen diseases, allergic disorders, metabolic disorders, endocrine disorders and in some instances factitiously (Ben-Shoshan, *et al.*; 1971). Petersdorf and Beeson (1961) in a study of 100 unselected patients with fever of unknown origin found that 19 had intra-abdominal pathological conditions. Apart from the characteristics of the fever already mentioned, one should look for other clues as to possible intra-abdominal disorder in order to help one to decide on laparotomy. Such clues include anorexia, loss of weight, anaemia (BMJ Editorial, 1971); a positive intra-abdominal finding like enlarged liver or spleen (Keller and Williams, 1965); biochemical abnormality, especially altered liver function tests (Keller & Williams 1965; Ben-Shoshan *et al.* 1971; Moossa and Skinner 1972). Indeed these workers consider the serum alkaline phosphatase to be the single most helpful test, though altered BSP retention and albumen/globulin ratios may also be significant. It should be emphasized that abnormal liver function tests in this context are not at all necessarily indicative of liver disorder but more particularly of positive intra-abdominal disease. A full radiological examination of gastrointestinal and genitourinary tracts is essential in all these patients.

In the largest series so far, Geraci *et al.* (1959) published a study of 70 cases of fever of obscure origin who underwent laparotomy with 80% positive results, Keller and Williams (1965) in a similar study of 46 cases had 82% positive laparotomy results while Ben-Shoshan *et al.* (1971) had 70% positive results in 23 patients. Hence laparotomy solves the problem of fever of unknown origin in over two thirds of the patients. Of these 40% are found to have malignant diseases and another 40% intra-abdominal infection. In spite of the possible risks of operation, its value is clear. Indeed, a negative laparotomy result may also be a worthwhile contribution to the management of the patient.

It is interesting to note that almost all

the series of cases mentioned (Geraci *et al* 1959; Sheon and Van Ommen, 1963; Keller and Williams, 1965, and Ben-Shoshan *et al* 1971) included among their patients with fever of unknown origin not only cases with lymphoma or Hodgkin's but also from one to three cases of cancer of the colon. Clanton (1950) remarks that it is sometimes forgotten that fever is often a symptom of cancer. In fact, in 70.3% of his series of 64 patients with cancer of the colon and rectum there was fever not otherwise explained and indeed 4.9% of these patients had fever as the only symptom of cancer of the colon. The fever may be due to toxic degeneration of the cancer or to secondary infection, especially in fungating, ulcerating lesions as in Case 1 above. (Bacon, H.E. 1949). While fever as the prominent symptom of Cancer of the colon was the most interesting feature of Case 1, the fact that such a grossly enlarged spleen was impalpable in Case 2 contributed in very large measure to the obscurity of the fever. In each case, the vital clue was provided by the radiologist, as seen in retrospect.

In conclusion, the above two cases of fever are but unusual clinical syndromes of otherwise commonly known diseases (Ge-

raci *et al*). They show that laparotomy may at the very least provide definite diagnosis of an intraabdominal disorder allowing rational management of the patient and may also in the best of cases cure such disorder.

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HAEMORRHAGIC CHICKENPOX

IN A RHEUMATIC CHILD ON STEROIDS

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Chickenpox is normally a highly infectious disease causing a mild illness. However, in patients with malignant disease or who are being treated with corticosteroids a severe haemorrhagic form of the disease may occur which is often fatal. We here report a case of varicella haemorrhagica in a nine year old girl who was being treated with steroids for rheumatic fever.

Case Report

A nine year old girl was admitted to St. Luke's Hospital in June 1972 with acute rheumatic fever following acute tonsillitis two weeks before admission. On examination she was feverish and found to be in heart failure, with tachycardia, tachypnoea, and enlargement of the liver. Investigations at this stage were as follows: Hb 14.2 g %; WBC, 24,200/cu.mm with 81% neutrophils, 11% lymphocytes and 8% monocytes; E.S.R. 132 mm in 1 hour; Antistreptolysin-O 833 units/ml; β -haemolytic streptococci were grown from a throat swab; agglutination reaction against *Brucella melitensis* and *Salmonella typhi*; negative; Blood culture sterile; routine urinalysis, normal. She was initially treated with Aspirin and intramuscular Penicillin. A few days after admission Prednisone 60 mg daily and Digoxin were added to the regime. She responded

to this treatment and Prednisone was reduced gradually to 25 mg. daily. In the meantime the child's general condition had improved and the E.S.R. came down to 2 mm in 1 hour. Digoxin was discontinued.

One week after her admission another child in the ward developed chickenpox and was sent home. The patient was given 750 mg γ -globulin by injection. Two weeks later she developed sparse vesicular rash over the abdomen and pain in the lumbosacral region. She was given another dose of γ -globulin. On the following day, the rash became more extensive, a diagnosis of chickenpox was made and she was transferred to the Isolation Hospital.

Over the next week she became critically ill. The vesicles became haemorrhagic and were extensive, and confluent in areas, mainly over the front and back of the chest, and over the abdomen which was distended (Figs. 1 and 2). She also had severe stomatitis and vulvo-vaginitis, with dysuria. Her temperature rose to 104-105°F. She complained of continual pain over the lumbar region, which at this time was free from lesions. She also developed petechial haemorrhages and bruises distinct from the haemorrhagic vesicles. Her fluid intake was difficult to maintain and her urine output was consequently diminished.

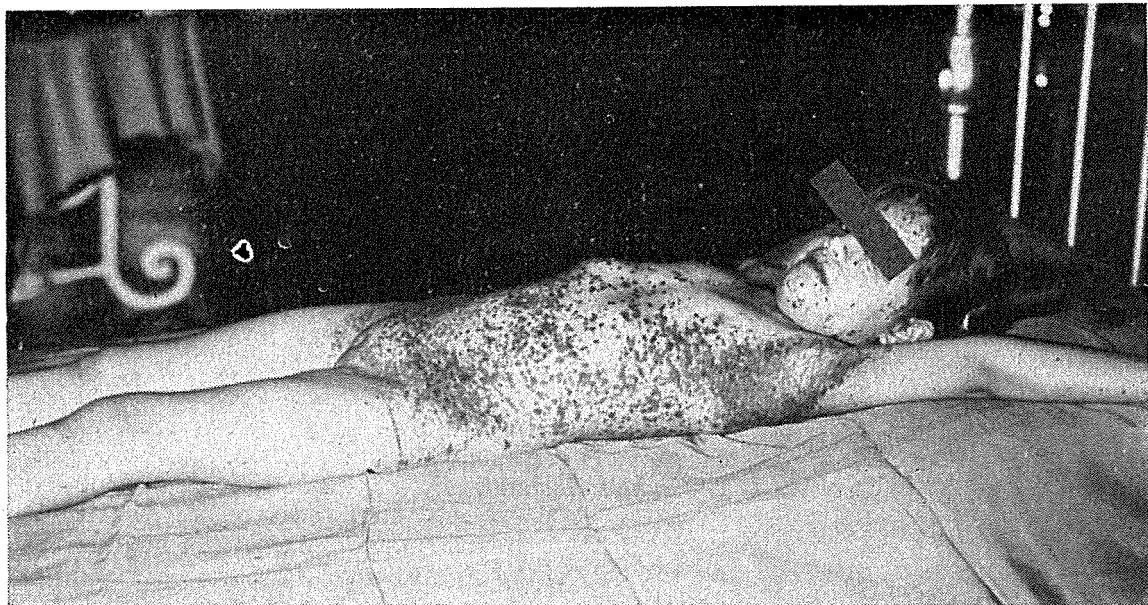


Fig. 1

Further investigations at this stage gave the following results: Hb fell to 8.8g% smear showed normoblasts; WBC 5,000/cu.mm; reticulocyte count 2.7%; platelets 150,000 per cu.mm; blood culture was sterile; blood urea 30 mg %; routine urinalysis normal; serum protein electrophoresis showed a relative decrease in albumin and β -globulin and a marked decrease in γ -globulin; an oral swab grew only a mixed flora. Microscopical examination of smear from base of lesions revealed giant and apparently malignant cells. Fluid and scrapings from vesicles and serum were sent to the Public Health Laboratory, Colindale, for virological studies.

She was treated with Chloromycetin, vitamins and the Prednisone was increased to 60 mg daily. Her Hb dropped to 7.5g% and a blood transfusion was given. Her general condition improved though a further extensive crop of haemorrhagic lesions, including deep confluent lesions in the lumbar region, appeared up to 12 days after transfer to the Isolation Hospital. These gradually regressed and the subsequent progress was uneventful. The lesions healed without scarring except for

two keloids (small) above the left nipple.

The virological report was as follows: Material seen to be full of Herpes group virus particles on the electron microscope and the gel-precipitin test is positive with varicella-zoster serum.

Discussion

The administration of steroids might alter the dermatological manifestations of chickenpox. Indeed, initially in this case there was some doubt as to the nature of the lesions. The possibility of disseminated herpes simplex, Kaposi's varicelliform eruption (which occurs in eczematous patients only) and even small-pox were considered in the differential diagnosis. Microscopical examination of smears from the base of lesions could not distinguish between herpes simplex and varicella, and the possibility of reticulosis involving the skin was suggested. The diagnosis was clinched by the distribution and evolution of the rash, by the known contact with a case of chickenpox in the ward two weeks before the appearance of the rash; and by the positive virological studies.



Fig. 2

The complication described in this case is extremely rare and is little mentioned in the literature. Most cases described have been in patients treated with steroids for another disease (Hagerty & Eley 1956) or on immunosuppressive therapy. But cases have also been described in patients not on steroids, notably in a series from Ceylon. (Krugman and Ward, 1968).

Opinions vary as to whether steroids should be increased or decreased, or even discontinued altogether in a child who develops chickenpox while on this treatment. In the case here presented it was felt

that since the patient was already on a relatively high dose of steroids, and the chickenpox represented a stressful situation, an increase in the dose of steroids was indicated. It cannot however be concluded that survival of the child could be positively related to the increase in the dose of steroids.

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MANDIBULO-FACIAL DYSOSTOSIS

A Case Report

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M.D.

Though the Mandibulo-Facial Dysostosis is a relatively rare congenital abnormality we thought this case deserved reporting because of the tender age of the patient — five months. Most reported cases were in considerably older patients. Moreover this is presumably the first case to be described in Malta. The syndrome is also known as the Treacher Collins or Franceschetti's Syndrome though it was first mentioned by Allen Thomson in 1847 and later by Berry in 1889. The genetic homogeneity of the syndrome was established by Franceschetti and Klein in 1949.

The fully developed syndrome shows the following features:-

1. An antimongoloid obliquity of the palpebral fissures, with a coloboma in the outer parts of the lower lids and sometimes of the upper.
2. Hypoplasia of the facial bones particularly of the malar bones and of the mandible.
3. Malformation of the external ears and sometimes of the middle and inner ears.
4. Macrostomia, a high arched palate and an abnormal dentition.
5. Blind fistulae between the angles of the mouth and the ears.
6. Tongue shaped projection of the hairline on the cheek.
7. Associated anomalies such as facial clefts and skeletal deformities.

Atypical, incomplete and unilateral forms have been described.

Our case presents all the main features except those that one would not expect to find at such an early age, such as dental abnormalities, tongue shaped projection of

the hairline on to the cheek, etc. The general appearance is of a fishlike face with sloping palpebral fissures, (antimongoloid obliquity of the palpebral fissures), flattened cheek bones, a large mouth (Macrostomia), a receding chin (Micrognathia) and absence of the Fronto-Nasal Angle. A striking feature is the deformity of both ears.

There is atresia of the pinna except for the tragus and a fold of skin extending upwards. There is also atresia of the external auditory meati. Hearing seems to be present on both sides but the child is too young for full auditory testing. The palate is highly arched and there is a bifid uvula. X-ray of the skull shows a small mandible with

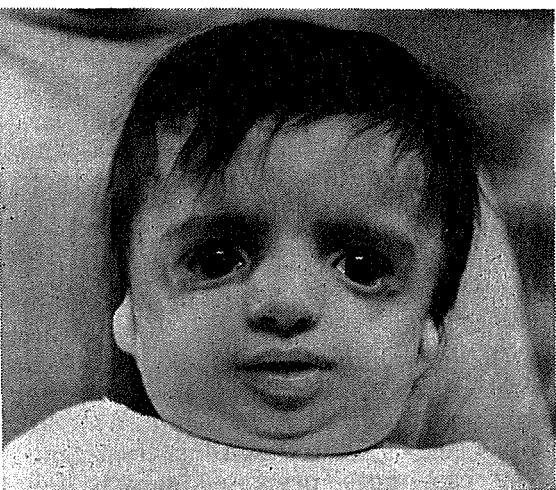


Fig. 1: Sloping anti-mongoloid palpebral fissures. Colobomata at the outer parts of the lower eyelids with bilateral ectropion. Macrostomia, flattened cheek bones and the malformed pinnae can also be seen.



Fig. 2: Showing absence of fronto nasal angle, micrognathia, atresia of the pinna of the auricle, and the typical fish-like physiognomy.

small rami and with especially small condylar processes. The inner ear appears normal with normal horizontal semilunar canals. X-rays of the left wrist showed some flaring of the lower end of the ulna. Lateral views of the lumbar spine show possibly some elongation of the pedicles of the lumbar vertebrae. The child seems otherwise normal. It is interesting to note that the only abnormality in the child's facies noticed by the parents was the abnormal shape of the ears.

The syndrome is described as having clearly established hereditary characters. It is inherited as an autosomal dominant trait with variable penetrance. This variability in penetrance of the gene is shown by

the fact that the features of the parents of this child do not show any abnormalities.

The mandibulofacial dysostosis is caused by a retardation of the differentiation of the maxillary mesoderm derived from the first visceral arch. There is a defective ossification of the bones of the face derived from the visceral mesoderm. An inhibiting process seems to become effective about the seventh week of foetal life when the supporting bony structures of the face are being laid down. There would follow secondarily as a result of the delayed ossification of the walls of the orbit, particularly in the temporal region, a displacement of the bones, and because support is missing, a hypoplasia and malposition of the associated soft tissues. Moreover an arrest of development at this stage accounts for the micrognathia, the macrostomia and the downward displacement of the entire ear.

As regards treatment it has been suggested that the malformation of the lid could be remedied by a plastic operation meant to raise the level of the outer canthus by transferring skin from the upper to the lower lid. At the same time the deficient malar region could be filled up with cartilage implants.

Summary: A case of the mandibulofacial dysostosis at the age of 5 months is reported. All the main features described in the syndrome are present in this case.

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HISTOPLASMOSIS

A pilot survey

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Introduction

Though Histoplasmosis was first recognized as a disease entity in 1905 by Darling in the Panama Canal Zone, it was still considered a rarity up till 1945. It was only when the frequency of the positive skin reaction to the histoplasmin test was reported first by Palmer (1945), and then by Christie and Petersen (1945), that the disease acquired epidemiological and clinical importance, with the result that it is currently estimated that 40 million people have been infected by the fungus, *Histoplasma capsulatum*, and that a significant proportion of the 500,000 annual infections are severe enough to require medical treatment (Chick, 1971).

Histoplasmosis is endemic only in the Eastern Central United States of America but cases have been reported in various parts of the World including some European countries, such as the Nederlands, England, France and Italy (Tassinari, 1948) as well as places in the Mediterranean.

In view of the presence of the disease along the Southern shores of nearby Italy where the fungus was cultivated from the soil (Murray, 1969), it was considered worthwhile to carry out a pilot survey to ascertain the local histoplasmin reactivity, even though so far no case of histoplasmosis has been diagnosed in Malta.

Methods

The population chosen to be tested consisted of a selected group having the following characteristics:

a) All had pulmonary tuberculosis, with the disease healed or in the inactive stage — thus having a pulmonary pathology similar to that of histoplasmosis;

b) All came from a rural or former rural area, and therefore were more likely to have come in contact with a possible source;

c) All belonged to the age-group 40-60 years, i.e. had already been born when a larger part of Malta could be described as rural.

A Histoplasmin Skin Test was carried out by the Mantoux Method in 461 persons (315 men, 146 women) coming from 30 rural areas and from 14 towns, the area representation being quite comprehensive; all the tests were carried out and read by the same individual.

The antigen used was a standardized sterile filtrate from cultures of *Histoplasma capsulatum* grown on liquid synthetic medium, equal in potency to Reference Histoplasmin; 0.1cc of this antigen was injected intradermally in the volar surface of the left fore-arm, the test being read 48 hours later. A positive reaction was taken as an induration of 5 mm or more; as with the Tuberculin Test, erythema without induration was not taken as a positive response.

All tests gave negative results.

Discussion

Systemic primary fungal infestation is rare in Malta. As far as could be ascertained only four cases of this type of fungal disease have been seen or reported locally: a Cryptococcal meningitis in a mid-

dle-aged man, a diffuse Nocardiosis in a young boy, localised pulmonary Nocardiosis in another case and a pleural effusion caused by *Penicillium lilacinum* (Fenech and Mallia, 1972) in a fourth.

No case of pulmonary aspergillosis, diffuse or localised, has been seen locally in spite of a careful look-out extending over 20 years, and no other fungi have been isolated at the Bacteriological Laboratories of the Health Department except those already mentioned (Agius, 1973; Spiteri, 1973).

It had been suggested that the best condition for the growth of *H. capsulatum* in nature include (a.) red-yellow podzolic soil under certain conditions of temperature (16° — 32°C) and humidity (relative humidity 50% or more), enriched by bird manure, and (b.) elevation above sea-level of from 500 to 1,000ft. (Addington, 1967; Manos *et al.* 1956); but it now appears that such soil is not indispensable for the growth of the fungus. In fact Chick *et al* (1972) have isolated the *H. capsulatum* from bat manure obtained from the concrete block wall of an abandoned building, and this was the source of infection in at least one case reported by them. There is no red podzolic soil in Malta, but bats are prevalent.

There is no evidence of direct spread from animals to humans or from humans to animals or that histoplasmosis is a contagious disease (Addington, 1967). Prior (1951) has however suggested that there may be transmission from animal to animal (dog), in fact in certain areas of the U.S.A. up to 50% of dogs are serologically positive, and the majority culturally positive on autopsy (Chick, 1971). The mode of infection is by inhalation of airborne spores, and the natural reservoir of the fungus is its saprophytic growth in nature from where it is spread to humans (Grayston and Furcolow, 1953; Furcolow, 1960; Lash, 1960).

Histoplasmosis has a clinical and pathological similarity to many diseases. It may be confused with Kala-azar (irregular fever, splenomegaly, leucopenia, inclusion bodies in endothelial cells), the Reticuloses (enlargement of liver, spleen, glands, leucopenia and anaemia), and, because of

the pulmonary changes, with tuberculosis. In fact it can simulate any illness, but it is primarily granulomatous in nature and the fungus is highly invasive to the reticulo-endothelial system.

As the disease is acquired by way of the respiratory tract, almost without exception the respiratory organs are the most common site of the primary infection, mimicking tuberculosis very strongly. Four types of pulmonary lesions are recognized:

1. A primary complex — having the same size, shape and localization as in tuberculosis.
2. Miliary lung — the most common.
3. Coin lesions, multiple or single, simulating malignancy.
4. Cavity formation, especially in adults.

Because of the multiplicity of the clinical manifestations, a diagnosis of histoplasmosis can only be confirmed by special laboratory investigations i.e. serology, mycology, and skin sensitivity tests.

