accuracy of diagnosis throughout the country, and should permit of the accumulation of valuable data on the epidemiology of ringworm, much of which at present is still speculative.

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SICKLING IN RELATION TO MORBIDITY FROM MALARIA AND OTHER DISEASES

BY

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Various indirect attempts have been made to test the hypothesis that children who are heterozygous for the sickling gene have a greater chance of surviving to reproductive age than normal children have when both are exposed to malarial infection. The evidence has been summarized (*British Medical Journal*, 1955). Direct proof is very difficult to obtain, for it would require not only accurate mortality statistics but also a knowledge of the sickling state of each member of a community.

One approach that has not been made, strangely enough, is a simple clinical comparison of sicklers and non-sicklers, to determine whether the former suffer less than the latter from malaria that is fatal or potentially fatal. Of course, the subjects must not possess an appreciable acquired immunity to malaria, and in a malarious country this can only be assured if they are children. Hospital patients are suitable subjects for this comparison. Malarial attacks must be of a certain degree of severity before patients are admitted, but admissions for so serious a complication as cerebral malaria may be taken as a fair sample of such cases in both the sickling and the non-sickling population. Death rates in hospital do not accurately reflect the death rates in the community, being influenced on the one hand by medical treatment and on the other hand by the selection of the more serious cases for admission. But it is permissible to compare the hospital death rates for sicklers and non-sicklers, provided the age-constitutions of the two groups are comparable.

Sickling and non-sickling children may of course differ in their susceptibility to diseases other than malaria, and information on this point is required, both for its intrinsic interest and to ensure that any differences that may exist do not unduly weight admissions in either group.

Present Investigation

Data have been collected on these subjects at Mulago Hospital, Kampala, over a period of about a year. Special care was taken to ensure that blood was collected for a sickling test from every case admitted to a children's medical ward, for the omission of children brought to the hospital moribund would have prejudiced the results. In each case the diagnosis accepted was that made on consideration of the evidence after the child's discharge, and a diagnosis of malaria was recorded only if this was the main cause of the child's illness. For this part of the investigation I am indebted to Drs. H. C. Trowell and J. Luder, under whose care the children were. In the period there were 31 cases of sickle-cell anaemia, and these have been omitted from the analysis, which is thus limited to a comparison of the morbidity and mortality in normal children and heterozygous sicklers respectively.

Table I shows the partition of sicklers and non-sicklers amongst the main groups of diseases causing admission. No difference emerges except in respect of hookworm anaemia, typhoid, and malaria. For the first two of these the numbers

TABLE I.—*Distribution of Diseases in Sickling and Non-sickling Patients in a Children's Ward*

Disease Groups	Heterozygous Sicklers	Non-sicklers	Non-sicklers / Sicklers
Pneumonia	18	100	5·5
Upper respiratory infections	13	46	3·5
Diarrhoea and vomiting	25	81	3·2
Poliomyelitis	4	22	5·5
Tuberculosis	8	29	3·6
Meningitis, purulent	5	21	4·2
Malnutrition	11	66	6·0
Miscellaneous	25	161	6·5
Hookworm anaemia	2	28	14·0
Typhoid fever	6	11	1·8
Malaria	13	123	9·5
Total	130	688	5·3

are small, and cannot interfere with any inferences regarding malaria. For hookworm anaemia the difference might well be due to chance. But the subject might usefully be pursued in adults, in whom the interfering effect of acquired immunity is probably negligible. Mackey (1953) thinks that only a small proportion of hookworm carriers in Tanganyika suffer disability from their parasites; moreover, he thinks the decisive factor in limiting the pathogenicity of hookworms is a genetic one. It is quite possible that the size of a hookworm population in the intestine may be affected by the nature of the host's haemoglobin, and since severe hookworm infestation has an appreciable direct and indirect mortality it may claim a place second to malaria as a selective agent. It is noteworthy that in the places in Africa in which Allison (1954) correlated high sickling gene frequencies with malaria endemicity a fair correlation with heavy hookworm infestation also exists: warmth and humidity favour both diseases. The apparent disadvantage of sicklers in respect of typhoid infections would hardly warrant remark if the Lambotte-Legrands (1951) had not made a similar observation. For malaria the lower incidence in sicklers is unlikely to be due to chance ($\chi^2=4.83$ for 1 d.f.).

Table II analyses the cases of malaria. It may be noted that, though *P. malariae* was recorded in a few cases and *P. vivax* once, the only species present in all children regarded as suffering from malaria was *P. falciparum*. Uncomplicated malaria was equally distributed between the

TABLE II.—*Incidence and Types of Malaria*

	Sicklers	Non-sicklers
Uncomplicated malaria	13	70
Cerebral malaria	0	47
Blackwater fever	0	6
Total malaria	13 (10%)	123 (17·8%)
Total admissions	130	688

two groups. The difference between the groups demonstrated in Table I is due to the presence of cerebral malaria and blackwater fever in the non-sicklers only; and of the 16 deaths from malaria in non-sicklers 9 were from the cerebral form. The age-constitutions of the two groups were not strictly comparable. Omitting 18 non-sicklers and 3 sicklers whose ages were not recorded, the non-sickling group contained 58% of children under 2 years, and the

sickling group 73%. There was, however, no significant difference between the two groups amongst the children suffering from malaria.

