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## CLINICAL SIGNIFICANCE OF SPLINTER HAEMORRHAGES

BY

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Splinter haemorrhages have been recognized as a characteristic physical sign of subacute bacterial endocarditis since Horder (1920) drew attention to their association with this disease. It has been stated by Lewis (1942) and White (1947) that their presence is due to an increased capillary fragility in this condition. Bramwell and King (1942), however, considered that they are embolic in origin.

Wood (1956) stated that they "are in no way diagnostic of bacterial endocarditis" and that they may also be present in septicaemia, rheumatic fever, and severe anaemia. Platts and Greaves (1958) found that they occurred in 44% of patients with uncomplicated mitral stenosis and in 15% of other patients. They also noted that they occurred with some frequency in patients who appeared to be in normal health, and suggested that their presence may be due to factors unconnected with disease.

The aim of this investigation was to determine what factors, other than the above diseases, are associated with this apparently common physical finding, in order to help the clinician assess its clinical significance when he elicits it.

In a pilot study 200 patients (from six wards) in the Whittington Hospital were examined. Details of their age, sex, occupation, duration in hospital, diagnosis, temperature, and blood-pressure were recorded. Hess's test was performed—according to the method suggested by Wood (1956)—and the urine of each patient was examined chemically for blood. The fingers and toes were examined for splinter haemorrhages. Other details which might have been relevant, such as purpura and the results of laboratory investigations, were also recorded.

The pilot study suggested that age, occupation, duration of the patient in hospital at the time of examination, and blood-pressure were factors which might be associated with the presence of splinter haemorrhages. It also showed that examination of the toenails was a fruitless task, because they were very often thick and opaque.

### Material and Methods

A group of patients who had all been admitted to 12 of the general medical and surgical wards of the Central Middlesex Hospital from April to July, 1962, were examined.

The age, duration in hospital at the time of examination, occupation, blood-pressure, and presence or absence of splinter haemorrhages were recorded for each patient.

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Each patient was examined for or questioned about the relevant factor in the order stated above, so as to avoid bias in classifying the occupational grade when the presence or absence of splinter haemorrhages was known.

Each patient was placed in one of four groups according to his occupation and activities. The patient was first classified as "manual" or "non-manual" according to the extent to which his hands might be exposed to trauma as a result of his occupation. The patients in each main group were then subdivided into a further two groups depending on the extent to which the patient in fact used his hands either at work or at home. There were thus four grades of occupation (1, 2, 3, and 4) based on increasing exposure to trauma.

For example, a motor mechanic would be classified as grade 4 if he actually wielded the tools himself, but as grade 3 if he had not worked for some weeks prior to admission to hospital, or if he was a foreman who rarely used his hands. Similarly, a housewife would be classified as grade 4 unless she had a servant to perform her heavy duties, in which case she would be grade 3. A clerk would be classified as grade 1 unless he indulged in a moderate amount of gardening or decorating at home, in which case he would be classified as grade 2.

Splinter haemorrhages were defined as longitudinally linear lesions, red, brown, or black in colour, not blanching on pressure, which were visible beneath the nail in the distal third of the vascularized part of the nail-beds of the fingers or thumbs. Any lesion which, by its appearance or from the patient's account, was due to an actual splinter was discounted.

### Results

A total of 267 patients were examined, and splinter haemorrhages were found in 51 (19.1%).

To estimate the strength of the association between splinter haemorrhages and each of the other factors, it was decided to calculate product moment correlation coefficients and partial correlation coefficients. It should, however, be appreciated that the data are not "normally" distributed in each of the factors analysed, and so this approach cannot be regarded as providing exact probability levels for the coefficients. The following interpretations have therefore been put upon the probabilities found: (1) 0.10, non-significant; (2) between 0.10 and 0.01, doubtfully significant; (3) less than 0.01, statistically significant.

Correlation coefficients were calculated between the presence or absence of splinter haemorrhages and various

other factors. The calculations were made on grouped data for "age" (14-24, 25-34, 35-44, 45-54, 65+ years) and for duration of stay in hospital (1-2, 3-4, . . . 19-20, 20+ days). As may be seen in Table I, there was a

TABLE I.—Correlation Coefficients of Various Factors with Presence or Absence of Splinter Haemorrhages

Factor	Correlation Coefficient of Factor with Splinter Haemorrhages	Probability Level
Age	-0.236	P<0.001
Duration of stay in hospital	-0.283	P<0.001
Occupational grading	+0.676	P<0.001
Systolic B.P.	-0.100	P>0.01
Diastolic "	-0.080	P>0.01

statistically significant correlation between splinter haemorrhages and age, duration of stay in hospital, and occupational grade.