Conclusion

The findings of the present pilot survey indicate that one is unlikely to come across endogenous histoplasmosis, yet, in view of the rapid increase in travel throughout the World, the possibility of meeting with imported disease has to be seriously considered.

Our thanks are due to Dr. J. Psaila Savona who carried out and read the Histoplasmin Tests, and to Messrs Parke-Davis Ltd., who very kindly supplied the Histoplasmin antigen.

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A NEW TOPICAL CORTICOSTEROID: CLOCORTOLONE CREAM

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Clocortolone pivalate (Purantix^(R) Sandoz) is a new dihalogenated corticosteroid for topical use, 9 α -Chloro-6 α -fluoro-II β , 21-dihydroxy-16 α methyl-pregna-1, 4-diene-3,20-dione 21 pivalate. Its anti-inflammatory action and good tolerance have been demonstrated in animal experiments. In the granuloma-pouch test, its activity when administered by the oral or subcutaneous route has been shown to be approximately thirty times that of hydrocortisone acetate. An open clinical trial was undertaken to evaluate its efficacy and tolerance, when used at a concentration of 0.1% in an oil-in-water base, in dermatoses normally responsive to topical corticosteroids.

Method

One hundred and one patients with the following diagnoses were treated:

Psoriasis vulgaris (20)
Contact dermatitis (23)
Lichen chronicus simplex (9)

Atopic dermatitis (6)
Pompholyx (3)
Seborrhoeic eczema (2)
Nummular eczema (2)
Pruritus in association with varicose veins (1)
Infective dermatitis (1)
Acne vulgaris (9)
Keloid scars (8)
Pruritus ani (5)
Herpes simplex (1)
Pityriasis rubra pilaris (1)
Dermatitis papillaris capilliti (2)

Fifty-three of these patients were male and forty-eight female. Only five were inpatients. Ages ranged from 3 months to 75 years but 87 were over 14. The cream was applied two to four times daily, in conformity with normal practice, and was continued until its maximum effect was deemed to have been achieved. This averaged 26.7 days (range 8-51 days). Two patients only were treated for part of the time with occlusive dressings which were changed 3 and 7 times per week respec-

Diagnosis	Acute-weeping	Acute	Sub-acute	Chronic	Total
Psoriasis vulgaris	—	1	9	10	20
Eczema	1	8	32	6	47
Others	—	4	19	11	34

TABLE I

tively. Both were cases of psoriasis. During the trial period, no other topical medicaments were applied except for potassium permanganate lotions or baths. No antibiotics or systemic steroids were administered.

Assessment

For the purposes of evaluation, cases were grouped into three categories, viz psoriasis vulgaris, eczema (including contact dermatitis, lichen chronicus simplex, pompholyx, atopic dermatitis, seborrhoeic eczema, nummular eczema, pruritus associated with varicose veins, and infective dermatitis) and 'other indications' (acne vulgaris, keloid scars, pruritus ani,

discoid lupus erythematosus, herpes simplex, pityriasis rubra pilaris, lichen planus, and dermatitis papillaris capillitii). Table I summarises the diagnostic distribution of the patients and the state of the lesions they exhibited.

Assessment of efficacy was based on:

- recording of the following target symptoms on a four-point severity scale before and after treatment: erythema, weeping, scaling, pruritus, lichenification;
- overall assessments at the end of the trial by the investigator and the patients separately of efficacy on a five-point scale.

Local and general side effects were also recorded.

Effectiveness	Eczema		Psoriasis		Other indications	
	Physician	Patient	Physician	Patient	Physician	Patient
very effective	25	35	2	9	9	16
effective	21	10	7	5	8	4
moderately effective	1	2	9	4	9	8
slightly effective	—	—	1	1	3	—
not effective	—	—	1	1	5	6
TOTAL	47		20		34	

TABLE II Overall Assessment

Diagnosis	Erythema	Weeping	Scaling	Pruritus	Lichenifications
Eczema	70.7% (41)	100% (10)	92.3% (26)	92.5% (40)	87.7% (7)
Psoriasis	20.0% (20)		44.4% (18)		
Other indications	35.7% (28)		50.0% (6)	100% (11)	50.0% (2)

TABLE III Percentage of Patients with Complete Regression of Symptoms
Numbers in brackets refer to number of cases showing each symptom at start of trial.

Results

Clocortolone was judged by the investigator as being effective or very effective in 71.3% of cases. It was considered moderately effective in another 18.7% and ineffective or only slightly effective in the remaining 9.9% (Table II).

Target symptoms in eczema resolved completely in between 70.7% (for erythema) and 100% (for weeping) of cases. Pruritus was relieved in 92.5% of cases of eczema and in 100% of the 'other indications'.

Average scores for target symptoms before and after treatment were calculated and the differences between pretreatment and post-treatment average scores were examined for significance by the t-test. The differences were highly significant in eczema for erythema, scaling and pruritus, and in psoriasis for both erythema and scaling (Table IV).

Discussion

In the *eczemas*, treatment was effective or very effective in no less than 46 of the 47 cases studied. In the remaining patient, clocortolone was judged moderately effective. In *psoriasis*, treatment was considered to be very effective in only 2 cases out of the 20 as judged by the investigator. Nevertheless, the improvement of both target symptoms was statistically highly significant and it is noteworthy that in the opinion of the patients

the treatment was very effective in 9 cases, effective in 5 and moderately effective in 4, only in one case being slightly effective and in 1 ineffective. Not unexpectedly, clocortolone proved disappointing in *acne vulgaris* and in *keloid* scars. In eight cases of *keloid*, treatment was moderately effective in 4, and slightly effective or ineffective in the other 4. In *acne vulgaris*, it was very effective in one case, effective in three cases, moderately effective in one case and slightly effective or ineffective in the remaining four. In the 5 cases of *discoid lupus erythematosus*, treatment was effective in 4 and very effective in 1. The result in the one case of *herpes simplex* was assessed as very effective. Of particular interest was the one case of *pityriasis rubra pilaris* who had been attending the clinic for 13 years and received numerous treatments without any effect but who responded rapidly and dramatically to clocortolone with complete resolution. The most striking experience in the trial of this new product was its effectiveness in pruritic states. In all 5 cases of *pruritus ani* relief was complete, prompt and enduring although most of them were long-standing. Of the 40 cases of eczema which presented with pruritus, 37 (92.5%) attained complete resolution of this symptom. There were no general side effects in any patients. The only local side effect encountered was a mild local irritation in one patient only.

Diagnosis	Symptom	Average Score		Difference	t-Test
		Pre-treatment	Post-treatment		
Eczema	Erythema	2.0	0.3	-1.7	highly significant
	Weeping	1.9	0.0	-1.9	significant
	Scaling	1.6	0.1	-1.5	highly significant
	Pruritus	2.2	0.1	-2.1	highly significant
	Lichenification	1.7	0.1	-1.6	not significant
Psoriasis	Erythema	2.0	0.9	-1.1	highly significant
	Scaling	2.2	0.7	-1.5	
Other Indications	Erythema	1.9	0.8	-1.1	
	Scaling	1.7	0.5	-1.2	not tested due to small numbers of each indication
	Pruritus	2.3	0.0	-2.3	
	Lichenification	2.0	1.0	-1.0	

TABLE IV Significance of differences between pre- and post-treatment average scores.

Summary

In a study of 101 cases, clocortolone was shown to be highly effective in the treatment of various forms of eczema and dermatitis. It was also shown to be effective or moderately effective in most cases of psoriasis. There were mixed results in a heterogenous group of 34 patients with other indications. Outstanding benefit was obtained in the relief of pruritus in all conditions in which this symptom occurred, and particularly in pruritus ani.

Local and systematic tolerance was excellent.

Acknowledgement

For their assistance with this study, I am grateful to Dr. J. Agius and to the sister and staff of the Outpatients' Clinic in the Department of Venereology and Dermatology at St. Luke's Hospital, Malta. I am also grateful to Sandoz Ltd. for providing the clocortolone cream and the data analysis.

MALIGNANT EPITHELIAL TUMOURS OF THE LIVER IN INFANCY AND CHILDHOOD

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Malignant epithelial tumours of the liver are the most common carcinomas of infancy and childhood. (Edmondson, 1958) Embryonic and adult type tumours occur; the morphological similarity of embryonic hepatic tumours to embryonic tumours of other viscera and the similar clinical presentation and behaviour of these tumours are two diagnostic pitfalls. In addition the distinction between adult type primary carcinoma of the liver and some embryonic hepatic tumours is not always possible histologically. This distinction may not be "theoretically valid" since it might only imply a different time of origin; embryonic tumours appearing during the development phase, the adult type tumours appearing later (Willis, 1967). Moreover, one cannot separate embryonic and adult type tumours on the basis of the time factor since the liver retains the power to regenerate actively throughout adult life. This inherent potential to regenerate presumably accounts for the occasional occurrence of an embryonic type tumour in an adult patient.

Aetiological factors

Primary tumours of the liver in childhood and infancy usually occur without antecedent cirrhosis and most case reports appear to be from parts of the world where, primary carcinoma of the liver with its possible relationship to cirrhosis, is a rare entity (Bigelow Wright, 1953). The occurrence of such a tumour in a 10 month old child with biliary cirrhosis has, however, been reported and the presence of giant cells throughout the parenchyma of the liver suggested a possible aetiological relationship between giant cell hepatitis,

biliary cirrhosis and primary carcinoma liver (Roth and Duncan, 1955). In a few cases primary tumours follow glycogen storage disease (Edmondson, 1958). That the tumour is congenital in some cases is suggested by the incidental finding of a liver cell carcinoma in a 7-hour-old infant who died of massive cerebral haemorrhage (Wilfer *et.al.*, 1944). In one case reported by Shorter *et.al.* (1960) a haemangioma of the right lobe of the liver had been irradiated with x-rays six years before the development of the malignant hepatic tumour. Christopherson and Collier (1953) rule out a possible relationship between hamartomas and primary liver cell carcinomas as hamartomas lack the property of uncontrolled growth; adenomas, however, are possible precursors since they are potentially malignant lesions. The presence of pre-existing adenomas is, however, difficult to establish. Review of the family histories does not usually reveal any significant findings.

Histologic classification

Primary malignant epithelial tumours of the liver in infancy and childhood can be classified histologically into three main varieties viz. primary carcinoma of the adult type, primary carcinoma originating from bile ducts and embryonic hepatic tumours. Embryonic tumours can be further subdivided into embryonic hepatomas (hepatoblastomas) and mixed hepatoblastomas.

The adult type liver-cell carcinomas, usually developing in older children, can be regarded as "late-appearing embryonic hepatomas or early-appearing carcinomas of adult type" (Willis, 1962). The structure

of the tumour reflects the degree of maturation of the liver parenchyma and provided the obviously embryonic. Moreover the liver parenchyma retains the ability to regenerate into late adult life; when this occurs the liver cell assumes an embryonic character which is partly reflected in the structure of some adult type tumours. As a general rule, however, most tumours appearing in infancy or early childhood are typically embryonic tumours while most of those occurring in late childhood are identical in structure to the hepatic cancers of adults. Various reports of adult type tumours, appearing in late childhood, are found in the literature. Kilfoy and Terry (1929) reviewed 44 cases of both hepatoblastomas and adult type tumours in children and reported an adult type tumour accompanied by cirrhosis in a 9-year old girl.

Hansen *et. al.* (1940) reported a liver-cell carcinoma in a 10-year old boy who also had lung metastases. Bodian and White (1952) reported two multifocal liver-cell carcinomas of adult type, one in a 6-year old girl and the other in a 12-year old girl, both with blood-borne metastases to the lungs and central nervous system.

One possibility that has to be considered in connection with the pathogenesis of the adult type tumours is that, like the nephroblastoma (Willis, 1962) and the neuroblastoma (Goldman *et. al.* 1965); Williams 1954) embryonic hepatomas may sometimes mature to form more benign, less embryonic tumours. The maturation process would result in an adult type liver cell carcinoma or perhaps an adenoma (Otaki, *et al.*, 1960). Although differentiation of an embryonic tumour with loss of malignancy probably occurs in some cases de-differentiation and enhanced malignancy is a more common event.

Hepatic tumours originating from bile ducts are very rare in children. Bigelow and Wright (1953) refer to only 3 cases in their review of the literature. Shorter *et al* (1960) describe a tumour in which the neoplastic cells were forming definite tubular structures resembling bile ducts in a 2-year old boy and suggested the term cholangiohepatoma for this type of tumour.

Embryonic hepatomas or hepatoblastomas are predominantly epithelial tumours more or less resembling embryonic or foetal liver parenchyma. These occur chiefly in young infants and some of them are congenital (Wilbur *et. al.* 1944; Knox *et. al.* 1958). In seven cases referred to by Willis (1962) the ages ranged between four months and seven years and six of the cases were below the age of three. Most of these embryonic hepatomas are highly malignant and metastasize rapidly within the liver, to lungs and bone. Reference has already been made to the possibility that some of these tumours could mature and develop into a more quiescent tumour. This is largely dependent on the rate of growth of the original tumour for most hepatoblastomas would kill the patient from liver replacement and metastases before they mature sufficiently to assume a less aggressive, perhaps benign character.

The *mixed hepatoblastomas* contain, in addition to embryonic hepatic parenchyma, mesodermal components in the form of osteoid, cartilage, bone and myxomatous connective tissue. The majority are seen in infants and in children under the age of eight years; although a few have been reported in adults (Milman and Grayzel, 1951). The epithelial components include liver cell tissue, bile-duct like structures or squamous cell foci with keratinization. The mesenchymal component may be highly cellular and undifferentiated or show varying degrees of differentiation into the above-mentioned components. Although some benign mixed tumours are reported in the literature it is doubtful whether any of these are truly benign. In a malignant mixed tumour either the epithelial or the mesodermal component is malignant; in a few cases both components are malignant. Malignant epithelial growths containing benign mesodermal derivatives are the most common. As the metastases from these tumours may also contain osteoid it is doubtful whether the mesodermal component is truly benign. Three reported tumours (Sheeham 1930; Williams 1954; Wuester and Knauer, 1961) differed from other mixed tumours of the liver in that the epithelial component consisted mainly

of bile ducts and cysts and not of liver cells and the mesenchymal component consisted predominantly of rhabdomyoblastic tissue and not cartilage or bone. Willis (1967) refers to these tumours as Rhabdomyoblastic Mixed Tumours and classifies them separately. However, this different terminology entailing a separate classification is not justified since the mesodermal component differs only in character but not in histogenesis. As for the prominent bile duct component this has been a feature of other epithelial tumours of the liver (Shorter *et. al.* 1960)

The first reported case of a mixed hepatoblastoma was that of Misick (1898) who labelled the tumour a "teratoma". The mesodermal derivatives found in mixed tumours, unlike the multiple tissues found in teratomas, are not foreign to the part; they represent metaplasia in the host stroma stimulated by a predominantly epithelial tumour or else from the second neoplastic component of a composite tumour.

Clinical findings

Most of the reported cases are in patients of Caucasian stock; there are only two cases reported in children from Japan (Bigelow and Wright 1953; Stainer 1938). In the 11 cases reported by Shorter *et al* (1960) the ages of the patients at the onset of signs and symptoms varied from 5 months to 13 years. In another series of 11 cases (Report, 1952) the first symptoms were noted between 5 months and 7 years of age; in one instance the abdomen was said to be prominent from birth. The adult type liver cell tumours tend to occur in the older age groups while the embryonic are found in infancy and early childhood.

The main symptom is gradual enlargement of the abdomen with development of a definite mass in the right upper quadrant. In most cases, at the time of first admission, the liver is enlarged down to the level of or just below the umbilicus. In the mixed hepatoblastomas calcification of the liver is often visible in the roentgeno-

gram of the abdomen. Apart from this, the commonest presenting symptoms are gastro-intestinal viz. vomiting and loss of appetite.

Pain in the right upper quadrant, becoming extremely severe in the terminal phases of the disease, is the rule. In some cases this pain radiates to the right shoulder; it is not usually related to food, movement or respiration. Jaundice and ascites are not often seen; the latter occurs in a few cases and is a late finding in the course of the disease.

In rare instances these tumours may be accompanied by hemihypertrophy and by serious disturbances in mineral and lipid metabolism (Report, 1952; Hansen. *et. al.* 1940). In two cases (Report, 1952) disproportionate enlargement of the right arm and leg was noted and subsequently at post-mortem the right kidney was also found to be enlarged. An appreciable degree of lipid storage in the reticulo-endothelial system, believed to be the result of hyperlipaemia due to liver insufficiency was found in two of eight children with hepatoblastoma and two primary adult type liver carcinoma (Report, 1952). The demineralization of the skeleton has been attributed to deficient calcium absorption due to lack of bile which is necessary for the action of fat soluble vitamin D (Roberts and Sullivan, 1955).

Anaemia, usually of the normochromic and normocytic type occurs as a complication in 80% of cases. Hypochromic anaemia with nail changes consisting of longitudinal ridging and brittleness is described in some cases; these were observed to regress after iron therapy. The total leucocyte count and differential percentages are usually within normal limits.

Serum proteins are usually normal and the serum electrophoretic pattern, may show an increase in the α_2 and β -globulin fractions with hypoalbuminaemia or agammaglobulinaemia (Otaki *et al.*, 1960; Report, 1952).

Prognosis: The duration of life from the onset of symptoms varies from 2 months to 2 years.

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HEPATOBLASTOMA:

A Case Report

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An infant aged 8 months was recently admitted to St. Luke's Hospital with massive enlargement of the liver and abdominal distension.

M.C. was the second child of healthy unrelated parents. He was a full term normal, delivery following an uneventful pregnancy; the birth weight was 3.8 Kg. There was no difficulty in the onset of respiration. His subsequent development was apparently normal. He was first seen at eight months of age with a three week history

of persistent crying. On examination he was a well-covered, dyspnoeic child, obviously in distress with abdominal distension. The temperature was 101°F, the pulse 140 and the respiratory rate 40. The heart sounds were normal but there were diffuse medium rales in his chest. The liver was markedly enlarged, the lower border extending below the umbilicus; the lower edge was hard and irregular. There was no clinical evidence of ascites. The spleen was not palpable. The Hb was 11.0g. per c.mm.

with a normal differential. Examination of peripheral blood film showed normocytic, hypochromic erythrocytes. The fasting blood glucose was 74 mg/100ml and the glucagon tolerance test revealed a 20% rise in the fasting blood sugar at 30 and 60 minutes. The serum bilirubin was 0.6mg% with an indirect Van den Bergh's reaction; the S.G.P.T. was 2 I.U./litre and the prothrombin times 22 secs, with a control of 16 secs. The urine was normal. X-ray films of the chest showed scattered focal opacities throughout both lung fields; a plain X-ray of the abdomen and an intra-venous pyelogram were normal. The serum electrophoretic pattern showed almost complete agammaglobulinaemia with relative increase in α^1 and α_2 , and a very marked increase in β -globulins; this pattern was considered to be non-specific.

His condition continued to deteriorate and he died five days after admission. The differential diagnosis included glycogen storage disease and tumour of the liver, either primary or secondary. Glycogen storage disease was excluded by the absence of hypoglycaemia, a normal response to glucagon and the absence of ketonuria. The plain X-ray of the abdomen and the intravenous pyelogram were helpful in excluding primary renal tumours and a neuroblastoma. In the light of the clinical findings of dyspnoea and rales over both lung fields, the X-ray chest was interpreted as a bronchopneumonia. The true nature of the hepatomegaly was determined at post-mortem examination.