TABLE III.—*Deaths from Malaria and Other Diseases*

	Sicklers	Non-sicklers	χ^2 (n = 1)
From malaria	0 13	16/123 (13·0%)	
,, other diseases ..	17/117 (14·6%)	53/565 (9·38%)	2·77
Total	17/130 (13·1%)	69/688 (9·99%)	1·1

The death rate in hospital from diseases other than malaria does not differ very materially between the two groups, nor indeed does the death rate from malaria (Table III). But the incidence of cerebral malaria shows a significant difference, and this is an indication that, without treatment, non-sickling children would be at a disadvantage.

This is not the first time this observation has been made. Before the importance of malaria in maintaining a high frequency of the sickling gene was proposed, the Lambotte-Legrands (1951) wrote from Léopoldville : " Nous signalerons . . . que nous n'avons pas vu d'accès cérébral de malaria chez les porteurs de sickle cell et qu'en comparaison de onze décès survenus suite à un accès de malaria chez des ' non-porteurs ' aucun décès n'a été constaté chez les enfants atteints de drépanocytose." The present results are entirely in agreement with that view, and, though it is not denied that occasionally a sickling child may die from malaria, they support the thesis that malaria is more likely to remove normal children than those carrying the sickling gene.

I wish to thank Dr. J. K. Lubega for his help in collecting blood specimens.

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Medical Memorandum

Multiple Villous Papillomata of the Gall-bladder

True multiple villous papillomata of the gall-bladder are exceedingly rare. There is considerable confusion in the terminology of new growths of the gall-bladder. Papillary overgrowth is common in chronic cholecystitis, and many pathological appearances have been called papilloma, cholecystitis proliferans, and cholecystitis polyposa with insufficient evidence of true neoplasia.

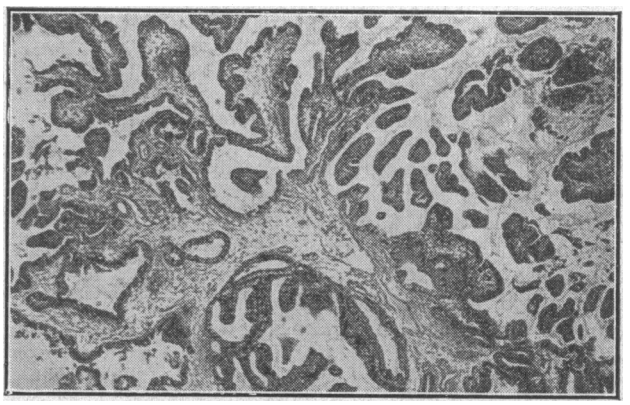
Kerr and Lendrum (1936) made an exhaustive study of the recorded cases of papilloma. They accepted seven cases, of which three were multiple, as true villous papillomata. Brown and Cappell (1937) described a further case in a man of 71, in which in addition to multiple papillomata the gall-bladder was heavily infected and contained multiple stones.

We describe a case of multiple villous papillomata without the presence of infection or stone.

CASE REPORT

In India, in 1940, a medical officer, then aged 34, developed pain and tenderness under the right subcostal margin after a severe attack of gastro-enteritis. A diagnosis of subacute cholecystitis was made. After three weeks' medical treatment symptoms subsided, but in 1941 there was a recurrence of the right subcostal pain, with tenderness, nausea, and vomiting. An excretion cholecystogram is stated to have shown a poor shadow. Since then mild attacks of pain, nausea, and flatulence occurred at irregular intervals. Further cholecystography in 1943 and 1949 showed only poor concentration of dye. From September, 1953, similar symptoms were more pronounced. In October an attack of diarrhoea was followed by severe upper abdominal pain, vomiting, and low fever. There was no tenderness over the gall-bladder, and a diagnosis of appendicular colic was made. In March, 1954, a similar attack occurred. Cholecystography (Telepaque) showed a normal-sized gall-bladder, throughout which were scattered numerous small round negative shadows. The appearance closely resembled that produced by multiple stones. The gall-bladder, however, contracted after a fatty meal to a size which would not have accommodated such a volume of stones had they been responsible for the shadows.

At operation (Lieutenant-Colonel R. S. Hunt) on March 29 the gall-bladder appeared normal, but numerous rubbery



objects were palpated through its wall. Cholecystectomy was performed. Convalescence was rapid and the patient has been in good health since.

Pathology.—The gall-bladder measured 6 cm. in length by 2 cm. in circumference after fixation. The wall was not thickened, but the mucosal surface was studded with numerous papillomata. These varied in size from 1 to 10 mm. in diameter and the larger growths were pedunculated. The gall-bladder wall between the tumours was normal and no stones were present. Histological section (see Fig.) showed the papillomata to consist of numerous fine villous processes, each composed of a loose connective-tissue stroma covered by columnar epithelium similar to that found elsewhere in the gall-bladder. In sections stained by Sudan III a number of the stromal cells were seen to contain lipoid. There was no evidence of any invasive tendency in the papillomata. The wall of the gall-bladder itself presented no evidence of infection.

We are indebted to Professor R. A. Willis for his confirmation of the histological diagnosis and to the Director-General, Army Medical Services, for permission to forward these notes for publication.

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The Royal Society of Health now has 14,000 members, which it claims to be a world record for such a body. 3,600 members were enrolled in 1955, an increase in one year which equalled that made in the first twenty-five of the society's existence. Last year over a thousand books were added to the society's library, which now contains 26,000 books on every aspect of public health. Questions on over 200 topics were answered by the information service.