lowered. The ratio was below this critical range in more than 70% of bile samples from patients with gallstone disease. The phospholipid + bile salt/cholesterol ratios in the isolated macromolecular aggregates which we studied were in agreement with Isaksson; of some interest being the observation that hepatic bile from patients with gallstone disease contained complexes with ratios below the critical range."

**SUMMARY**

There is a variety of macromolecules in bile, all of which, on theoretical grounds at least, might contribute to gallstone formation. The role of the bile proteins is probably the least significant. Mucous substances contained in bile are certainly components of gallstones. They might aid stone formation not only by providing a matrix for the lipid components of the stone, but also by increasing the viscosity of the bile with consequent bile stasis. Of greatest significance are the lipid-containing macromolecular complexes, which are now known to be mixed micelles of bile salts, cholesterol, phospholipids and probably the bile pigments. These micelles are large, polymolecular aggregates with molecular weights varying from 11,000 to 75,000 depending upon the concentration of the bile. Cholesterol, one of the major components of gallstones, is mainly (or only) transported in bile in micellar solution. Thus the possibility of a reduction in, or instability of the cholesterol-holding capacity of the mixed micelles in bile is an aspect of bile physico-chemistry that requires further investigation. Of equal significance, but less well understood, is the relationship of the bile pigments to the mixed lipid micelles in bile.

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**HYPOCHROMIC ANAEMIA IN CHRONIC INFECTIONS**

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Textbooks of haematology and medicine, a review of 378 patients in Oxford, and a recent annotation in The Lancet indicate that iron deficiency is usually considered to be by far the commonest cause of hypochromic anaemia. When there is a block in the incorporation of iron into haemoglobin, as in thalassaemia, pyridoxine-responsive anaemia and refractory sideroblastic anaemia, hypochromia may also occur. However, these conditions are apparently uncommon among the Bantu in South Africa.

Some years ago we were impressed by the frequency with which hypochromia was reported in patients admitted to this hospital suffering from a variety of chronic infections. We found this surprising in a hospital population composed largely of Bantu patients, in the majority of whom high tissue-iron deposits may be expected and in whom iron-deficiency anaemia should therefore be relatively infrequent.

We accordingly started a controlled investigation of the anaemia associated with long-standing infections. Our results in Bantu patients with amoebic liver abscess have already been published. We have since studied a further series of 34 patients selected on the grounds only that they suffered from chronic infection. Thirty-two were Bantu and 2 Indian, and all but 6 were male. Pulmonary tuberculosis was the commonest infection (23 cases). Six patients had pyogenic lung abscess, while the remainder suffered from bacterial endocarditis, polyarthritis, empyema, pleural effusion and tuberculous peritonitis.

For the purpose of control our results were compared with the haematological findings in 51 subjects, all of whom were in apparent good health (30 Bantu males, 8 White females and 13 White males).

**METHODS**

Morning specimens of blood were taken shortly after admission to hospital and before treatment had been instigated. Haemo-
globin was estimated as oxyhaemoglobin in an EEL colorimeter and the packed-cell volume was determined by a microhaematocrit method, as described by Dacie. Both were done in duplicate.

The methods of Bothwell and Mallett and Bothwell et al. were used for the plasma iron and the unbound iron-binding capacity. From these 2 estimations the total iron-binding capacity (TIBC) was calculated by addition.

A specimen of bone marrow was aspirated from the sternum in each case. It was stained for iron by hydrochloric acid and 3% potassium ferrocyanide, the iron stores being graded 0-6 as described by Rath and Finch. The technique of Douglas and Dacie was used for sideroblast counts.

Hypochromic anaemia was diagnosed when the Hb. was under 12.0 G./100 ml. and the mean corpuscular haemoglobin concentration (MCHC) was 30% or less.

RESULTS
Examination of the bone marrow showed that erythropoiesis was normoblastic in all patients and all showed the presence of haemosiderin, which we graded 1-2 in 6 patients and 3-6 in 28.