Necropsy Findings

Gross examination. The body was that of a well-developed, well-nourished, white male infant weighing 10 Kg and showing slight central cyanosis and a markedly distended abdomen; there was eversion of the umbilicus and fullness of the epigastrium and both flanks. There was no palpable lymphadenopathy. The peritoneal cavity contained approximately 200 c.c. of straw-coloured clear fluid. The liver weighed 1260 gm (normal 254 gm); its lower border extended downwards to the level of the pelvic brim. There was a yellowish-white tumour mass within the right lobe of the

liver and several smaller satellite nodules in the immediate vicinity. The entire external surface of the liver was peppered by small, haemorrhagic, often cystic lesions averaging 0.2 cm in diameter. The main tumour mass in the right lobe of the liver measured 10.0 cm in diameter. It had an irregular outline with tongues of tumour tissue invading with tongues of tumour tissue invading the surrounding, compressed parenchyma: the main mass was confluent with some of the satellite nodules. The cut surface of the main tumour mass showed areas of necrosis haemorrhage with pseudocyst formation and pools of clotted blood. The smaller tumour nodules varied in shape and size but otherwise had the same gross appearance. Inspite of their small size most of them consisted of necrotic and haemorrhage tumour tissue. The extra-hepatic biliary system was normal and there was no obstruction to the flow of bile into the duodenum.

The lungs together weighed 250 gm (normal 97 gm). Several elevated, well-circumscribed tumour nodules, averaging 1.0 cm in diameter, were seen on their external surfaces. On serial sectioning these tumour nodules were seen to occupy the immediate sub-pleural region: they consisted of haemorrhagic, necrotic tumour tissue identical in appearance to the smaller tumour nodules in the liver.

The lymphnodes in the region of the porta hepatis and the paratracheal and parabronchial lymphnodes were partly or completely replaced by tumour tissue. All the other organs were normal.

Microscopic examination. This showed predominantly an epithelial growth structurally resembling embryonic or foetal liver tissue. The tumour consisted of sheets and cords of closely packed cells, of uniform size, with hyperchromatic nuclei and a small amount of cytoplasm. The cytoplasm was more basophilic and less abundant than one sees in the normal parts of the liver. The nuclei showed coarse chromatin clumping with prominent nucleoli; the latter, however, were less acidophilic than those seen in mature liver cells. The tumour sheets and cords were arranged around large vascular channels partly lined by endothelium and partly by neoplastic

cells. Large haemorrhages within sheets of tumour cells and large areas of necrosis were seen. The cytoplasm of some of the tumour cells contained granules of bile pigment. Irregular, disorderly bile duct proliferation was a prominent feature. The stroma was of scanty or moderate amount, somewhat oedematous, but mature in form with collagen formation. The tumour was not sharply demarcated from the surrounding hepatic tissue; the latter was compressed and distorted and showed infiltration by neoplastic epithelial cells. Apart from these changes the adjacent hepatic tissue appeared normal. The metastases in the lung and in the paratracheal and porta hepatis lymphnodes showed the same histological picture. Haemorrhage and necrosis were particularly prominent in the lung lesions.

Discussion

This case presented with the typical clinical and histological picture of the hepatoblastoma. These tumours are usually highly malignant and metastasize rapidly to the liver, lungs and bones. They occur chiefly in young infants; Willis (1962) refers to seven cases from his collection whose ages ranged between 4 months and

7 years with six cases below the age of 3. Like all reported cases the main presenting feature in this case was an enlarging mass in the upper abdomen associated with an increase in the size of the abdominal girth. Pain was a factor in 45% of the cases reported by Shorter *et al* (1960) and this became particularly severe towards the terminal phase of the disease. The occurrence of pain in our case could not be determined with certainty but the infant presented with a three week history of persistent crying. There was no clinical evidence of ascites and at post-mortem only 200 c.c. of fluid were found in the peritoneal cavity. In Shorter's series ascites developed in 3 out of 11 patients and was a late finding in the course of the illness. The histological picture tallied with that of the typical hepatoblastoma and the liver parenchyma surrounding the tumour showed no indication of a possible aetiology.

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ARGENTAFFIN CARCINOMA OF THE TERMINAL ILEUM

(An Incidental Finding During Hysterectomy)

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The purpose of this paper is to emphasise the importance of routine exploration of the abdominal viscera in all patients undergoing elective abdominal surgical procedures. We report here a case in which an unsuspected and asymptomatic argentaffin carcinoma of the small bowel was discovered in the course of hysterectomy carried out for intractable metrorrhagia.

Case Report

The patient, a 52 year old multipara, was referred to the gynaecological out-patient department on October 5, 1972. She gave a history of irregular and heavy menstrual periods during the previous twelve months. Her last menstrual period had occurred in June 1972 since when the patient had also complained of hot flushes, tiredness, slight dyspnoea on effort and recent loss of appetite. There was no recent change in bowel habit and micturition was normal. No significant information could be obtained from the patient's past history.

On examination, the patient was moderately obese, pale and hypertensive (blood pressure 220/100 mm. Hg.). There was a soft apical systolic ejection murmur radiating towards the left axilla. Both breasts were normal to palpation and no abnormal abdominal masses could be felt. Pelvic examination showed the uterus to be

enlarged by a fundal fibroid, but no other abnormality was noted.

The following pre-operative investigations were carried out: Haemoglobin 8.3 g.; blood group A Rhesus positive; haemagglutination-inhibition pregnancy test negative; and blood urea 19 mg. Urinalysis (Labstix) was negative. The patient's haemoglobin level rose to 12.0 g. following the transfusion of 1000 ml. of blood given one week prior to admission for hysterectomy.

At operation on November 24, 1972 the following findings were noted: the uterus was enlarged by a fundal myoma 7.5 cm. in diameter; the ovaries were normal in size but cystic. On further exploration of the abdominal cavity, a hard intraluminal tumour was encountered in the terminal ileum with its pedicle attached to the anti-mesenteric border, puckering the muscle layer and serosa. The growth was obviously infiltrating the mesentery which was haemorrhagic and rubbery in consistency. The liver and abdominal lymph nodes were normal to palpation as were the stomach, spleen, kidneys, adrenals and colon. There was no ascites.

The operative procedure consisted of total hysterectomy and bilateral salpingo-oophorectomy. This was followed by resection of part of the terminal ileum 10 cm. on each side of the tumour together with a wedge of mesentery which included the infiltrated area. End-to-end anastomosis of

the small intestine was effected about 7 cm. from the ileo-caecal junction.

Post-operative naso-gastric aspiration and intravenous fluids were discontinued on the second day when the patient started passing flatus and had a bowel action. Subsequent recovery was uneventful and the patient was discharged from hospital on the tenth day. She was re-admitted on December 11, 1972, 2½ weeks after her operation, with signs and symptoms of intestinal obstruction. This was thought to be due to adhesions and was treated conservatively with good result. The patient was discharged home after four days and when last seen for follow-up on April 2, 1973, her condition had remained satisfactory.

Histology of the uterus showed adenomyosis and leiomyoma. The report on the bowel specimen read: "The nodule in the ileum is an argentaffin carcinoma. There is pronounced permeation of the lymphatic channels with tumour cells within the deeper muscle layers".

Discussion

Argentaffin carcinomas or carcinoids arise from argentaffin or Kulchitsky cells in the intestinal mucosa which secrete serotonin (5-hydroxytryptamine, 5-HT); similar tumours may be found in other sites such as the bronchus, pancreas and ovary where mature Kulchitsky cells are not to be found. The term 'carcinoid' was coined by Oberndorfer (1907) to distinguish these slowly-growing and relatively benign tumours from adenocarcinomas.

Serotonin released into the portal circulation is rapidly destroyed by the hepatic enzyme monoamine oxidase so that only minute amounts of this substance are normally found in the blood. The presence of hepatic metastases, by interfering with the destruction of serotonin, may cause excessive amounts of this substance to be released directly into the systemic circulation to give rise to the so-called carcinoid syndrome. This syndrome, first described by Thorson *et al.* (19g4) includes episodes of cutaneous flushing, lobster-red discolouration of the face, diarrhoea and valvular lesions of the heart affecting mostly the

right side. The syndrome is found in association with metastatic carcinoid tumours which secrete excessive amount of serotonin and other vaso-active substances including braykinin, histamine and prostaglandins. Confirmation of the diagnosis is made by demonstrating an increased urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA) which is a metabolite of 5-HT.

Incidental discovery of carcinoid tumours of the small intestine at operation for some unrelated complaint, or at autopsy, is not uncommon. Carcinoid is the commonest single malignant tumour of the small intestine and accounts for one-third of all small bowel tumours. Spread occurs in 40 per cent of cases, at first to the mesenteric lymph nodes and later on to the liver. Nevertheless, these tumours metastasise slowly and even the presence of liver metastases is compatible with many years of life.

The case we have described underlines the importance of routine exploration of the abdominal viscera in all patients undergoing elective abdominal surgery. Unrelated pathological conditions, such as the asymptomatic carcinoid in this case, would otherwise be missed. A carcinoid tumour of the bowel without obvious distant metastases should be treated by wide excision of the affected loop and its mesentery. It may be justified, on occasion, to perform a partial hepatectomy in cases where metastases affect only one part of the liver. The use of tryptophan hydroxylase inhibitors to block tumours 5-HT production is still in the experimental stage.

Acknowledgement

We wish to express our thanks to Professor A.P. Camilleri under whose care this patient was admitted. We are also grateful to Professor G.P. Xuereb for the histological examination of the specimens submitted.

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THE PROBLEM OF DIARRHOEA IN INFANTS AND CHILDREN

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Diarrhoea is a common problem in paediatric practice and is due to causes ranging from unwise eating in older children leading to trivial brief episodes to those producing severe and potentially fatal gastroenteritis in infants. Diagnosis and treatment are not usually difficult, but at times both can be extremely so necessitating the admission of the child to hospital. In practice, however, the commonest reason for admitting a child with diarrhoea is the necessity of giving intravenous fluid and providing electrolyte replacement.

The fully breast-fed baby normally has loose, golden-yellow, sometimes green, frequent stools and mothers often complain that their baby has diarrhoea, when in fact the stools are quite normal. One should therefore always have a look at the stools oneself and it is wise to enquire if the mother is taking purgatives, as some of these are secreted in the milk. It is also important to bear in mind that the fully breast-fed infant hardly ever suffers from gastroenteritis.

Gross underfeeding of a young infant produces small, green, loose stools. This may be mistaken for diarrhoea leading to more withdrawal of food by the mother. It is vital to stress to the mother that, in contrast to underfeeding, overfeeding is virtually never the cause of diarrhoea, for a full-term infant knows when to stop. In such a case, if the food intake is increased, the stools will rapidly revert to normal. In the bottle-fed infant looseness of the stools may be produced by the excessive addition of sugar in milk feeds or else by the administration of orange juice. Teething is commonly said to cause many symptoms in infants and it is important to remember that diarrhoea is never due to teething. Another commonly supposed cause is milk intolerance or allergy.

This is actually extremely rare and one is hardly ever justified in changing from one brand of milk to another for this or indeed for any other reason.

Acute gastroenteritis is the commonest problem in practice and usually occurs in the summer months though cases are seen sporadically throughout the year. Vomiting usually precedes diarrhoea but may be completely absent. An extremely common mistake is for the mother to continue feeding the baby as usual, often adding more solids in an attempt to "keep the feeds down". Often, though the baby's feeds are rightly replaced by 'clear fluids', these are constituted badly. Too much salt produces hypernatraemia with its many possible harmful effects especially on the central nervous system; excess sugar often produces more intestinal hurry through an osmotic effect and thus further diarrhoea. Oral or intramuscular antibiotics, commonly of the broad spectrum type, are often prescribed. These do not help and may be positively harmful. The child's condition, especially in infancy, can deteriorate at an alarmingly rapid rate because of fluid and electrolyte loss and if there is little or no response to home treatment, there should be no delay in referring the child to hospital. It is particularly easy to miss dehydration in an obese infant. In particular the skin and subcutaneous tissue will show no obvious change and the important signs are sunken eyes, depressed fontanelles and dry mucosae. It is vital not to mistake dehydration and rapid acidotic breathing in an obese baby for a respiratory infection with parenteral diarrhoea. The latter is common, especially with otitis media and urinary tract infection, and antibiotics should be used for the primary condition.

Not uncommonly, after an apparently

complete recovery from an attack of gastroenteritis, there is a relapse. On re-introducing full-strength milk feeds, the loose stools return, often causing marked soreness of the baby's buttocks. In most cases, this is due to *lactose intolerance* which results from damage to the superficial part of the small intestine mucosal surface and a decrease in the sugar-splitting enzyme lactase, which is essential for the absorption of lactose. On pH testing, the stools are found to be acid and reducing substances are detected in the stools by the usual tests for sugar. Typically, Clinitest (which detects any reducing agent) is positive, while Clinistix (which is specific for glucose) is negative. All milk and milk-products must be excluded from the infant's diet for a variable period of time till the intestinal mucosa recovers fully its absorptive functions.

Diarrhoea brought on by *drugs*, usually broad-spectrum antibiotics, is also fairly common. The indication for antibiotic therapy is very often dubious and the child would no doubt have been better off if left 'untreated'. Most childhood infections are viral and if the child is on antibiotics his diarrhoea usually clears on stopping chemotherapy. In gastroenteritis, the indiscriminate use of antibiotics is common practice. As mentioned above, the treatment of this condition is basically that of fluid and solute replacement and perhaps, oral intestinal antibiotics should be reserved for cases from the faeces of which a pathogen has been cultivated. It has been shown conclusively by several workers that antibiotics do not improve the child's symptoms, often do not eradicate the bowel infection and may indeed prolong the carrier state. However, in the critically ill child, especially one that remains so after a period of adequate rehydration, it is wrong to withhold systemic antibiotics, for in such cases septicaemia is a real possibility.

The child with pale, loose, greasy, bulky and offensive stools has steatorrhoea, which is the cardinal feature of the '*malaabsorption syndrome*'. The motions typically stick to the nappy and are difficult to flush down. In some cases, however, the

stools may not look abnormal at all. The commonest cause in Malta is *coeliac disease* (gluten-sensitive enteropathy) while *Cystic fibrosis* which is common in the United Kingdom seems to be rare. Coeliac disease nowadays presents around the age of six months because of the current practice of introducing cereals early into the infant's diet. It responds dramatically to a gluten-free diet, but before starting treatment it is important to confirm the diagnosis by special investigations in hospital. This is essential because the diet, which is not an easy one to stick to, will need to be continued to well beyond puberty.

In the older child, *spurious diarrhoea due to constipation and faecal soiling* is another commonly encountered problem. The diarrhoea is produced by the fluid part of the stool above a hard faecal mass in the rectum leaking through out of the anal canal i.e.: encopresis. It is important to make a proper diagnosis for in such cases anti-diarrhoea measures are quite obviously useless. Inspection of the anal orifice for the presence of a fissure, especially common in infants, and a rectal examination are essential. Treatment is that of constipation and its cause. One must remember that Hirschsprung's disease (aganglionic megacolon) can also present in a similar way with diarrhoea rather than constipation.

In the preadolescent child, *emotional stress* often causes mild diarrhoea. This is ascribed to intestinal hurry and is usually brought on by stressful situations like those caused by overdemanding parents, imminent examinations, and worries about puberty. Similar to this '*nervous diarrhoea*', but less well understood, is the so-called '*irritable colon syndrome*'. This typically occurs in the pre-school child who is otherwise healthy and who presents with chronic or recurrent mild bouts of loose stools, often offensive and blood-streaked, with three or four motions a day. There may be periods of constipation in between. It is difficult to make a proper diagnosis in these cases and most of them are probably due to dietary indiscretion. The condition usually returns to normal

when fried foods, fruit and sweets are excluded from the child's diet. Some cases may be due to a low grade infection with an enteropathogen.

Lastly, there are occasional cases of diarrhoea which are extremely difficult to diagnose or treat in the home and which need to be managed in hospital. Two such cases were seen recently: Case I — Coeliac disease with secondary lactose intolerance; and Case II — Primary Sucrase-Isomaltase deficiency with a complicating lactase deficiency following gastroenteritis.

Case I

M.S. (date of birth: 6.3.69).

This child was first seen at 14 months of age with a history of failure to thrive. She was born of unrelated parents, after a normal pregnancy and delivery. Birth weight was 6 lbs 9 oz. She took milk feeds well up to the age of 5 months when she weighed 17 lbs. At this time cereals and other solids were introduced and from then on the child fed poorly, vomited frequently and had bouts of bulky, greasy, offensive stools, about four times a day. There were two healthy older sibs in the family. Examination showed a pale, miserable and extremely irritable child who was markedly underweight at 15 lbs. She had marked wasting of the subcutaneous tissue and loose folds on the buttocks. The abdomen was distended. She was tentatively put for a period on a milk-free and lactose-free diet but made no improvement. She was then started on a gluten-free diet and there was an immediate improvement both in the child's behaviour and in the nature of the stools. However, the mother found it rather difficult to keep up this strict gluten-free lactose-free diet and on 7.6.70 the child was admitted to hospital because of frequent, watery stools. Her weight on admission was 13 lbs 4 oz and the subsequent weights during her 10 week stay in hospital are shown in the figure. It should be noted that once more there was no improvement on low-lactose milk and during this period she had several relapses of severe diarrhoea needing intravenous fluid therapy. When a strict gluten-free diet was re-introduced the diarrhoea soon

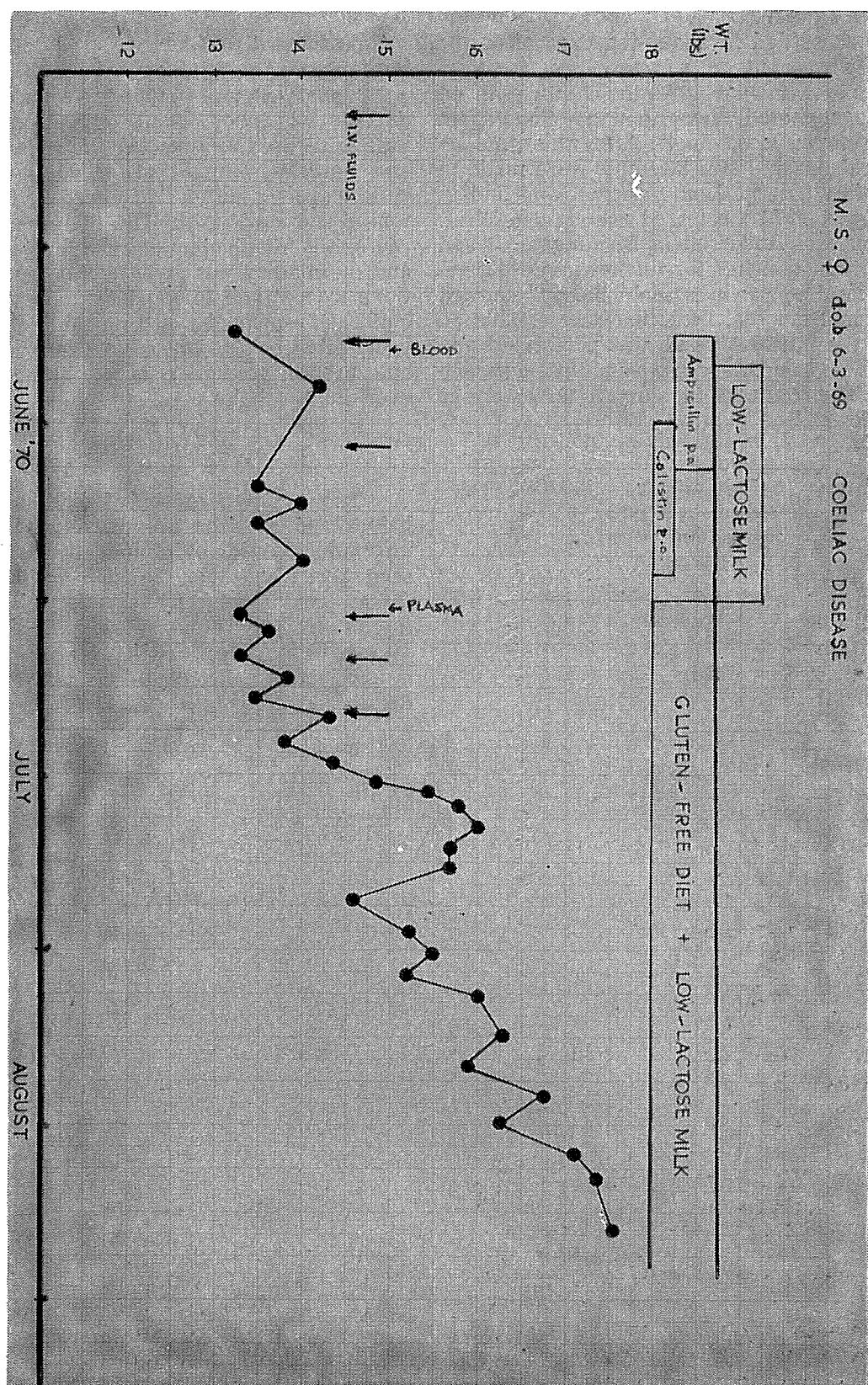
settled and the child's weight continued to increase steadily. The child was discharged home well on 22.8.70 weighing 17 lbs 8 oz and has remained well since. She can now tolerate milk and milk-products but has to continue on a gluten-free diet.