As there was evidence of some association between age and occupational grading and between age and duration of stay in hospital, partial correlation coefficients were evaluated (Table II).

TABLE II.—Partial Correlation Coefficients of Various Factors with Splinter Haemorrhages

Correlation Coefficient of Splinter Haemorrhages		Correlation Coefficient	Probability Level
With	Allowing for		
Age	Duration of stay in hospital	-0.196	P<0.001
	Occupational grading	-0.050	P>0.10
Duration of stay in hospital	Occupational grading	-0.355	P<0.001
	Duration of stay in hospital	+0.696	P<0.001

Allowing for the effect of occupational grading in the correlation of age with splinter haemorrhages leads to a much reduced value of the coefficient (-0.050). This value does not reach statistical significance. Since the relationship of splinter haemorrhages and occupation accounts for most of the association between splinter haemorrhages and age, age will be ignored subsequently.

The correlation coefficient of duration of stay in hospital with splinter haemorrhages, allowing for occupational grading, was -0.355 (P<0.001) and that of splinter haemorrhages with occupational grading, allowing for duration of stay in hospital, was 0.696 (P<0.001).

There is therefore evidence that splinter haemorrhages are more likely to be found in patients in occupational groups which lead to more exposure of the hands to trauma, and also in patients examined shortly after admission to hospital.

It is of interest that the subdivision of each of the basic occupational groups leads to differing proportions of patients with splinter haemorrhages—39% of 76 and 18% of 34 patients in the manual group, and 18% of 44 and 6% of 113 patients in the non-manual group (Table III). Each of these differences is statistically significant at the 5% level.

The distribution of the values of duration of stay in hospital for the group of patients with splinter haemor-

TABLE III.—Presence of Splinter Haemorrhages According to Occupational Grading

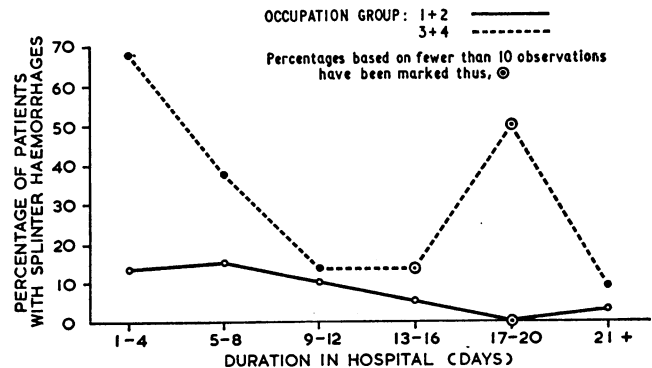
Occupational Grading	Total Patients	Patients with Splinter Haemorrhages	
		No.	%
1	113	7	6
2	44	8	18
3	34	6	18
4	76	30	39

rhages ranges from 1 to 63 days, with a medium value of 5 days.

Discussion

In spite of the imprecision of the boundaries of the occupation grades, it appears from the analysis of the results that the incidence of splinter haemorrhages is related to the occupation or activities of the patient. In so far as these have been graded, the occupations or activities which exposed the hands to frequent trauma tended to be associated with a higher incidence of splinter haemorrhages.

Furthermore, the incidence of splinter haemorrhages was highest in those patients who had been most recently admitted to hospital, and tended to decrease with duration in hospital (as shown in the Chart).



Decline of the incidence of splinter haemorrhages in manual (groups 3 and 4) and non-manual (groups 1 and 2) groups of patients with increasing duration of stay in hospital. Percentages based on fewer than 10 observations are marked thus ⊙.

It can be shown, by marking finger-nails with pinpricks at the junction of the distal third and the proximal two-thirds of the vascularized part of the nail (those being the limits of the area where splinter haemorrhages are commonly found), that these marks travel beyond the vascularized part of the nail by 14 days (approximately).

During the collection of the data presented here it was noted that in two patients who had six splinter haemorrhages each when first examined, and who were subsequently examined daily, all of the splinter haemorrhages had outgrown the vascularized part of the nail by the twelfth day.

This gives additional weight to the "trauma hypothesis" that the decline in the incidence of splinter haemorrhages with increasing stay in hospital is due to two factors: (1) the gradual growing out of the splinter haemorrhages already present, and (2) the cessation of occupational trauma, leading to fewer or no further splinter haemorrhages.