Our findings in the peripheral blood are summarized in Table I while Table II shows 5 examples of haematological patterns encountered. It was noted that the MCHC ranged from 25% to 33% and that hypochromic anaemia was a common feature in this series (24 out of 34 patients), despite the adequacy of the iron stores, while there was no anaemia and only 1 case of hypochromia (MCHC 30%) in the controls.

As expected in infection, and unlike iron-deficiency anaemia, both plasma iron and TIBC values were reduced (with means of 44 and 162 µg./100 ml. respectively) and in most patients the percentage saturation was normal (mean 27%) although the range was wide (9-62%). Among the controls the results were similar to those of other workers, except that in a few of the Bantu the plasma transferrin was almost fully saturated with iron (Table I).

Four patients had plasma iron patterns similar to those found in iron-deficiency anaemia. Their plasma iron levels were very low (10-35 µg./100 ml.) and the saturation less than 16%. Iron deficiency was excluded in these patients, however, by the presence of adequate amounts of haemosiderin in the bone marrow (grades 2, 3, 3, 4).

Sideroblasts, counted in 20 patients, were all abnormally low (under 20%) with one exception (33%); in 12 cases no sideroblasts could be seen. Ring-sideroblasts were not observed, and this fact together with the absence of hyperferreraemia effectively excludes the sideroblastic anaemias as the cause of the hypochromic anaemia in this series.

DISCUSSION
The anaemia observed in our patients appears to be the anaemia of chronic infection. What is surprising is the frequency with which it is hypochromic. This has been previously observed but insufficiently stressed, so that the terms 'hypochromic anaemia' and 'iron-deficiency anaemia' still tend to be regarded as synonymous, probably because most of the extensive literature on hypochromic anaemia has come from studies on patients in whom anaemia was the major clinical feature.

When low MCHC values are encountered, iron deficiency can readily be excluded by examination of the bone marrow for iron, and this was done on every patient. In iron-deficiency anaemia the stores are depleted, whereas normal or increased amounts are found in the presence of infection, as shown in our cases.

Although the plasma iron pattern usually also helps to distinguish between these 2 conditions, this is not invariably so. It will be noted that 4 patients in this series had patterns like those of iron-deficiency anaemia, but their iron stores were adequate. Case 4 (Table II) is a good example. The MCHC, plasma iron and saturation suggest iron-deficiency anaemia, which is ruled out by finding a normal amount of iron in the marrow.

How frequently is hypochromia found in the anaemia of infection? In our experience with chronic infections the incidence appears to be high. Among Bantu patients in the medical wards at King Edward VIII Hospital, where severe infection still dominates the scene, infection is probably the commonest cause of hypochromic anaemia. Twenty-four out of 34 patients in the present series and 15 out of the 31 patients with amoebic liver abscess previously reported had hypochromic anaemia, an over-all incidence of 60%.

These results are comparable with those of Bainton and Finch in Seattle, although the incidence in Durban is somewhat higher.

When severe hypochromic anaemia is encountered in patients with chronic infection, treatment with iron is irrational since the anaemia is due to a block in the incorporation of iron into haemoglobin and not to an inadequate supply. In such cases, the only rational therapy is blood transfusion. If circumstances permit, examination of the bone marrow for iron should be undertaken but, in the absence of facilities, transfusion should not be delayed and...
valuable time wasted by embarking on a trial course of iron to the detriment of the patient.

SUMMARY

Hypochromic anaemia is shown to be a common feature in a series of 34 patients with various chronic infections. Iron deficiency anaemia was found as the cause in each case by demonstrating the presence of haemosiderin in the bone marrow.

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AMOEBIC LIVER ABSCESS CAUSING CAVAL THROMBOSIS, PULMONARY EMBOLIC DISEASE AND COR PULMONALE

THREE CASE REPORTS

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The purpose of this paper is to present the aetiological role of amoebic liver abscess in the production of venous thrombosis and subsequent pulmonary embolic disease leading to cor pulmonale. Cor pulmonale associated with amoebic liver abscess has not been encountered here previously, nor has an extensive search of the literature revealed any published reports.