Case II

J.N. (date of birth: 14.4.71)

This infant was born at 37 weeks gestation following a normal pregnancy and delivery. Birth weight was 6 lbs. 11 oz. and there were no immediate neonatal problems. During the first 2 months she was a poor feeder, had infantile colics and her buttocks were constantly sore. In August 1971 (at four months of age), she had an episode of diarrhoea and very sore buttocks. This recurred in September when the family was on holiday in Malta. Seen at this time a diagnosis of "probably lactose intolerance following gastroenteritis" was made and the child started on a lactose-free milk formula ('Nutramigen'). The diarrhoea soon cleared up. Back in London, she was seen by Dr. A.P. Norman and the mother was to introduce the usual milk feeds slowly.

In October the child was given a full-strength milk feed by mistake and immediately she started vomiting and developed diarrhoea and sore buttocks. On 16.10.71 she was admitted to Great Ormond Street Hospital under the care of Dr. Norman and the diagnosis made was again one of secondary lactose intolerance. Investigations done were: Hb and Blood film Urea, Electrolytes, Urinalysis, X-Ray Chest — all normal; urine culture-sterile. Sweat Na-17 and 15mEq/lit. Swab from buttocks grew coagulase negative *Staphylococcus*. Stools for sugars contained 300 mg lactose and 100 mg galactose per 100 grams. 24-hour urine contained less than 5 mg/100 ml of sugar and the amino-acid pattern was normal. The stools were shown to be persistently acid on pH testing. The child was put on lactose-free milk 'Galactomin' and her diarrhoea settled soon after. She was sent home on 20.10.71, and remained well till April 1972 when during an attempt at restarting cow's milk and sugar her diarrhoea and sore buttocks recurred. On the same day, the child had also been given 'junior' aspirin' in syrup form. The diar-



rhoea settled in about ten days after the baby was put on a lactose-free, fructose-free diet. In June 1972, the child was given a sugar-coated 'Phenergan' tablet and again developed loose stools. After this time several unsuccessful attempts were made to restart the child on a normal diet and in August 1972 I referred the child to Prof. Charlotte Anderson in Birmingham, and she was admitted for further investigation. Peroral upper intestinal biopsy showed normal mucosa. Disaccharidase estimation on the mucosal tissue was performed and this revealed a sucrase-isomaltase deficiency. The results of the enzyme tests were as follows:

Enzyme	Units activity (u/mole substrate split/g wet weight mucosa)	B.C.H.lab range
Lactase	0.9	(1.0 — 5.7)
Sucrase	0.3	(4.0 — 8.6)
Maltase	11	(14.6 — 33.0)
Palatinase	0.3	(1.2 — 6.8)

This showed that lactase was on the borderline of normal, probably indicating a secondary lactase deficiency earlier on. Sucrase was almost completely absent. Palatinase is used as a marker for isomaltase and there was only a trace of activity. The child was first put on half and half 'Galactomin' and cow's milk and then just on cow's milk. She had no diarrhoea after this and the mother was given dietary instructions to continue to avoid sucrose. The child has remained well since and it is expected that as she grows older she will be able to tolerate more sucrose than she ever did as a baby.

Summary

The common causes of diarrhoea in babies and children are discussed. Two uncommon causes of prolonged diarrhoea seen recently — one a case of coeliac disease complicated by secondary lactose intolerance, the other a case of primary sucrase-isomaltase deficiency with acquired lactase deficiency — are reported in detail.

PROBLEM EVENTS AND PSYCHOSOMATIC DISORDERS IN FAMILY PRACTICE

G. T. FIORINI
M.D.

In April, 1970 a group consisting of 134 patients was chosen and studied, with results which were published in this periodical for June 1971. It will be recalled the group consisted of 77 patients suffering from what were diagnosed as psychosomatic illnesses, and of another 57 patients who had come to the office for some reason such as pregnancy, an injury, a minor cold etc who served as controls. In that survey patients had been questioned about the occurrence in their lives of recent or chronic psychotropic events, as well as about their hobbies or tension relief activities. Each event had been given a score of one. The number of events had been recorded and an attempt was then made to relate the incidence of psychotropic events to psychosomatic illnesses. The following had been the score obtained by the psychosomatic cases and by the control group:

and to see how their lives had evolved in the process. In this way more insight was gained into the patient's problem and the effect of treatment could also be assessed. It became even more apparent than ever that events do indeed play an all important part in the causation of emotional and somatic illnesses. Undoubtedly there is a certain degree of emotional participation or concern on the part of the family physician with the upheavals in a patient's life and rightly so. It has to be realized that a patient coming to a family physician may not only accept a professional, medical appraisal but may also appreciate non-medical advice.

In reviewing the previous study it became apparent that the assessment of the psychotropic events had been inaccurate. All psychotropic events had been given a score of one regardless of the type of event.

Psychosomatic Cases	No. of Events	Acute	Chronic	No. of Tension Relief Activities
77	372	204	158	303
Average	4.93	2.6	2.05	3.9
<hr/>				
Control Group				
57	187	127	60	256
Average	3.28	2.23	1.05	4.5

The same 134 patients were reviewed two years later, in 1972. Most of the patients had been followed as they either returned to the office for other complaints or else members of their family had come to the office for other reasons enabling us to obtain a continuous history and to assess the effect of treatment. It became very interesting to follow these patients

Marriage, pregnancy and bereavement had each been given a score of one. In many instances even the same event may have a different psychotropic effect on different individuals depending on circumstances. A first pregnancy to a married woman may not have the same effect as a first pregnancy to an unmarried girl. The accidental death of a young father in a young family

will not have the same effect as the death of an elderly father after a wearying, long drawn out illness. It has to be equally emphasized that even a happy event by causing a high degree of excitement can be equally stressful and exhausting. On the other hand the same event may not be equally stressful. As soon as the patient's history and event history are studied in depth the patient will be seen in a different perspective. An insight is obtained in the mechanism of operation in the home life of that particular person weighing the conflicting stresses acting on the family unit from the outside in the form of economic and social stresses, while, the conflicting stresses and strains between the members of the family can also be studied.

It was obvious from studying these patients that while their complaints were persistently somatic there was a degree of emotional disturbance which required direct individual consideration apart from its somatic counterpart. It also became apparent that on many occasions by concentrating therapy on the emotional disturbance the somatic symptoms improved without it being necessary to have recourse

to any of the standard somatic prescription items. However, to prevent a recurrence or to effect a lasting cure the emotional disturbance had to be treated for longer than the somatic complaint warranted. On studying the event history closely in relation to the medical history and findings it became apparent that the events of greater relevance were those that presented the patient with problems which were insurmountable or unresolvable by him. It has to be emphasized that while a psychotropic event may create a problem for one patient, it may not do so for another patient. The physician will have to judge whether an event will create a problem for the patient or not, even though in some instances the patient may deny that a particular situation (event) actually does so.

The main problem events affecting these patients were found to fall mostly within ten main groups. A relationship was established between the problem events, the age and sex of the patient and the presenting symptom. The symptoms have been divided into four groups. They are usually limited and surprisingly repetitive.

The incidence of the ten problem Psychotropic events in the two groups.

Problem Psy. Event	Psychosomatic Pts.	% of Total	Control Group	% of Total
1 Immigration	15	19.5	5	9.4
2 Teenagers in Home; Son or Daughter to be married	11	14.0	2	3.5
3 Major Debts or buying a house	6	7.8	6	10.5
4 Newly wed and/or First Pregnancy	4	5.2	9	11.8
5 Elderly spinster or widow	2	2.6	0	0
6 Alcoholic Spouse	1	1.3	0	0
7 Unemployed husband or both husband & wife unemployed	8	10.4	0	0
8 Bereavement or chronic illness or disabling injury in member of family	13	17	4	7
9 Infertility or sterility in either of married couple	4	5.2	2	3.5
10 Separation or Divorce	2	2.6	1	1.7
 TOTAL	 66	 85.6	 29	 46.4

In Group 9 symptoms are related to the head and general well being consisting of headaches, dizziness, mental confusion, irritability, bad nerves, lassitude.

In Group B symptoms are related to the gastro-intestinal tract consisting of burning in the epigastrium, epigastric pain or epigastric bloating, abdominal discomfort etc.

In Group C symptoms are related to vague aches and pains usually in the muscles such as dorsal spine, rib cage, lumbar or sacral region which are usually diagnosed as myalgias or mild rheumatoid arthralgia but to which the patient reacts

vigorously.

In Group D symptoms consist of pruritus ani and paraesthesia all over the body.

In analysing these figures it will be noticed that immigration, teenagers, unemployment and bereavement form 60% of the Problem Psychotropic events, while in the control group these four events form only 19.9%. On the other hand buying a new home and newlyweds and/or first pregnancy show a higher incidence in the control group, forming 22.3% of Problem events against 13% in the psychosomatic group of patients. The stress factors in-

Control Group

1. Immigration — 5 cases Ages 20-27 — 4 cases	4 F 1 M
Age 57 — 1 case	
Presenting Symptom — Injury	— 1
Scars on face	— 1
U.R.D.	— 1
Sinusitis	— 1
Diabetes	— 1
2. Teenagers in Home — 2 cases Ages 40-47	2 F
Presenting Symptom — Bells' Palsy	— 1
Injury	— 1
3. Buying a House — 6 cases Ages 22-36	4 F 2 M
Presenting Symptom — Respiratory Diseases	— 3
Lumbosacral strain	
Pregnancy	— 1
4. Newly Weds or est. Preg. — 9 cases Ages 21-27	8 F 1 M
Presenting Symptom — Pregnancy	— 8
Tinea versicolor	— 1
5. Elderly Spinster or Widow — no cases	
6. Alcoholic Spouse — no cases	
7. Unemployed Husband or both Husband and Wife unemployed — no cases	
8. Bereavement or Chronic Illness in Family — 4 cases	
Ages 49-59 —	2 F 2 M
Presenting Symptom — Lumbosacral strain	— 1
Tennis elbow	— 1
Diabetes	— 1
9. Infertility or Sterility — 2 cases Ages 39-55	2 M
Presenting Symptom — Bronchial Asthma	— 1
Chest Pain	— 1
10. Marital Separation or Divorce — 1 case Age 42	1 F
Presenting Symptom — Pap Smear & Diabetic Child	

Relationship Between Problem Psychotropic Event, Age, Sex, Presenting Symptoms in Psychosomatic Group

herent in these events are self evident in some cases and not so clear in others. Many people go over these hurdles in life successfully unaided. The fact that not everyone will succeed in getting over the hurdles is a fact we all know and happens at any age. As infants and children we need nursing and assistance and loving care. Through education we become more and more independent and self reliant. However great or strong we may be, even when we are adults and mature, there again may still come a time or two when calamity strikes, our reasoning becomes confused, our emotions cause us to behave erratically, our whole system gets out of gear and again we need the protecting hand of a friend or of a member of the family. When these are lacking or insufficient there is the protecting hand of the medical profession. It would be wrong for a physician to fail to understand the socio-economic problem along with the medical problem afflicting a patient. At this stage the patient may not only require the sympathy and understanding, which he normally expects from his family physician, but also the assistance which could help him in his particular socio-economic problem.

Three of the patients in the psychosomatic group, through the occurrence of other subsequent aggravating events, required psychiatric help eventually. In the control group there was only one patient who required psychiatric help.

In an age where bacteriological illnesses are on the decline emotional illnesses are becoming more prevalent and more apparent to the medical profession. It is also being understood that emotional disturbances, caused by events, may cause psychiatric conditions as well as organic illnesses.

The conditions affecting these patients, such as lassitude, are repetitive and referred mostly to the gastrointestinal tract or to the general health, but there are other illnesses such as thyroid dysfunction, bronchial asthma, cardiovascular diseases that have an emotional connotation that in many cases precedes the organic illness.

The stresses induced by the ten psychotropic problem events are understandable.

However, there are two problem events, immigration and teenagers in the home, which are worthy of some additional comments.

Immigration

Immigration, at whatever level, is expected to disturb the milieu. Leaving one's homeland is a traumatic experience. The prospective emigrant has to sever his relationship with his immediate family and close friends and his familiar terrain. It is true that in the young the whole episode could be tinged with a spirit of adventure. The hurdles an immigrant has to overcome may be the language barrier, job insecurity, a demanding economy, competition, isolation from what could have been a closely knit family, loneliness, a different way of life with its different social customs, a different climate requiring a different leisure time, a change of job, with what might be considered a loss of self esteem. It is true that many immigrants overcome these challenges and are able to improve the image they have of their own self. That others are not so fortunate is not very surprising. The fact remains that the recent immigrant, for the first few years, is more vulnerable and a contrary event can be very unbalancing. Illness, injury, unemployment will become even more traumatic to a landed immigrant without any friends or relative to rely on. Such a momentous event is bound to cause psycho-physiological problems and reactions. Whether this biological reaction will be contained within the limits of normality will depend on subsequent events and on the potential and personality of the individual concerned. It is interesting to note that the incidence of psychosomatic illnesses between the ages of 20 to 40, when immigration seems to be a problem, is twice as prevalent in the female sex, while in the ages between 40-60 the ratio is reversed, being twice as prevalent in the male sex. This would suggest that women between 20 and 40 and men between 40 and 60 have a harder time adapting to a new environment.

Teenagers in the Home

Watching children grow from a state of complete helplessness to mature, articulate, competent adolescents who are inform-

ed and sensitive to events around them inspires wonder. Parents, very often, find it hard to believe that their children, whom they completely possessed when they were infants, have grown beyond their influence. These so-called children have become almost unrecognizable distinct entities with their own morality, intellect and outstanding capabilities and they have ceased to be objects or things. They cannot be manipulated anymore, and they are being influenced by extraneous forces which the parents may not completely understand, and over which they have no control. The resulting reaction, between parents and children, may be one of conflict unless there is an accomodating mental and emotional readjustment by all parties concerned.

Naturally the so called generation gap that exists between parents and their teenage children is not a problem in all families. In some families there is complete harmony between parents and their children, while at the other extreme there is a breakdown in understanding and communication in the home with the usual behaviour problems. However, to the ordinary stresses in a teenage home other special ones may commonly appear in some segments of non-English speaking immigrant families. This is the case when the parents in their own country have been badly educated and will therefore find it very difficult to assimilate the English language. The generation gap in the family, in such instances, will be accentuated by a language and cultural barrier between parents and children. It is a fairly common experience to find the parents speaking their own ethnic mother tongue between themselves and to their children while the children answer in English and speak English amongst themselves. In the early stages when the children are young, the bilingual structure in the home may be considered as amusing. However, subsequently as the children become older and their emotional demands more complex the language barrier becomes frustrating. For guidance the children will rely on school teachers whose social and cultural values could be in conflict with those of the parents. As the children grow older the

parents may feel that they are losing their influence and their control over the children, and also that the children are losing respect for them. The final outcome may result in stress disorders of a psychological or somatic nature or behaviour problems affecting the children and parents alike, such as drug abuse or increased alcohol intake.

Events may affect man's destiny and well being. Psychotropic events may cause mental and somatic aberrations. Disturbing events if of long standing and productive social problems may cause mental or somatic illnesses. Patients coming to the office for so-called functional illnesses should not be discharged from the office or hospital with a few well-chosen words of reassurance at one extreme, (although this could be sufficient with some patients), or referred immediately to a psychiatrist at the other extreme. The family physician should have a comprehensive appraisal of the disturbing factors in an individual's life. Any socio-economic cultural illness should be handled through the appropriate channels. The family physician should also try to establish rapport with the patient, developing a line of communication which allows him to exert influence gradually while watching the progress of the patient. Public health nurses, social workers and other agencies should be used readily when required. An attempt was made here to show that psychotropic problem events may cause psychiatric and organic illnesses if not treated and checked at an early stage. The number of psychosomatic illnesses listed here were restricted to certain conditions affecting the brain and the gastrointestinal tract, to menstrual disorders, and to neuro-dermal conditions. There are other conditions such as rheumatoid arthritis and other related conditions, cardiovascular disturbances such as essential hypertension, bronchial asthma, thyroid disturbances, and upper respiratory tract infections — all of which have an emotional connotation which it would be negligent to disregard and it is more than likely that these conditions are triggered by stress factors and events. In other words while events may be a product of man, man is also a product of events.

MAN AND HIS ENVIRONMENT

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This is an abridged version of a Public Lecture given under the auspices of the Royal University of Malta Department of Architecture in the series "Man and Architecture" in February 1973.

Man has both an internal and an external environment. The internal environment is the environment within his own body and this is kept constant by complicated and elaborate means; the external environment on the other hand is that which is found outside and around his body. The human body is continuously being played upon by a multitude of external environmental factors but it resists the impact of these external forces and maintains its internal environment in a steady state with the external. The ability to survive in varying environments is the central physiological characteristic of living things.

Man is the main purpose of architecture. This talk will deal with the physiological factors that influence architectural expression (Fig. 1) — with the relation of man to chemical, physical and biotic factors in his external environment, his adaptation to atmospheric temperature, pressure, oxygen concentration, light, radiation as well as contamination of the atmosphere.