It will be seen that no attempt has been made to correlate the incidence of splinter haemorrhages with the diagnosis with which the patient was admitted to hospital. In order to confirm that the tendency for manual occupations to be associated with the presence of splinter haemorrhages is not spurious, owing to a possible association between manual occupations and subacute bacterial endocarditis, a review was made of the incidence of this disease in the Central Middlesex Hospital for the years 1960 and 1961. There are 25 recorded cases of bacterial endocarditis in the two-year period, in which time 27,000 in-patients were admitted to the hospital. Thus the incidence of this condition was 0.09%; it seems unlikely that the incidence of splinter haemorrhages in this series would have been seriously affected by bacterial endocarditis.

**Summary**

A total of 267 hospital in-patients were examined for splinter haemorrhages. These were present in 51 (19.1%).

They were found to occur more often in those patients whose occupations or activities exposed their hands to frequent trauma. They were also found more often in those patients who had recently been admitted to hospital, their incidence tending to decrease with increasing length of duration in hospital.

It is suggested that they may be traumatic in origin.

Other details which were recorded—namely, age, sex, temperature, blood-pressure, capillary fragility, and haematuria—were apparently irrelevant.

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## RELATION BETWEEN CIRRHOSIS AND TRACE METAL CONTENT OF LIVER WITH SPECIAL REFERENCE TO PRIMARY BILIARY CIRRHOSIS AND COPPER\*

BY

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The aetiology of cirrhosis of the liver is often obscure. In about 34% of cases in this country no factor can be incriminated, and these are designated as idiopathic or cryptogenic. Others we refer to by certain labels, but that does not necessarily mean that we understand what the cause is or how it produces its effect. An example of this type of obscurity is the so-called primary biliary cirrhosis. Cameron and Hou (1962) state that "we may as well frankly admit that we have little or no idea of the causation of primary biliary cirrhosis."

The knowledge that heavy metals could in some circumstances give rise to pathological changes within the liver suggested that the trace metal content of cirrhotic livers should be studied. In our own series of 450 cases we have encountered arsenical cirrhosis in 7 (1.6%), haemochromatosis (iron) in 7, Wilson's disease (copper) in 2 (0.44%), and gold cirrhosis in 2. This experience encouraged us to think that we might discover similar but more obscure evidence of some such cause for other types of cirrhosis, and perhaps a factor linking cirrhosis with primary carcinoma of the liver.

**Methods of Analysis**

Substantial samples of about 1 g. or more were obtained from a representative area of the liver, at operation or at necropsy, from patients suffering from a variety of pathological conditions including cirrhosis. "Normal" liver samples were taken from cases of sudden accidental death.

The concentrations of iron, zinc, cobalt, copper, and gold in liver were determined by neutron activation analysis. The procedures, by which all five elements may be determined in less than 0.5 g. of liver, are described in detail elsewhere (Parr and Taylor, 1963). The principle of this extremely sensitive method of analysis is as follows.

Weighed samples (about 0.1 g.) of the dried tissue, together with standards consisting of weighed amounts of the pure elements under study, are rendered radioactive

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by bombardment with neutrons in a nuclear reactor. The desired elements are then separated chemically and their radioactivity is identified and determined with a  $\gamma$ -ray scintillation spectrometer. The content of the element in the tissue is then calculated from the relative amounts of radioactivity in the samples and standard. With these particular techniques the overall error is less than 5%.

In order to reduce the risk of spurious results it is necessary to take great care to prevent the contamination of the sample prior to activation. Immediately after removal the tissue specimens are placed in clean polythene envelopes, sealed, and frozen until required for analysis. During subsequent processing prior to activation the specimens are handled with plastic forceps, and glass knives are used for cutting off outer surfaces of the sample. The samples are then dried and ground up in plastic vessels.

Blood samples are collected through platinum-iridium needles into specially cleaned syringes.

In a few cases it has been necessary to analyse fixed specimens, and in these instances samples of the preservative have also been analysed.

**Results and Discussion****Iron**

The concentration of iron in the liver of normal subjects and that of patients suffering from a variety of diseases is shown in Table I. The range of values observed is very wide, and, except for the single case of haemochromatosis in which the iron concentration is almost 1%,

TABLE I.—*Concentration of Iron in Human Liver*

Diagnosis	No. of Patients	Iron Concentration ( $\mu$ g. g. Wet Weight)		
		Mean	S.D.	Range
Normal adult	6	183	$\pm 86$	42-252
Cirrhosis of liver (excluding cancer)	18	282	$\pm 360$	39-1,570
Cancer (all sites)	40	409	$\pm 326$	33-1,820
Cardiovascular disorders	10	249	$\pm 224$	34-816
Haemochromatosis	1	9,100	—	—
Other disorders	13	262	$\pm 135$	48-515