Three cases of amoebic liver abscess complicated by thrombosis of the inferior vena cava are reported: in 2 of these pulmonary embolic disease leading to right ventricular failure occurred.

CASE REPORTS

Case 1

A previously healthy African male, aged 25 years, was admitted to hospital complaining of pain in the right upper abdomen of 1 week's duration. The pain was aggravated by coughing. He admitted to dyspnoea on exertion, orthopnoea, swelling of the ankles and headache.

On examination oedema of the ankles and sacrum was found, with puffiness of the face. The jugular venous pressure was raised. Tachycardia, cardiomegaly and a presystolic gallop rhythm were present. The blood pressure on admission was 145/108 mm. Hg. Gross ascites and a right-sided pleural effusion were found. The liver was enlarged 3 fingerbreadths below the right costal margin and was tender.

Special investigations. Hb. 12.5 G/100 ml., WBC 16,000/ cu.mm. The CSF had xanthochromic supernatant fluid. RBCs scanty, polymorphs +++, lymphocytes +++, protein 504 mg./100 ml., globulin 290 mg./100 ml., sugar 24 mg./100 ml. X-ray of the chest showed elevation of the right hemidiaphragm posteriorly and a small effusion at the right base. A clinical diagnosis of congestive cardiac failure was made on admission, but the aetiology was undetermined. Treatment consisted of bed rest, digoxin and diuretics. Two days later the patient developed neck stiffness, bilateral extensor plantar reflexes and pin-point pupils. Clinically, meningitis or an amoebic brain abscess was suspected and a lumbar puncture was performed. Emetine hydrochloride was added to the treatment. The patient became confused, lapsed into coma, and died on the 4th day after admission.

Necropsy findings. The body weighed 130 lb. Oedema of the legs and sacrum was noted. The liver weighed 2,700 G and a large amoebic abscess was found in the right lobe posteriorly. The diaphragm was adherent anteriorly and a loculated subphrenic abscess was present. The liver abscess communicated with the inferior vena cava through a small perforation, and a polypoidal thrombus was found adherent at the site of perforation. The lungs (750 and 650 G) showed minimal oedema and numerous emboli adherent to the walls of the arteries. Haemorrhagic infarction was not found. The heart weighed 350 G and gross examination demonstrated hyper trophy and dilatation of the right ventricle and a relatively normal left ventricle. Mural thrombi were present in the right atrial appendage. The brain revealed a large abscess situated in the left frontal lobe. The colon showed no abnormality. The other organs were congested. Bilateral small hydrothoraces and moderate ascites were also present.

Microscopic examination of sections from the liver disclosed an amoebic abscess but no amoebae were seen. The absence of amoebae in sections may have been due to emetine therapy. Sections from both lungs revealed recent and organizing emboli in the pulmonary arteries at all levels. Sections from the brain showed an abscess but again amoebae were not seen.

Case 2

An African male aged 70 years was admitted to the King Edward VIII Hospital acutely ill and unable to give any history of himself. The patient's daughter testified that her father had been admitted to another hospital recently complaining of swelling of the ankles, shortness of breath and upper abdominal pain. He left hospital about 10 days before the present admission and had discontinued his maintenance therapy. Swelling of the ankles and shortness of breath at rest recurred and he was brought to hospital.

On examination he was very ill, dyspnoeic, pale, and had oedema of the ankles and sacrum. The jugular venous pressure was raised. Tachycardia and cardiomegaly were found and the blood pressure was 130/90 mm. Hg. The abdomen was slightly distended and a firm liver was felt in the epigastrium. Free fluid was present in the peritoneal cavity.

A diagnosis of congestive cardiac failure of undetermined aetiology was made. The patient died within hours of admission and no special investigations were done.

Necropsy findings. The body weighed 120 lb. Oedema of the lower limbs was noted. The liver weighed 1,650 G, was siderotic and dense adhesions were present on the diaphragmatic surface. An amoebic abscess 5 cm. in diameter was found in the right lobe of the liver. Thrombosis of the right hepatic vein extending into the inferior vena cava was noted (Fig. 1). Examination of the lungs showed extensive emboli in