Man and his environment is a fascinating topic which has attracted the attention of biologists for centuries. The Greek physician Hippocrates and his associates appreciated the role of the environment in relation to health and disease in man, emphasising the importance of "Airs, Places and Waters" in regard to well-being. This tradition was consolidated throughout the medieval period, first by the Arabs and later by Western European scholars, but it began to be questioned during the Renaissance. Santorio gave a tentative back-

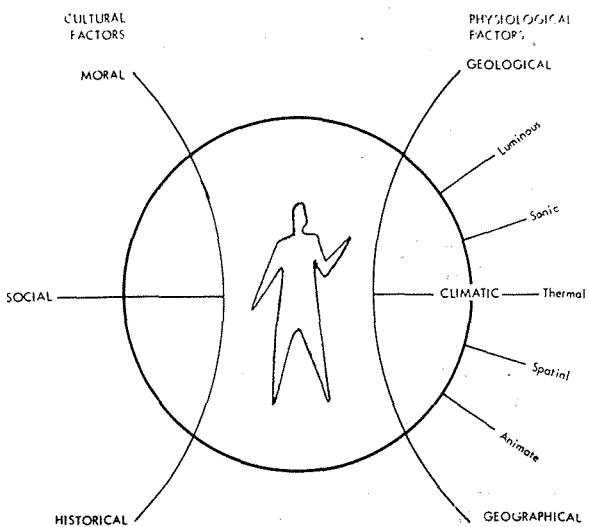
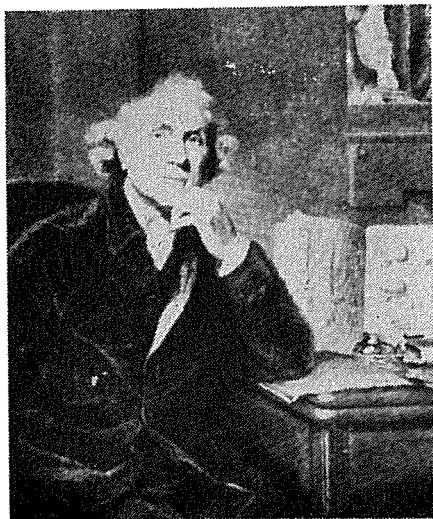


Fig. 1

ground for systematic studies of the cyclic relations of humans with the environment. John Hunter (Fig. 2) made observations on living organisms in relation to their surroundings and disease. It is however to Claude Bernard (Fig. 3) that we owe our greatest knowledge of the adjustment of living things to environmental conditions. He developed the concept of the "milieu interieur" in which internal regulating mechanisms are related to feedback systems from the various parts of the living material itself and from its environment — preservation of internal stability and constancy in an organism, despite any external change, is the central characteristic of life. We are now becoming aware of the importance of the environment at social and ecological levels, in such matters as over-population, air and water pollution, and the destruction of nature's eco-



John Hunter.

logical areas. Indeed so blind are we in what we do that we are in danger of destroying for ever the environment in which we took so long to evolve.

Man is throughout life being subjected to the effects of the external environment; this is evident from his very existence in utero where he is subjected to the external environment of the amniotic fluid, right up to old age when the effects of the external environment may be very manifestly evident. Throughout life, multiple physiological processes act as adaptive mechanisms by which the equilibrium between the external and internal environment is achieved. These mechanisms consist of a series of interrelated, integrated and dynamic changes which affect the various organ systems of the body.

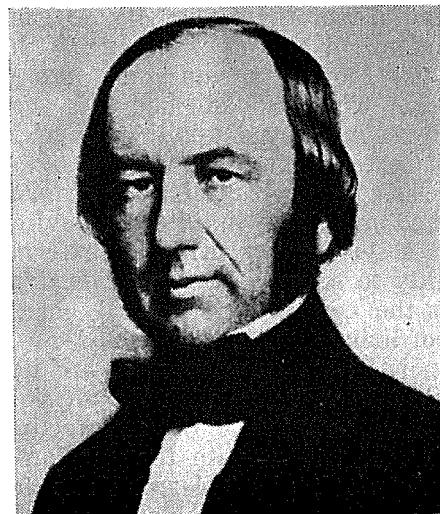
In the nervous system, adaptation by habituation is apparent; in other words if sensory stimuli are repeatedly applied, the response to them gradually diminishes or disappears. Arctic man has adapted himself to cold by setting his temperature thermostat at a lower level so that he responds to cold with less shivering.

Muscular tissue, which forms a large proportion of the human body, can adjust its strength and endurance to increased mechanical requirements. Muscular work also contributes to temperature regulation

by heat production, as in shivering and increased muscular tone, or by actual contraction. In birds, shivering, especially of the chest muscles, is the most important adaptive mechanism in cold exposure.

On the heart, heat and exercise produce an increase in the rate. Training is said to produce a slower heart rate — this, in fact, is the only difference between trained and untrained subjects at rest.

The lungs are the means by which man can obtain his most urgent molecular requirement from the environment: oxygen. Lung ventilation has many functions — it is related to surface water loss by evaporation and it regulates temperature by producing heat dissipation, as is well seen in the panting of dogs and other mammals.



Claude Bernard.

The digestive system is in direct contact with the external environment at both its oral and anal ends, and, though its contents are part of the external environment, they are separated from the internal environment for the most part only by a single layer of cells. Thirst controls water intake hence water balance; hunger, appetite and satiety adjust the food intake to body needs; while the intestine regulates and limits absorption and rejects most noxious substances.

The kidneys are of importance in conserving water, as well as excreting salt and

nitrogenous products. Completely terrestrial forms must conserve water at all times. Indeed, some of the most successful terrestrial animals, mammals and insects, have kidneys capable of producing highly concentrated urine, and these animals can survive in deserts with no access to drinking water.

The skin protects man from mechanical injuries and invasion by organisms; it serves as a sense organ; it helps in the regulation of body temperature; it participates in metabolism as, for example, by forming a fat depot; and it also takes part in water and salt metabolism by perspiration.

Mechanical protection of the skin results from its thickness, the hardness of its outermost keratin layer, and its pigmentation. The importance of keratin is evident when repeated mechanical stimuli in one area cause callosities, as often appear on the palm of a farmer's hand. Normal skin colour is due to the black pigment melanin, to the red pigment of blood, and to the yellow carotene stored in skin. Racial differences in skin colour depend largely on the amount of melanin and this pigment may possibly account for the well known greater resistance of black skin to external irritants.

Temperature regulation is contributed to by heat loss through the skin. Below 31°C , heat loss depends on the dilatation of the blood vessels of the skin — this leads to the shifting of blood from the interior to the surface so that the skin temperature is raised and heat is lost. Above 31°C , heat loss is mainly from sweating. Man is foremost in the animal kingdom with respect to the development of the sweat apparatus and it is in fact this that has allowed the human race to inhabit the whole earth including the most torrid zones. Frequent and continuous exposure to high temperature causes an increase in sweating; the excessive sweating of newcomers to the tropics is well known. The total number of sweat glands is the same in all races, but the number of active ones differ; for example, Ainos have the fewest, Russians have slightly more, Japanese still more and Filipinos living in the tropics have the most.

The skin has important functions in relation to water and salt metabolism. Insensible water loss through the skin proceeds continuously and unconsciously throughout the day and night and is associated with heat loss. In dehydration this insensible water loss is diminished.

We shall see now, how man reacts to weather and climate. Weather and climate conditions in the atmosphere are continuously interacting with the internal physiological processes of man. The weather affects the human body in five ways: it stimulates the skin by changes in temperature; it may stimulate the eyes and head by solar radiation; the internal mucous lining of the nose may be stimulated by olfactory substances, changes in the humidity of the air or possibly allergic reactions to allergens in the air; the lungs may be stimulated by changes in the ion content of the air, by trace substances such as ozone, by air pollutants, by reduced pressure of oxygen, especially at high altitudes, and by thermal stresses. Weather may stimulate directly the peripheral nerves possibly by electro-static and electro-magnetic fields, by diastic changes in atmospheric pressure, and by microvibration of the earth and of its buildings.

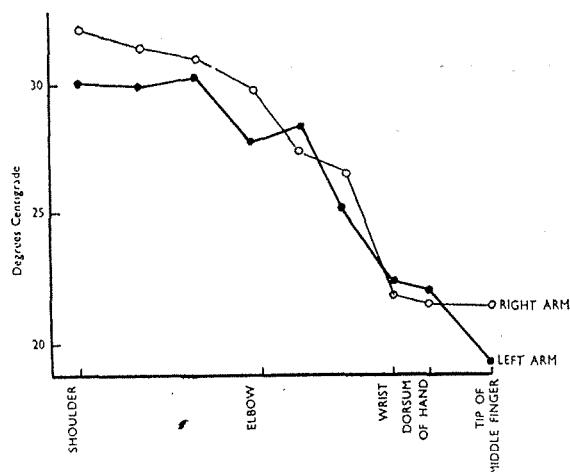


Fig. 4

The temperature of a healthy human being is kept relatively constant at 37°C , but this is the temperature in the mouth

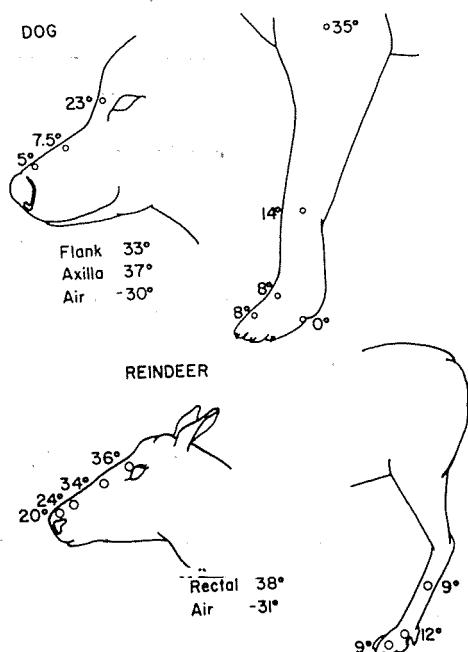


Fig. 5

or rectum. There are variations in temperature in the different parts of the human body and even in different parts of the same limb (Fig. 4). The same holds

for animals, such as the dog and reindeer (Fig. 5). The body temperature of a healthy human being varies at different times of the day, and it also varies in relation to external temperature and body activities (Fig. 6).

One may ask, how does the body manage to keep its temperature relatively constant at 37°C ? The temperature regulation in the body depends on the balance of heat production and heat loss. The balance of these factors is illustrated in Fig. 7. The factors which affect the heat exchange of the clothed body are shown in Fig. 8.

Human beings are known to live in climates where the extreme cold winter may reach -50°C , as in the interior of Siberia and North America. Although it is known that man has lived in Arctic Alaska for the last 5,000 years or so, physiological adaptation to cold accounts for only a small part of Man's conquest of cold; his adaptation is in fact mostly cultural.

Man responds to cold by increasing his metabolism and altering his peripheral insulation, at the same time improving his muscular activity through shivering. Continuous exposure makes man more tolerant to cold; for example, young Norwegian males and Eskimos develop a marked re-

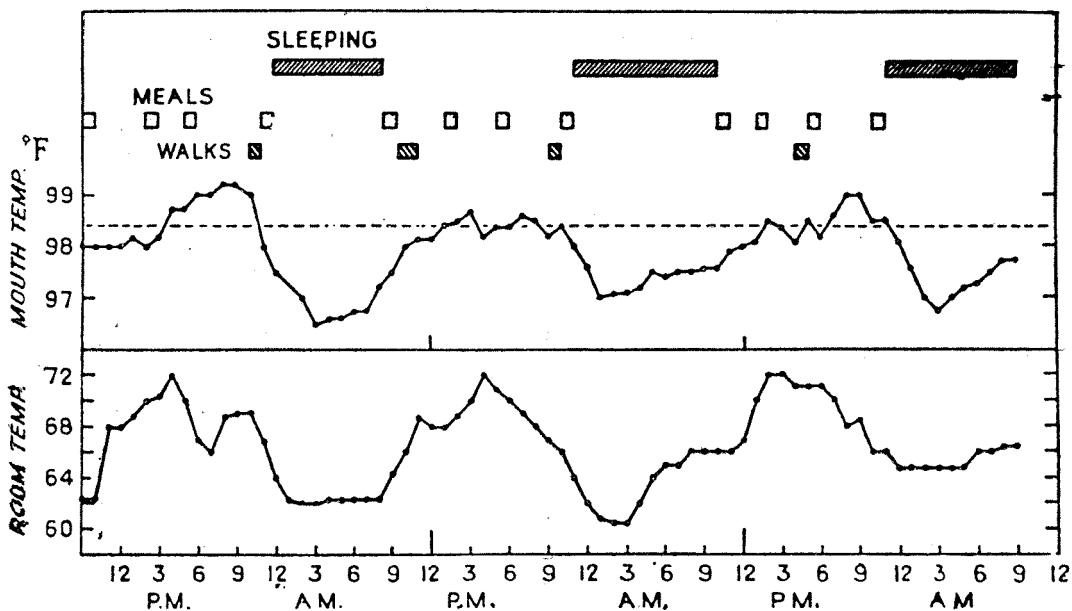


Fig. 6

sistance to cooling of their limbs.

Another interesting adaptive function of man to cold is that cold feet fail to melt the snow under them; the people of a religious sect who go about barefooted can, in steady cold a few degrees below zero, walk on snow with bare feet without trouble from icing. Sir Cedric Hicks investigated a group of Australian aborigines who live naked in areas of marked variation in temperature and who sleep naked in extreme cold near small fires. He found the skin temperature of these aborigines to be far below that of Europeans; it seems that these people control their heat loss at night by reduction in the blood supply going to the colder areas of exposed skin.

What about man's adaptation to heat? Over a fifth of the world surface, an area equal to that of Africa, is occupied by desert or semi-desert. Man living in hot dry climates is mainly concerned with preventing dessication and keeping cool. Reliance has to be placed on the evaporative cooling of the skin rather than on an increase in skin blood flow. Evaporation takes place mostly through sweating; respiratory ventilation is of minimal importance in man; increased surface area is not useful under desert conditions as heat would be added to the skin by solar radiation; decreased activity and work is impractical, while reduction in the metabolic rate seems to be minimal.

Heat produces an increase in the heart rate and swelling of the feet which may

reach disabling proportions in inactive people, as is often seen in ship passengers passing through the Red Sea. There is a reduced motility and tonicity of the digestive system which accounts for the reduced appetite we all experience in hot conditions. Failure in adaptation to heat may result in heat stroke, heat exhaustion, heat cramps, and dehydration.

We in Malta have a particular interest in the effects of radiation from the sun on the human body. Sunbathing is said to be a route to health and, though no doubt giving subjective pleasure, its true relation to health is still unknown. Solar radiation directly affects body heating, vision and the general sensitivity of the body surface; it is concerned with vitamin D synthesis, with the ultra-violet radiation damages of sun burn and pigmentation, as well as with changes in skin colour.

Sunburn produces dilatation of the skin blood vessels and deposition of the pigment melanin. The relationship of hair, skin and eye colour to solar radiation is well known; light skinned, blonde and red-headed, blue-eyed frecklers are known to be more sensitive to sunlight. A dark skin protects from sunburn but not from heat gain, for infrared radiation absorption is the same for both white and black skin.

What is the effect of high altitude on the human body? With increasing altitude, the pressure of atmospheric oxygen falls. Above 10,000 feet most persons require the addition of oxygen to the air they breathe, and at 35,000 feet 100% oxygen must be

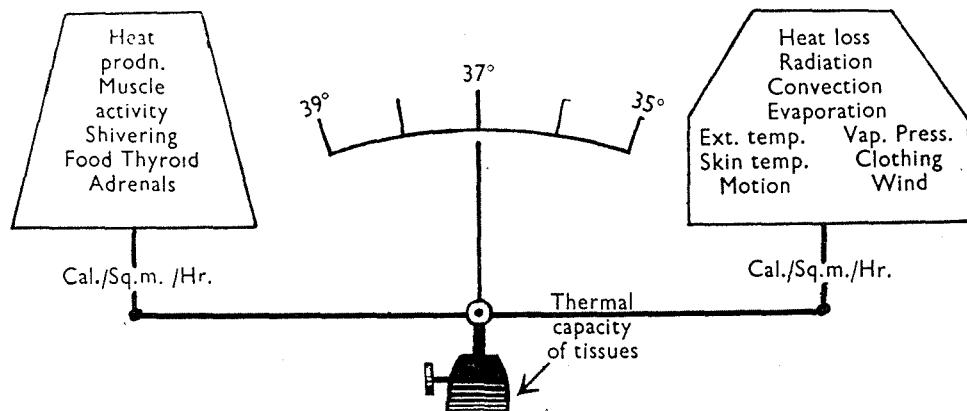


Fig. 7

Primary factors	Secondary factors
Metabolic rate	Clothing temperatures
Air temperature	Air motion beneath clothing
Mean radiant temperature	Skin temperature
Air motion	Sweat rate
Vapour pressure	Wetness of skin and clothing
Clothing type and materials fit	Cooling efficiency of sweating

Fig. 8 *Factors affecting the heat exchange of the clothed body*

breathed. It is surprising to learn that both Hilary and Tensing in 1953, when on the summit of Mount Everest, removed their mask and spent ten minutes breathing atmospheric air, though Hilary reported that he soon felt clumsiness of movement and impairment of thought.

Man can become partially but never fully acclimatized to high altitudes and those who acquire acclimatization never reach a high degree of physical and mental activity, though this is not the case in

native high altitude residents. The low oxygen tension at high altitudes causes hyperventilation in man as well as increase in the number of red cells in his blood. Loss of natural acclimatization to high altitudes may cause chronic mountain sickness or Monge's disease.

Early balloon flights and more recently space flights have provided more information on the effects of altitude on man. In space, man depends for his existence on an artificial environment based on bio-

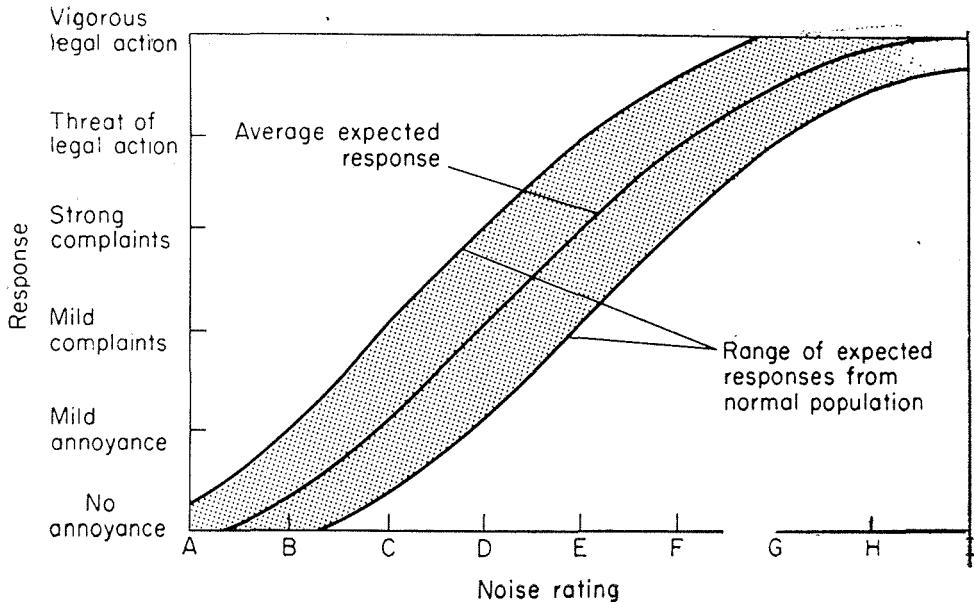


Fig. 9

instrumentation. Manned orbital space flights have brought us in relation to our ultimate environment, the universe.

How does pollution affect the human body? Man is influenced by the contaminants found in the atmosphere of industrial and urban environments. These consist of gases, mineral dusts, combustion products, radio-active fall-out, vegetable poisons and micro-organisms. Tobacco smoke and the exhaust of automobiles in congested urban areas are specialized types of local pollution.

Ionizing radiation can occur naturally in minimal amounts, but it is mostly man-made, as from X-Rays used in medical diagnosis and therapy and from the atomic fall-out from the testing of nuclear weapons in air. Radiation causes changes in the structure, bio-chemistry and genetic constitution of cells, as was well evident in the Hiroshima survivors of the atomic bomb.

The human eye is a complex structure. The eye can adapt to darkness — the so-called day and night vision — as well as to visual acuity, depth perception, binocular vision and colour perception. Dark adaptation depends on the regeneration of photo-pigments, but recently the photo-chemistry of the fluids of the eye such as the vitreous humor have come into prominence. The form and texture of an object seen by the eye depends on the direction of light. It is known that the sensitivity of the eye varies to different wave-lengths both for day and night vision.

The ear is also a complex organ. Sound waves are propagated either by air borne means or by impact. In man the external ear has little importance as a megaphone and the intensity of a sound can be increased by cupping the hand over the

ear; but it has some importance in that it renders sounds coming from the front more audible than those coming from behind.

The more intense the sound the greater the fatigue effect, though it has been found that industrial and engine noise with high frequencies is more easily damped than the human voice containing many low frequencies, so that speech intelligibility may actually be increased in noisy environments by the use of ear plugs! It is also known that loudness declines during the continual presentation of a sound. During sleep, certain sounds become more audible and can produce arousal, independently of their intensity. The behaviour of man exposed to noise varies in different individuals and in the same individual at different times (Fig. 9). Higher and intermittent noises tend to be more annoying than continuous and lower ones. On the other hand man can adapt psychologically so that an individual can "put-up" with even very loud noise.

In normal life there is a continuous flow of impulses from the sensory organs to the brain. If these are completely eliminated, as by suspending a person in water for long periods in total silence and darkness, a remarkably disagreeable reaction producing oppression and even alarm may result, for this would constitute a situation which man rarely encounters and to which he is not adapted.

In conclusion then we may say that man is indeed dependent on his environment and must respect it for the sake of his own survival and happiness. From this arises his urge to control, manipulate, and understand the environment around and within him which ultimately determines his success or failure.

THE HOLY INFIRMARY OF THE ORDER OF ST. JOHN

JOSEPH BORG

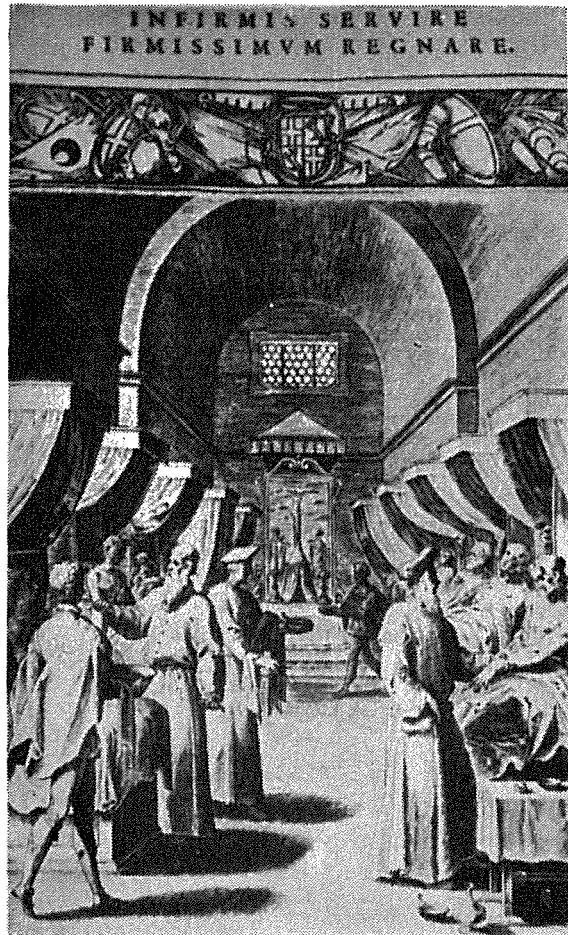
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The "Holy Infirmary" or hospital of the Order of St. John was the chief *raison d'être* of the Brotherhood. The very first concern of their founder and first rector, the Blessed Gerard Tom de Martigues from Provence, after Pope Paschal II had by his Bull "Pie postulatio voluntatis" issued at Benevento on the 15th. February 1113 confirmed

the establishment of the order and taken it under his protection, was the erection of a hospice and a hospital annex in Jerusalem for the benefit of the sick or weary pilgrims who had gone there to visit the places which had been sanctified by Our Lord's presence. The oldest document in the Royal Malta Library is one dated 1107 and relates to a donation by King Baldwin of Jerusalem to the Order of some property on Mount Tabor for the noble purpose of building a hospital thereon. By 1104 the hospitalers had already become armed monks. When Saladin drove the Christians from Jerusalem in 1187, the Knights retreated to Acre, which had been called Ptolemais under the Greeks, in the north of Palestine or present-day Israel, where they built a hospital for the benefit of the sick besides some fortifications for its proper protection, the place then being called St. John of Acre.

Incidentally, the skull of Blessed Gerard had been jealously kept by the Knights, first in the Holy Land and then at Rhodes. When this stronghold fell, the skull was taken in 1535 by Fra John de Boniface, Lieutenant-Grand Master and Bailiff of Manosque, to his Commandery of Manosque (in the Lower Alps at Provence in the South of France), the Order's chief property in the Priory of St. Gilles, and Blessed Gerard's presumed native place. In 1792 the French revolutionaries sacked the Order's church and the skull, deprived of its silver repoussé', was somehow sent to the Order's seat at Malta, where it is still preserved with loving care at the Order's nunnery of St. Ursula, in St. Ursula Street, Valletta. These Ursuline nuns of Valletta, who had been under the Order's special protection, bearing the white eight-pointed Cross on their black habits and hence also called the Jerusalemite Sisters, had been brought to



The great ward of the "Holy Infirmary".

Malta from Aracoeli in Syracuse in 1583 by the French Grand Master Cardinal Fra Hugh de Loubenx Vardale (1582-1595). They had first settled at Vittoriosa but later moved to Valletta when their church and convent were built in 1595. The reliquary in the form of a head, commissioned in 1674 by Fra Francis Carbonel de Lussan, then Bailiff of Manosque, made of silver and measuring 33 by 26 cm., was saved, and is now to be found in the Hotel de Ville at Manosque.

At Rhodes and wherever the Knights had settled they made the tending of the sick their chief and immediate duty, and the Head of the Hospital or "Hospitaller" was the Bailiff of the Langue of France. In Rhodes the hospital had even been provided with the first Apothecary recorded since 16th August, 1473, working under the general direction of the "Commissarius Sanitatis", while the first clerk of the hospital "scriba Infirmariae" was employed on 3rd December, 1476: (cf. Arch. No. 75); and the first ever Maltese to work therein and, indeed, the first to join the Order, was Fra Gonsalvo Vella, who was enrolled in the



Blessed Gerard's skull at Valletta

Langue of Italy at Messina on 15th September, 1480 and later attained the high rank of Bailiff (cf. Arch. No. 76).

When the Knights came to Malta on the 26th October, 1530 and settled at Borgo, they erected there in 1531 a very large hospital with a small church adjoining dedicated to St. Anne. When they crossed over to the new City of Valletta in 1571 they also constructed between 1574 and 1575, during the rule of the French Grand Master Fra Jean Levesque de la Cassiere (1572-1581), a very fine hospital "The Holy Infirmary", which was enlarged and improved by the Spanish Grand Master Fra Raphael Cotoner (1660-1663). On completion the "Sacra Infermeria" was one of the earliest organized hospitals in the world. It had six large wards, each provided with an altar, the four larger ones called "Gran Sala", "Sala Nuova", "Sala Vecchia" and "Sala dei Feriti" respectively; the first, dedicated to the Most Holy Trinity, was 505 feet long, 34 feet 9 inches wide and 31 feet high, overlooking the Grand Harbour. It was one of the longest rooms, unsupported by pillars, in Europe and consequently lon-

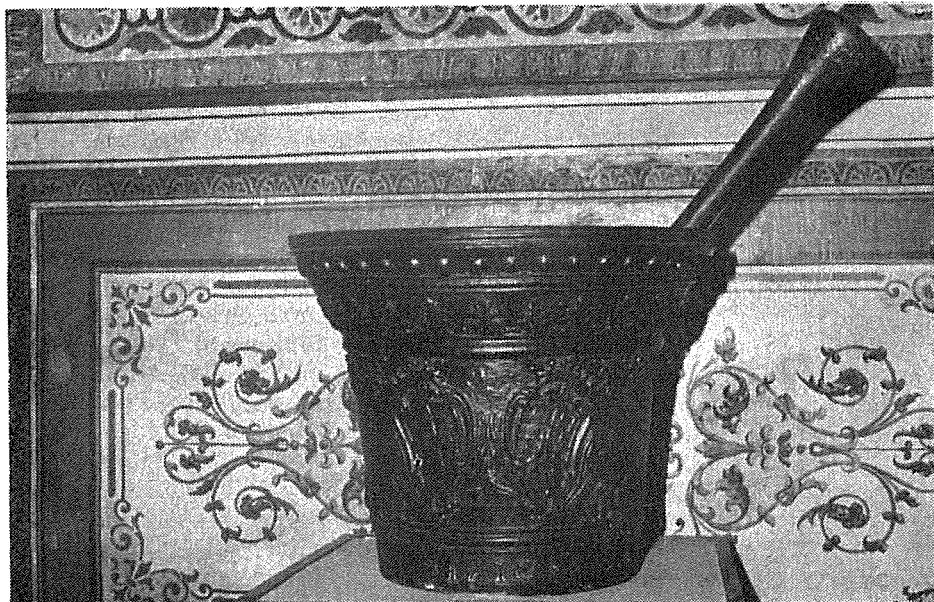


Grand Master Wignacourt's spherical pharmacy jar

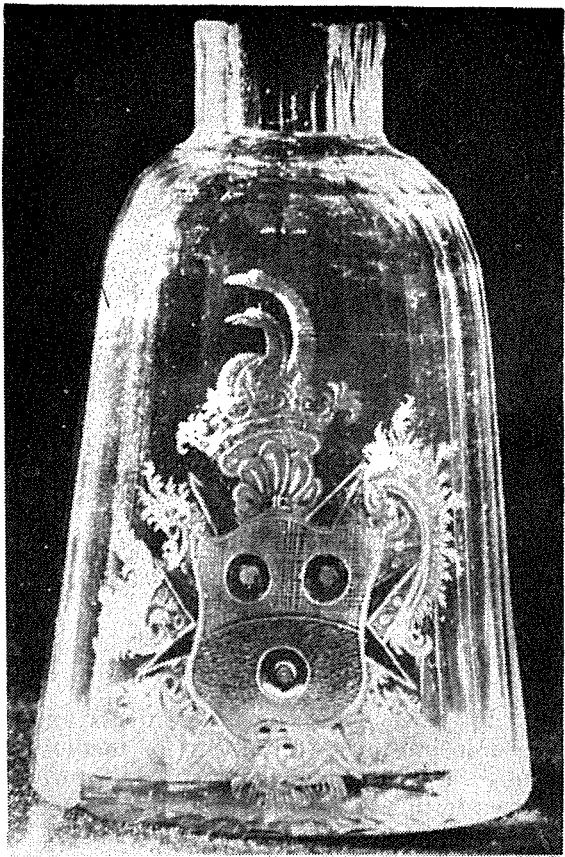
ger than the wards of any other hospital in the whole world; at one end of it was a valuable picture representing the Sultan of Turkey, Bayezid II giving the left arm of St. John the Baptist in 1484 to the French Grand Maser Fra Peter d'Aubusson (1476-1505) wearing Cardinal robes. Usually the hospital had 500 beds, at times even 745 and this number could be increased to 2,000 in case of need; its patients were most efficiently looked after, and it was considered one of the most advanced hospitals in Europe at the time. About 2,000 patients were admitted per year.

Patients took their meals from silver dishes, drank from silver bowls and ate with silver spoons, forks and knives, and it was the duty and honour of all the Knights as servants of the hospital to attend at meals to "their Masters the Sick". The food of all the patients was better and more carefully cooked than that of the Knights who served them; every Knight performed this service one day of each week. Grand Masters Alof de Wignacourt (1601-1622) and Anton Manoel de Vilhena (1722-1736) gave to the infirmary very fine sets of tin-glazed chinaware pharmacy jars, Wignacourt getting these from Urbino in Italy while Vilhena obtained them

from Caltagirone in Sicily and from Venice. It is recorded that 780 medical substances were available in them. Some of these pharmacy jars are now at the Valletta National Museum and some with representations of St. Anthony Abbot or St. Andrew or larger bluish ones at the Governor-General's Palace at Valletta. The Spanish Grand Master Fra Raymond Perellos y Roccaful (1697-1720) provided the hospital in 1710 with new sets of instruments and appliances necessary for the proper and smooth running of the pharmacy; while the German Bailiff Fra Francis Anton von Schonau von Schwrstatt provided a complete set of polygonally-shaped, Bohemian fine glass drinking bottles for all the patients and staff. This Knight was Bailiff of Brandenburg and had served the Order as Captain of the galleys, Commander of the Maltese Militia and Head of the Common Treasury. He was greatly beloved by his nationals, his fellow-knights and the Maltese, and, when he died on the 11th January 1743, was buried at St. John's Conventual Church inside his Langue's chapel at the extreme right side near the altar. All the officers, with the exception of the medical ones, were Conventual Chaplains. The Knight of Provence took charge of the sick on Sundays and were



Grand Master Perellos y Roccaful's bronze mortar and pestle

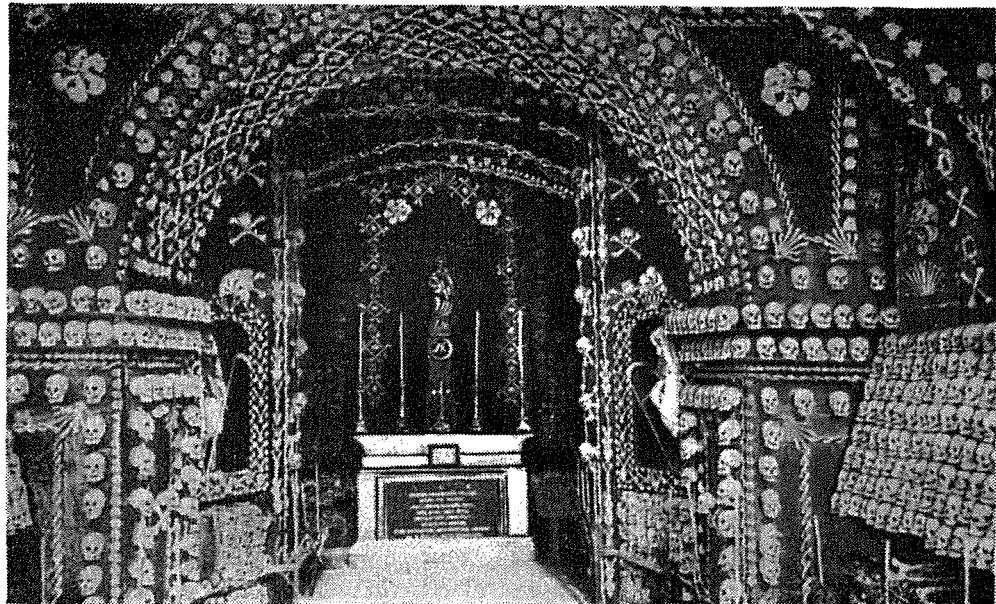


Bailiff Fra Francis Anton von Schonrau
von Schwrstatt's drinking glass bottle.

followed by the other Langues according to seniority, the Anglo-Bavarian and German serving together on the last day of the week. There was no discrimination in the nursing of the sick, except that if one happened to be a Knight he was entitled to have a brother-knight look after him, while if he were a slave he was accommodated in the ward underneath. The motto for this noble work was "*Infirmis servire firmissimum regnare*", as appears in Grand Master Cardinal Verdale's Statute of the Order issued in 1586, giving the duties of the Knights at this noble charitable Institution with this motto on page 30, over a drawing of the great ward. Mattia Preti's painting showing Saints Cosmas and Damian originally hung in the "Hall of the Wounded" of this hospital; it is now to be found in the main sacristy of St. John's Conventual Church.

In 1788 the annual cost for the running of the hospital was £7,947 or about one shilling per person per day. During the French occupation it was used as a military hospital and afterwards as a wine store. Under the British it was again used as a Military Hospital and lastly as Police Headquarters. During the Second World War it sustained great damage, but the "Gran Sala", which was not a total loss as the upper structures were, is now being restored by Mr. Michael Ellul a government Architect in charge of Antiquities. Just across its lower side street was a small cemetery with a chapel, dedicated to the "Holy Name of Mary" and built at the expense of the Italian Commendatore Fra Giorgio Nibbia in 1619 with a rather large room at its back where hundreds of skulls of Knights, Priests, Civilians and Slaves alike were arranged along all its walls to remind the onlookers of the inevitability of death, a point which had also been made in the epigram on the marble slab of Baron Bailiff Fra Wolfgang Philip von Guttenberg's tomb in St. John's "Fumus, Humus Sumus; et Cinis est nostra ultima Finis" — "we are like smoke and dust and we will end in ashes". This small church was appropriately called the "Chapel of Bones".

Not many years after the building of the "Sacra Infermeria" at Valletta, the French Grand Master Fra Jean Paul Lascaris Castellar (1636-1657) built the "Lazzaretto" on the islet, in Marsamxett Harbour. This hospital was greatly improved during the plague which ravaged the Islands for nine months in 1675-1676 and carried off 11,300 of the population, "when the corpses were thrown out into the streets remaining unburied so that the sky was their only cover, while the houses were turned into sepulchres", by the then Spanish Grand Master Fra Nicholas Cotoner (1663-1680), who also on the 19th December, 1676 instituted the School of Medicine and Surgery including Practical Anatomy at the "Sacra Infermeria". It was again enlarged during the time of Grand Master De Vilhena, who added a chapel and naturally had it dedicated to St. Anthony, the saint after whom he had been called. He also constructed a fortress in 1726, on designs previously made in 1715 by the two famous



The Chapel of Bones

engineers of King Louis XIV of France Chevalier Gion de Mondion and Brigadier Chevalier René James de Tigné.

These notes serve to show how the Order of St. John, in its Maltese period,

lived up to its long cherished ideals and helped foster the development of medical practice. These objectives it still faithfully pursues to this day, in many countries and in various ways.

EYE DISEASES IN MALTA AT THE TURN OF THE CENTURY

FRANCIS J. DAMATO
M.D., D.O., D.O.M.S., F.R.C.S.

This work is based on reports published by three ophthalmologists working between the years 1890-1909, namely on Prof. L. Manchè's "*Rendiconto degli ammalati ammessi durante il Biennio 1890-91 (per il Dottor Salvatore Cassar) nel Comparto Ottalmico dell'Ospedale Centrale di Malta*: on "*Le Malattie Oculari in Malta: Appunti Clinici e Statistici 1899*" by Dr. Giuseppe Norsa an "oculist" from Rome and on an "Annual Statistical Report of the Eye Diseases treated at the Ophthalmic Institute of Malta from July 1908 to July 1909" by Dr. C. Manche, M.A., M.D., O.S.U.K. This report was dedicated to the author's father "the Founder of Ophthalmology in Malta in token of love and gratitude".

The report by Dr. Norsa is considered first because it is the most comprehensive and detailed, besides being the work of a foreigner. I think it will be more profitable to start at the end and consider the summary of the report which runs as follows: In Malta one comes across all eye diseases usually found on the continent. As on the African littoral the predominant disease is Granular Conjunctivitis (Trachoma) with its complications and sequelae. Norsa recommended the establishment of Ophthalmic Outpatients Department, free of charge for poor patients in the main centres of the island, along with Medical and Ophthalmic Boards to supervise crowded places such as schools, workshops and homes for the aged. He suggested that public talks should be held on Ocular Hygiene and prophylaxis, that more water should be provided for every inhabitant especially during summer; that the planting of trees and vegetation should be encouraged; that laws should be enacted to check abuses in the consumption of alcoholic drinks. Nowadays we can say that Trachoma has become a rarity. The water

supply has been improved, but as regards vegetation, inspite of recent efforts, the island still presents the same, dry brownish appearance, seen by Norsa seventy years ago. Dr. Norsa had been coming to Malta for seven years in summer-time, when eye diseases were more prevalent. He could not avail himself of any statistics on eye diseases in the Government Health Department as none were to be found.

Ignorance, prejudice and carelessness, and a low standard of living contributed then to the diffusion of the trachomatous infection all over the island, and to the increase in the incidence of blindness. People resorted to treatment only during the last stages of the disease. Moreover, the necessary treatment was not easily available. There was an Ophthalmic Department attached to the Central Hospital, created twenty years before through the initiative of Prof. L. Manchè. The beds available were 8 for male patients and 7 for female patients, that is, 1 bed for every thousand persons. Only very serious cases were admitted and patients were discharged as soon as they improved to make room for others.

Norsa used to make regular visits to Tunisia, Tripolitania and Egypt besides practising in Rome. He could thus present a comparative study of eye diseases in the Eastern Mediterranean Basin. The number of patients who came for treatment was 499: Males 297, Females 202. (The age period 21 — 31 years was represented by 18.63%). In Rome the incidence according to sex was more or less equal. In Malta the incidence was higher in males, in spite of a larger female population. This can be explained by the more frequent exposure of men to wind, dust, sun and trauma. The population in Malta in 1893 was 163,314 with 80,370 males and 82,944 females.

The more frequent diseases of the eyes were those of the conjunctivae with 24.67%, diseases of the lids 6.8% and diseases of the cornea 10.80%. In Rome the comparative figures were higher, with the conjunctivae giving 30.32%, the lids 18% and the cornea 17.9%. The main cause of these afflictions was Granular Conjunctivitis (Trachoma) with its palpebral, conjunctival and corneal complications and sequelae.

Trachoma could be found everywhere in the cities, villages and countryside. Although one cannot rule out the possibility that it had been brought to Malta by French soldiers coming back from the Egyptian campaign, there is evidence that it was present in the island a long time before the conquest of the island by the French. The short distance separating Malta from Tunisia and Tripolitania where Trachoma infection was all pervasive and the old and intricate commercial ties with these countries would have been quite enough to explain its presence here. The contributing factors were the climate, the prevailing scirocco winds that might have brought with them pathogenic matter, the geological formation of the island giving rise to irritant dust and the bright sunshine unmitigated by the presence of vegetation. Other factors which could possibly be remedied by the authorities were the scarcity of water especially in summer-time and over-crowding. That the incidence of Trachoma had become higher and endemic could be seen by the fact that not only the poor people living in overcrowded and dusty surroundings suffered from it, but also the middle and upper classes enjoying a higher standard of living. Irrigation of the eyes by sublimate solution was introduced by Norsa in 1892. It had a beneficial effect on the course of the disease and was accepted and extensively used by his colleagues in the island. He also introduced the use of copper sulphate crystals which replaced for some time the silver nitrate stick used either pure or mitigated by potash.

Pterygium was rather frequent. This was to be expected in a place where climatic conditions were so favourable for

its appearance. Norsa suggested that it could have been caused by tiny wounds and small ulcerations at the corneal border. Ophthalmia neonatorum does not seem to have been a problem, Norsa reporting only one case. Corneal diseases were represented by 10.8% of the cases. This compared very well with 17.97% in Rome. Neglected Granular Conjunctivitis was to blame for the majority of the cases. Norsa noticed that Phlyctenular Conjunctivitis, usually found in debilitated children, was much less prevalent in Malta (4 cases) than in Rome where he dealt with 58 such cases in a group of 227 patients. Did this mean that the children in Malta were healthier because they breathed marine air and bathed frequently in the sea? Lens changes — cataract — were more common in Malta with 11.02% compared to Rome's 5.14%. Moreover, these changes appeared at an earlier age. This usually happened in hot countries where individual development and organic evolution take place at a quicker pace. Another factor was Diabetes which in Malta was very frequent. Diseases of the uvea showed more or less the same percentage as in Rome with 4.44% and in Malta 4.04%. The main cause was Syphilis. This was to be expected in a place with a garrison of 12,000 soldiers and sailors and which was a port of call for ships from all over the world. More than half the cases of retinal diseases encountered by the author were caused by Retinal Detachment. Syphilis was another cause. Diseases of the optic nerve were more common in women than in men, the opposite of what he found in Rome. Most of these cases were to be attributed to Syphilitic infection. Treatment by an electric current gave satisfactory results. This was applied either directly to the globe or in an 'ascending' sense to the vertebral column. Along with Charcot Norsa deprecated the use of mercurials and of potassium iodide in syphilitic infection as the condition might thereby be made worse.

Norsa was surprised to find that the various forms of Glaucoma were more common in Malta (4.20%) than in Rome (0.63%). Half of the cases were chronic. He performed a Graefe iridectomy which in his hands was a safe and effective

remedy. In surgery he followed the motto "Cito, tute et jucunde". He came across a good number of cases of Toxic Amblyopia due to the simultaneous consumption of alcohol and tobacco. Whisky, gin and cognac were being imported on an extensive scale, whilst the cost of inferior quality tobacco, full of nicotine, was very low. In North African countries where light tobacco was used along with strong coffee no such cases were met with. The author concluded that, whilst coffee seems to be an antidote to nicotine, consumption of alcohol heightened its effect.

Disorders of ocular muscles were more frequent in Malta (6.18%) than in Rome (2.77%). The causes were errors of refraction and central corneal opacities following Trachomatous infection. The incidence of Myopia was high. The frequency of astygmatic errors of refraction could be attributed to scarring of the corneal tissue by Trachoma. He performed 59 operations. Cataract surgery constituted about a third. The rest almost all consisted of Trachoma surgery on the lids, conjunctivae and iris. He operated on 20 cases suffering from Cataract with very satisfactory results, no complications being reported. Up to this time (1895) Cataract extraction was performed, according to Prof. Liebreich's technique. The lens was delivered through a small corneal incision and iridectomy at the lower part of the cornea. Extraction was an extracapsular one. Dr. Norsa was the first to introduce in Malta the modern technique of a broad incision of the upper part of the cornea and a cataract extraction without complete iridectomy. In four cases he performed an Intracapsular extraction according to Gradenigo's technique. This surgeon used a zonulotome to break the lens ligaments and deliver the lens along with its capsule. A round black pupil free from lens remnants was the usual result. This technique prevented the appearance of a secondary cataract and inflammatory reactions associated with the presence of large masses of lens matter in the anterior chamber. Fifty years were to pass before an Intracapsular extraction was performed in Malta.

Dr. Norsa seems to have been a bold

and resourceful surgeon. His visits to Malta were short and he could not afford to wait. He expected quick results. In two children, seven years old, suffering from congenital cataract instead of the usual discussion operation, he attempted a cataract extraction under chloroform anaesthesia. In spite of a stormy convalescence the results were very satisfactory. He attributed his success to strict antisepsis. He advocated and resorted to the ancient operation of couching in those cases where the patient was too old, and uncooperative to allow an ordinary extraction. Expulsive haemorrhage in the other eye was one more indication. With regards to diseases of the lachrymal apparatus he limited himself to incision of the lachrymal canaliculi and of the lachrymal sac. He discussed the treatment carried out by other surgeons. He obtained better results by improvement of the general condition of the patient and by the application to the lachrymal region of faradic and galvanic electric current. He also showed interest in squint surgery. Squint seemed to have been more common in Malta (6.8%) than in Rome (2.77%). He performed Strabotomy in six cases.

In December 1891 Prof. L. Manchè, a Surgeon Major in the R.M.A., presented a report to Dr. S. Cassar on 341 cases treated in the "*comparto ottalmico dell'ospedale Centrale di Malta*" during the two years 1890-1891.

In this department there were eight beds for male and seven beds for female patients. There was no proper out-patients department. Many patients were refused admission and others were discharged as soon as possible to make room for other patients. Although Prof. L. Manchè was very busy fighting Trachoma and its complications and sequelae, he found time to publish in 1885, a textbook on Ophthalmology "*L'Ottalmologia in Quadri Sinottici da servire come guida ai Pratici ed agli studenti*". He was encouraged to write it by professors. Wecker, Liebreich and Meyer, whose clinics he was attending in 1870.

In his report trachomatous infection accounts for no less than two thirds of the cases. He treated Granular Conjunctivitis by means of light touches with a silver nitrate stick and instillation of glycerin and

tannic acid. Extensive scarring of the conjunctive was very frequent. Gaillard's technique was found quite useful in simple Trichiasis. Plastic operations were resorted to in cases of Entropion. Seven cases of Purulent Conjunctivitis were reported. Treatment could not have been very effective as only three were reported to have recovered, the others being left with an adherent Leucoma. The incidence of Kerato-Hypopyon was quite high. He treated ten cases. In a paper read in a meeting of the "Malta and Mediterranean Branch of the British Medical Association" he described the successful treatment of these cases over a period of ten years, by means of the instillation of 2% Eserine Sulphate drops. This treatment rendered unnecessary such heroic treatment as cauterization of the ulcer by means of the thermocautery and a corneal incision of the ulcer. Five cases of Interstitial Keratitis (Celtic Keratitis) treated by mercurials and atropine suggest that the incidence of Syphilitic infection was high. He reports the loss of one eye through Panophthalmitis in a series of 19 cataract extractions using Liebreich's technique. The only antiseptic measure used was irrigation of the eye by means of 1 in 2000 corrosive sublimate solution. Anaesthesia was obtained by means of an instillation of 2% cocaine solution.

The Third Report is by Dr. C. Manchè, the son of Prof. L. Manchè.

His annual statistical report deals with 1251 cases treated between July 1908 and July 1909 at the "Ophthalmic Institute in Malta". The Institute was founded in order to enable Prof. L. Manchè to carry on with his work after he resigned from the Government service after forty years of "Incessant Professional Service". The site at Hamrun chosen for the Institute was very convenient "being within reach of nearly all the towns and villages of Malta, owing to the train running on one side of the building and the Electric Tram on the other".

The Institute was open on all weekdays between 9 and 12 a.m. The poor were treated free of charge. The higher classes were expected to contribute voluntarily for the maintenance of the establishment.

Out of 1251 cases, diseases of the conjunctiva accounted for 954 cases, that is,



Surg. Major L. Manche'.

*By courtesy of the Hon.
Mr. Justice W. Harding.*

76.2%. Trachomatous infection was represented by 62.3%; complications and sequelae of Trachoma involving the lids and cornea, raised this percentage to over 85%. Trachoma was still the all pervading prevalent disease of the eyes. The usual treatment was scraping of the Conjunctive twice a week, supplemented by copious irrigation by Corrosive Sublimate solution, Protargol drops, yellow oxide of mercury and Picric Acid. Treatment by the Silver nitrate stick seems to have been dropped. The average duration of attendance was between two to three months.

He reports 52 cases of Cataract. This was a large number considering the population of Malta at that time. However, he operated only upon 7 cases. Cataract was not operated upon unless it was completely mature. People could not afford to pay the small fee for the operation and stay in hospital. Other patients were reluctant to ask for an operation before they lost vision in the other eye. The results of the operations seemed to have been very satisfactory. His technique — corneal section above, complete Iridectomy and entracapsular extraction was a modern one for that time. Though Squint was very common he only saw 6 cases. People did not care to ask for treatment unless they were suffering from Double Vision. He did not perform any Squint operation, as 3 cases responded to treatment by glasses and the other cases refused operation. Parents did not seem to care about the appearance of their children. They were quite happy with good vision in the stronger eye. In penetrating injuries of the eyeball treatment was prevention of infection, cleaning of the wound and excision of Iris prolapse when present. No mention at all is made of the Giant Magnet. In a

reported case of Intraocular foreign body the surgeon waited until the foreign body luckily came out spontaneously at the surface. Two cases of Retinal Detachment were treated by rest in bed and subconjunctival injection of Sodium Chloride solution and Potassium Iodide by mouth. The same treatment was in use until 1940, when Diathermy was introduced. In this report no mention at all is made of Diabetes Mellitus and its complications. Today this disease is responsible for 17% of the blind population in the islands. Is it possible that at that time the incidence of Diabetes was much lower?

These reports show that eye diseases at the turn of the century were being treated by the best means available at that time. The surgeons were very well informed about developments on the Continent and tried to do their best. What was needed was the raising of the standard of living, especially better housing to avoid overcrowding, a good water supply, good sanitation, the establishment of suitable centres for treatment all over the island and education of the masses on ocular hygiene and early treatment.

NOTICE

This periodical is published biannually in June and in December. Contributions for the December issue are to reach the Editor at the Bacteriology Laboratory, St. Luke's Hospital, Malta, by the 1st November. They must be typewritten, with double spacing. References should be given by the author's name and by the year of publication. Papers, which are accepted on the understanding that they have not been published elsewhere, are to consist of reports of original work or studies or case histories.

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VESTIGES OF THE PARTURITION CHAIR IN MALTA

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The position adopted by women in childbirth has varied throughout time and locality among both primitive and civilised communities. Different peoples have favoured squatting; or tying the woman to the trunk of a tree or hanging her from a branch by means of a rope passed under the armpits. Others preferred the kneeling posture; sitting on the knees of an assistant who holds the parturient woman around the abdomen; sitting on a semi-circle of stones or on a backless stool or on a birth-chair; or lying down on a bed. The stool as a birth appliance dates at least since the 4th century B.C. (Cyprus). It was still being recommended at the beginning of the 17th century A.D.

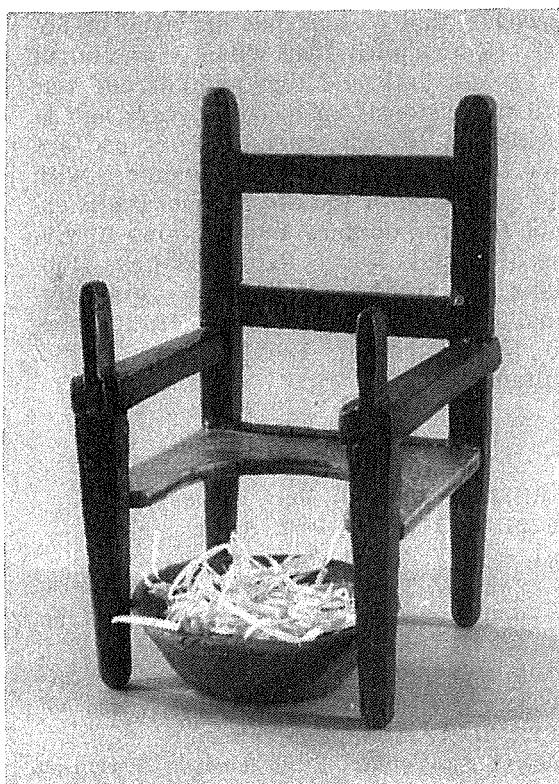
The birth-chair, which was already in use in the 2nd century A.D., survived with modifications to render it more comfortable until the present century (1921) in various parts of the world such as Turkey, Syria, Japan, Egypt, etc (Scarano, 1968; Cope, 1957). The birth-chair differed from an ordinary one in the following features:— (a) the seat was made of wood and had an aperture cut in it in the shape of a horse-shoe; (b) the chair was provided with a back, either fixed or movable, to permit a sitting up or semi-reclining position; and (c) an arm-rest was attached to each side of the seat so that by grasping these rests during her pains the woman was able to strain more effectively during the expulsive stage. A chair in use at Xaghra and Zebbug (Gozo) had a leather belt attached to its back which was brought forward, and fastened over the woman's abdomen to

prevent her from sliding (Bezzina, 1973). The midwife usually seated herself on a low stool, or knelt, in front of the chair to receive the baby while another woman stood at the back of the chair to hold the patient in place (Cianfrani, 1960).

The first attempts to replace the chair by the bed and the lying down position were made in the 17th century by Francois Mauriceau (1637-1709). The bed, in turn, began to be substituted by the delivery table towards the end of the 19th century (Cianfrani, 1960).

The writer has found no trace of the employment of birth-stools in the Maltese Islands but he has come across fragmentary evidence of the use of the parturition chair amongst us. It was called *is-siggu tal-qabla or maqghad tal-qabla*.

It is not known when the birth-chair was introduced in the Maltese Islands. It was recognised as an item of the armamentarium of the midwife and obstetrician by the 18th century. Comments on its disadvantages and the best way of constructing it are found in one of Dr. Francesco Butigieg's lectures to medical students in 1804. "Various forms and shapes of labour-chairs (*sedie di travaglio*) called *selle*", he states, "have been devised by obstetricians. Some of them have been found to be uncomfortable, troublesome and dangerous for the patient as they have been responsible for tearing of the vagina and the perineum and are, therefore, to be avoided. Others, however, may be recommended such as that designed by G.W. Stein (1731-1803) and the one produced by



A small scale model of the parturition chair showing two uprights projecting from the arms rests which the woman grasped during her pains to increase the force of the uterine contractions during the expulsive stage of labour. Note also the horse-shoe shaped seat and the earthenware bowl filled with straw underneath the chair.

H. van Deventer (1651-1724) and modified by L. Heister (1683-1785) so that it approaches the shape of that used in the Kingdom of Naples and Sicily". Dr. Butigieg, however, was not quite satisfied with the Neapolitan type of chair and he advocated its modification as the seat was too narrow from side to side so that the woman could not open her thighs wide enough to allow the exit of the baby from the vagina when its head happened to be unduly large, with consequent compression of the infant's skull.

Some of the chairs of Malta were hinged so that they could fold down flat

(*siġġu li jingħalaq*) for easy conveyance by the midwife (Birkirkara); the non-collapsible type was usually carried for her by a boy or young man on his head. From this custom derives the Maltese saying *qrieh għax kien iġorr is-siġġu tal-qabla* i.e. he has become bald from carrying the birth-chair (on his head), the implication being that he lost his hair from the constant friction of the chair on his scalp (Zammit, 1966).

As the final expulsive phase of labour approached, a large earthenware bowl (*lembija*) was filled with straw and placed on the floor beneath the chair so that if the baby was not caught in time by the receiving hands of the mid-wife as it came out of the birth canal, it would slip on to the soft straw inside the bowl (Aquilina, 1963).

A variant of the *lembija* custom was the attachment of a kind of drawer underneath the opening of the seat. This drawer was made of strong cloth like a hammock and was pulled out from under the seat to receive the baby during the last pangs of delivery (Sultana, 1964).

In 1852 Dr. G. Clinquant designed an obstetrical bed which could be converted into a birth-chair "adapted to every sort of parturition for the use of lying-in women". He exhibited this apparatus at the Central Hospital, Floriana, where he demonstrated its mechanism to obstetricians and midwives and explained the "facility and comfort by which every manoeuvre" of delivery could be effected (*The Malta Mail*, 1852).

In the eighties of the last century one of the successors of Dr. Butigieg in the Chair of Midwifery in our University did not hesitate to condemn outright the use of the parturition-chair. This was Professor Salvatore Luigi Pisani (1828-1908) who warned midwives against using the chair mainly because, with the patient in a sitting position, the midwife could not maintain adequate flexion of the baby's head by supporting the perineum, allowing the slow escape of the infant's head from the vagina and thus preventing the laceration of the perineum. Owing to this complication the use of the birth or labour

chair by midwives was made illegal by Art. 143, Chapter XIV, of the Police Laws of 1883 (Police Laws, 1883).

It was not easy, however, to convince parturient women to do away with the chair. Indeed as soon as the law prohibited midwives from using it, some families had a chair constructed for their own private use. "Others", wrote Professor Pisani, "delivered their offspring sitting on two chairs approximated to each other while there were some who told the midwife that they would do without her services unless she allowed them to deliver their babies the way they wanted". He exhorted midwives not only to abide by the law in spite of the remonstrations of their clients but also to remove the chair from their homes lest they should be tempted to use it (Pisani, 1883).

In spite of legal sanctions and the endeavours of Professor Pisani, the usage of the chair persisted for many years afterwards. It was still employed at Birkirkara at the beginning of the present century. A ninety-nine year old man, recently deceased, recalled in 1971 that his sixty year old son was born on a parturition chair belonging to the village midwife. A member of another family from the same locality states (1972) that they had their own private chair (Zammit Maempel, 1972).

It seems that the chair began to disappear from the midwifery scene in our Islands after World War I (1914-18). No

specimens have been traced. It is known, however, that a chair had survived at Rabat ((Gozo) until 1942 when it was burnt as useless junk and that another one was still in existence up to some years ago at Birkirkara. Reminiscences of its use are now fading out from folk memory with the extinction of the older generations except for fragmentary recollections surviving at Dingli, Mosta, Rabat (Malta), Floriana, Birkirkara and Rabat (Gozo) (Bezzina, 1973; Zammit Maempel, 1972; Debono, 1964; Sansone, 1964; Calleja, 1964, Sultana, 1964).

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CHOLERA

Some Historical Reflections

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"Those who cannot remember the past are condemned to repeat it". — Santayana.

Introduction

It seems only a short time ago that, in order to bring my knowledge of tropical diseases up to date, I bought my third copy of Manson-Bahr's book on Tropical Diseases, as beffited an army man liable to see service in foreign lands, and a pathologist to boot who would have to think of exotic diseases when confronted with the duties, responsibilities and problems met with in the Armed Forces Medical Services.

Yesterday I had occasion, while trying to put my study-room in some sort of order, to take down from its customary prominent place in my meagre medical library my dogeared copy of this justly world famous reference book which happens to be the 15th edition, reprinted in 1961 from the 1960 edition; and as I thumbed my way through the various sections and their constituent chapters my fingers chanced to stop on chapter 31 — Cholera.

Now cholera has been one of the biggest, if not the biggest, public health problem that the World Health Organisation had to tackle in 1971-72, and medical interest in this disease which had stagnated so much during my years of medical studentship, and even in my post-graduate days, has had perforce to be rekindled and reviewed and indeed forced to make rapid advances when that notorious rogue variant the El Tor Vibrio quite unexpectedly in 1961 sprung its prison boundary in the island of Sulawesi and relentlessly made its way not only through the semi-dormant Asian continent catching many

countries therein unawares, but even succeeded in leap-frogging to the virgin ground of the Dark continent by 1971-1972, taking Europe through its southern flank en passant.

And these were the thoughts that floated nebulously through the labyrinthine recesses of my mind, as I pensively held Manson-Bahr in my grasp.

Etiology

I quote from page 31: 'The cholera vibrio was first discovered by Koch in Egypt in 1883; this he confirmed in Calcutta in 1884 by finding it in every case of the disease examined'.

As everyone agrees, this was an excellent piece of research, as was to be expected from that immortal master, with the French team, in the unavoidable absence, due to ill-health, of the equally immortal Pasteur, made up of Pasteur's best pupils' acting as a pace maker in Egypt, but it would appear that some merited honour even at this late hour should be given to the Italian Pacini who during the 1854 cholera epidemic in Florence detected the motile vibrios in the faeces of cholera patients and not only described their general morphological appearances but also correctly attributed an etiological relationship to the "immense number of vibrios which I have found in the distended intestines".

Pathology

'The cholera endotoxin causes a superficial denudation of epithelium, and increases its permeability; so that there is

a great outpouring of water and electrolytes with loss of fluid from the tissue and the blood' reads a statement on page 435.

By work on living specimens, involving the manipulation of elaborate gadgets like Crosby capsules it can be shown nowadays, both macroscopically and microscopically, that in cholera the patient's intestinal epithelium is more or less normal; which statement physiologists injecting some fashionable highly artificial laboratory macro-molecule like ^{131}I -PVP into a patient's circulation hasten to confirm in their turn.

Cohnheim lecturing a century ago told his students that "in order to understand cholera it is indispensable that we should possess an accurate acquaintance with the mechanism and processes on which the discharge of fluid into the intestinal canal depends. Naturally, it was at first hoped that the desired information might be obtained by an accurate examination of the intestine, the locality affected by the disease; but it was found to present no well-marked pathologico-anatomical changes. Nor is microscopic examination of any avail. One fact it is true, and that a very striking one, is revealed by the microscope, namely a deficiency of the intestinal epithelium. In the intestinal fluid there float, as a rule, quantities of epithelial shreds, both single cells and more especially connected cell-groups, some being pretty long membranous pieces of epithelium. This extensive shedding of the epithelium was formerly regarded as, and is still held by many to be, the criterion distinguishing cholera from other acute diseases of the intestine accompanied by diarrhoea, to be, so as to speak, the anatomical basis of the disease. But is the desquamation really a pathological process? All speculation is rendered superfluous in cholera by the ease with which the intestinal contents may be examined with the greatest accuracy *intra-vitam*; for if the epithelium is shed during the attack we must necessarily find it in a corresponding amount in the dejections. Yet, however often and confidently its discovery in the stools has been asserted, this is not the case. During the epidemic of 1866, many hundreds of rice-water stools were

examined in the various cholera lazarettos of Berlin by Kuhne, Bruberger, Hirschberg, myself and others; but although we all directed our attention especially to the presence of epithelium we only rarely succeeded in finding a few undoubted epithelial cells therein; and even with regard to these it was not possible to exclude absolutely an accidental contamination. Accordingly, there cannot, in my opinion, be a doubt that the entire desquamation of the epithelium is nothing but a result of post-mortem maceration."

Pathophysiology

I read on, 'Vibrios do not apparently produce any exotoxin. The endotoxin results from the destruction of the vibrios within the bowel lumen' (vide page 434).

Mainly through the impetus of renewed medical interest in cholera, resulting directly from the current 7th Pandemic, it has been discovered, without a shadow of doubt, that the vibrios do in fact secrete an exotoxin(s) (Choleragen: Diarrhoeal Factor: Permeability Factor) which stimulates the enzyme adenylyl-cyclase sited on the surface of the epithelial cells (and possibly located inside the cells as well) to trigger off a mechanism leading to the profuse watery gut contents, so characteristic of florid cholera.

Was this what that genius John Snow had in mind, albeit chemically-speaking not so word-perfect, not ten but one hundred years ago, when he opined, 'From all that I have been able to learn of cholera, both from observations and the descriptions of others, I conclude that cholera invariably commences with the affection of the alimentary canal. It follows that the morbid material producing cholera must be introduced into the alimentary canal; and the increase of the morbid material or cholera poison must take place in the interior of the stomach and bowels.

It would seem that the cholera poison, when reproduced in sufficient quantity acts as an irritant on the surface of the stomach and intestines, or what is still more probable, it withdraws fluid from the blood circulating in the capillaries, by a process

analogous to that by which the epithelial cells of the various organs abstract the different secretions of the healthy body.

Treatment

I thought that page 442 summarises very well the lifesaving treatment as practised today. I quote, 'Maintenance of biochemical equilibrium:- these measures are

- (1) Replacement of fluids.
- (2) Maintenance of blood and tissue chlorides at their natural levels.
- (3) Counteraction of acidosis.

Intravenous salines:— In the stage of collapse, which is due to the loss of a large amount of fluid, intravenous injections of salines must be resorted to, to restore the balance. Three to four pints may be necessary. The modern drip transfusion method should be used whenever possible.

It is assumed that in this day and age every medically qualified man (and para-medical personnel as well) is familiar with the recommended treatment of cholera, which, as stated above in Manson-Bahr, is the immediate introduction into the human body of fluid/electrolyte replacements. This vital procedure rapidly corrects the hypovolaemia, restores the lost ions, and neutralises the acidosis.

But lest our younger medical colleagues, perhaps not as well acquainted with medical history as they should be, should think that this is indeed a marvelously modern method of bio-physical therapeutic resuscitation, let them hark back to John Snow (1894): 'It is only necessary to allude to the effects of a weak saline solution injected into the veins in the stage of collapse. The shrunken skin becomes filled out, and loses its coldness and lividity; the countenance assumes a natural aspect; the patient is able to sit up, and for a time seems well. If the symptoms were caused by a poison circulating in the blood it is impossible that they should be suspended by an injection of warm water, holding a little carbonate in solution. The whole quantity of fluid that requires to be effused into the stomach and bowels, in order to reduce the

blood of a healthy adult individual to the condition in which it is met in the collapse of cholera is, on the average, 100 ounces or 5 imperial pints. This calculation may be useful as indicating the amount of fluid which ought not to be exceeded in the injection of blood vessels'. And I daresay one or the other of my Scottish confreres would demand redress on a matter of national pride and prestige if I do not reproduce hereunder at least a paraphrase of the following relevant document.

Malignant Cholera

Letter from Dr. Latta to the Secretary of the Central Board of Health, London, affording a view of the Rationale and Results of his Practice in the Treatment of Cholera by Aqueous and Saline Injections:

Leith, May 23, 1832.

Sir,

My friend Dr. Lewins has communicated to me your wish for a detailed account of my method of treating cholera by saline injection into the veins.

I have no doubt that it will be found, when judiciously applied, to be one of the most powerful, and one of the safest remedies yet used in the second stage of cholera, or that hopeless state of collapse to which the system is reduced.

I beg leave to premise that the plan which I have put in practice was suggested to me on reading in 'The Lancet' the review of Dr. O'Shaughnessy's report on the chemical pathology of malignant cholera, by which it appears that in that disease there is a very great deficiency both of water and saline matter in the blood.

So as soon as I learnt the result of Dr. O'Shaughnessy's analysis I attempted to restore the blood to its natural state. I resolved to throw the fluid immediately into the circulation. In this, having no precedent to direct me, I proceeded with much caution. I dissolved from two to three drachmas of muriate of soda and two scruples of the subcarbonate of Soda in 6 pints of water and injected it at a temperature of 112°F.

As soon as the pulse fails again, or the features again shrink the venous injection must be repeated, taking care that the fluid in use retains its proper temperature.

The quantity to be injected depends on the effect produced, and the repetition on the demands of the system, which generally vary according to the violence of the diarrhoea; the greater the degree of collapse, the greater will be the quantity needed.

The apparatus I have used is Read's patent syringe, having a small silver tube

attached to the extremity of the flexible injecting tube. The syringe must be quite perfect, so as to avoid the risk of injecting air.

I am Sir,
your most obedient Servant,
Thomas Latta, M.D.

Oscar Felsenfeld has well said that "It is natural that most logical brains follow similar pathways, and newcomers in the field will sooner or later follow the trek that was travelled by the old".

PUBLICATIONS LIST

The following are recent publications by graduates of our Medical School:

ATTARD, R. and WARRINGTON, A.J. 1972. Beitrag zur Behandlung des Prostatakarzinoms. *Arztliche Praxis*, 84, 3999-4000.

CUSCHIERI, A. (With BANNISTER, L.H.) 1971. The fine structure and enzyme histochemistry of vomero-nasal receptor cells. *Olfaction and Taste: Proceedings of IV International Symposium on Olfaction and Taste*, 4, 27-33.

CUSCHIERI, A. 1973. The development of the Olfactory Mucosa in the mouse.

J. Anat, Apr.

CUTAJAR, C.L. (With MARSTON, A. and NEWCOMBE, J.F.) 1973. Value of cuff occlusion pressures in assessment of peripheral vascular disease. *Brit. Med. J.*, 2, 342-395.

ELLUL - MICALLEF, R. 1973. Airway smooth muscle in health and in asthma. *Brit. J. Dis. Chest*, 67, 107-113.

GRASSO, P. 1973. The range of carcinogenic substances in human food and the problems of testing for them. *Proc. Roy. Soc. Med.*, 66, 26-27.

VELLA, E.E. (with GOODE, D.) 1973. Holiday Brucellosis. *J. Roy. Army Med. Corps*, 119, 1-6.

MEDICAL NEWS

At a meeting of the British Medical Association (Malta Branch) held at the Medical School on the 25th. March, Dr. Edwin Besterman of St. Mary's Hospital, London spoke on "The Use and Abuse of Drugs in Heart Disease"; at another meeting on the 27th. April, Dr. Roger Ellul Micallef spoke on "Asthma — Facts and Fancy". At the Annual General Meeting in January, Dr. Frederick F. Fenech was elected Branch President for the year. This year's B.M.A. prize for an essay on a medical subject was awarded to Dr. Paul Cassar for his paper on "The teaching of midwifery in Malta at the beginning of the nineteenth century".

This year also the B.M.A. organised a refresher course for general practitioners in December, with a record number of attendances.

The B.M.A. (Malta Branch) Gold Medal for the best student in the Course of Nurses was awarded to Miss Therese Mintoff.

Members of the B.M.A. (Malta Branch) are advised that the B.M.A.-R.U.M. Travelling Fellowship will be awarded next year. Funds will be available to a selected member who would like to go abroad for a short period to continue study on some special topic. A call for applications will be issued probably in March. Anyone who by then will have already carried out or have been engaged on work which a short tour abroad would enable him to round off will obviously have a fair chance of getting the award.

At the recent Committee Election, Dr. Frank Callus was chosen to be the President of the Medical Association of Malta for 1973-75; Dr. L. J. German is the new Honorary Secretary and Dr. J. Paris the Honorary Treasurer.

Under the auspices of the 'Association of Surgeons and Physicians of Malta', Professor Ian Scott Smillie, professor of orthopaedic surgery at Dundee University, who was visiting Malta for the World Health Organization, lectured on the 2nd. March on "Athletic Injuries of the Knee".

At a meeting of the Anatomical Society of the University on the 7th.

February Dr. A. Cuschieri, Dr. R. Ellul Micallef and Dr. A. Lanfranco took part in a discussion on "The Bronchial Tree"; the same society met on the 21st. March, the subject of the day being "The Pharynx: some aspects of its anatomy and pathology" with Professors J.L. Pace and G.P. Xuereb as main speakers.

The Department of Dental Surgery of the University held a successful refresher course for Dental Practitioners. Professor George Camilleri, at the first meeting dealt with "New Equipment and Materials in Dentistry". At the second meeting Mr. John Portelli lectured and demonstrated on "Impression Taking". The third and fourth meetings concerned "The Management of Traumatic Injuries to the Anterior Teeth in Children" and were conducted by Mr. Hector Galea. At a special meeting on the 4th. April, three films on dental subjects, supplied by the British Council, were shown.

We congratulate young David Bartolo on his getting the M.R.C.S., L.R.C.P. last February and on obtaining the M.B., B.S. degree from the University of London last May. David, who is the son of Dr. Albert Bartolo, studied at St. Mary's, in London. Congratulations also to Professor Frank Vella, now of Saskatchewan University on his election to the Fellowship of the Chemical Institute of Canada; to Dr. Joseph L. Grech and to Dr. Joseph Mifsud on their election to the Fellowship of the Royal College of Pathologists; to Mr. John Portelli on his being awarded the Fellowship in Dental Surgery by the Royal College of Surgeons (England); and to Dr. Paul Vassallo-Agius on his appointment as Senior Lecturer in the Department of Medicine in our University.

On the 21st. May the Minister for Health, Dr. D. Piscopo, inaugurated a Cobalt Treatment Unit at the King George V Hospital; this will be run by our radiotherapy specialists. Dr. Colin Jones, senior physicist from the Royal Marsden Hospital of London guided the setting up of the plant.

We record with deep regret the death of Dr. Cesarin Attard ('19), as he was known to a vast circle of friends, which occurred last February. Dr. Attard was

a surgeon with a very wide practice and one of the team with the late Professors Peter Paul Debono and A.J. Craig in the old Central Civil Hospital. He worked assiduously throughout the II World War, starting at the Emergency Hospital in the Mater Boni Consilii School. The writer recalls the calmness with which Dr. Attard, who was serving at Holy Mass at the moment of the first air-raid on Malta, like the officiating priest and indeed the whole congregation, carried on to the conclusion of mass completely unflurried.

Dr. Walter Fava ('31) died at the Cambridge Military Hospital in Aldershot on the 5th February 1973. Colonel Fava had made the Army Medical Corps his career, joining almost immediately on qualifying. He specialised in Radiology. He came frequently back to Malta to renew his many friendships among us.

Dr. Edgar Azzopardi of Dingli Street, Sliema died on the 9th April 1973, mourned by many people in Sliema and elsewhere.

The death of Dr. John Borg ('58) at the early age of thirty-nine was a shock all round. Dr. Borg worked in Zejtun and Birzebbugia and was already very well loved by a large clientele.

On the 3rd. June the death occurred of Dr. Victor T. Camilleri ('25). Dr. Camilleri had great gifts as a surgeon, as a teacher and as a family physician, and was trusted and respected by all who knew him. To a circle of friends he was also known for his skill as an amateur artist; he designed the cover of this periodical. His death severs a link with a period of surgery in Malta which was dominated by

Professor Peter Paul Debono, a period in which many doctors still in practice obtained their medical education.

It is important to know that that august body the Council of Europe frequently gives its attention to varied medical problems especially such as are common to its component states. Within the last six months it has adopted a programme of assistance for handicapped persons, and it has gone into details about the use of cereals treated with pesticides. The Council has publicised rules which ten of its member states have issued for the control of radioactive pharmaceutical preparations. A series of measures designed to reduce the number of accidents caused by drivers under the influence of alcohol have recently been adopted by the Council, while 17 member states have accepted a comprehensive programme to combat the illicit use and sale of drugs. Such difficult matters as the possibility of standardising automated blood grouping in Europe and the drafting of an agreement to facilitate organ transplants are under very active consideration. Anybody with a medical problem, especially of a social character, would be well advised, before he tackles it, to see whether the Council has studied it already and whether it can give him any help in that direction. In these days of mounting prices and shrinking supplies it is also encouraging to note that the Council has prepared a 28-article Consumer Protection Charter, which has been adopted by the parliamentary assembly and will now go to the component governments for acceptance and application.