trait incidence of 26·9%[1] and 20·6%[2] respectively, and while accepting that such foci of the gene do exist, it is important not to lose sight of the major areas where problems associated with the sickle gene are more likely to occur. There is no doubt that should screening programmes for aircrew be adopted, these must be applied regardless of race. The present policy of some authorities in screening only people of Negro origin would miss examples of sickling in other ethnic groups and is to be deplored. Dr. R. A. Lewis (8 January, p. 113) feels that we have misquoted a statement from his book,[3] and in fairness to this author we would like to produce the relevant passage in its entirety.

"With respect to occupational ability, individuals with G-6-PD deficiency do not suffer from any occupational handicap, and people with sickle-cell trait are only at risk when the type of work entails frequent exposure to reduced oxygen pressure. Although there are military and civilian pilots who have sickle-cell trait and who have not suffered from any disability during their career, there is still some risk involved, especially that of splenic infarct. It is therefore advisable to discourage individuals with sickle-cell trait from entering a career which involves frequent airplane flights. On the other hand, it is not necessary to dismiss or ground individuals who have already been trained or employed before the sickling trait was noted. These individuals deserve the benefit of medical supervision."

We apologize to Dr. Lewis for our inadvertent substitution of the word "patient" for an individual who deserves the benefit of medical supervision. The use of the word individual or patient for those rare cases of the sickle-cell trait in which symptomatic episodes are or might be related to the presence of Hb S is a semantic problem. In his book Dr. Lewis has summarized the situation:

"Sickle-cell trait is not a disease. For this and other reasons it is almost impossible to make the clinical distinction between a person with normal haemoglobin and one with sickle-cell trait. The only clues to the existence of sickle-cell trait are idiopathic haematuria and infarction following airplane flight." To these should be added the hazards of anaesthesia, and Dr. F. I. D. Konotey-Ahulu[4] stated "While the difference in haemoglobinopathy between normal homozygotes and persons with the sickle-cell trait is qualitative, that between persons with the sickle-cell trait and those with sickle-cell anaemia is quantitative; so that the same conditions which would cause crises in patients with sickle-cell anaemia could, if pushed to a further unphysiological degree, also cause in-vivo sickling in persons with the sickle-cell trait." We submit that exposure to altitude is such a condition.

It has been inferred that cases of infarction in flight previously reported as the sickle-cell trait were perhaps examples of other sickle-cell syndromes. It was suggested that ignorance of Hb C prior to 1951 may have confused the diagnosis but only one case report preceded that time. Case reports since 1951 (which include all but Sullivan's (1950) case) have been queried by your correspondents on the grounds that there was insufficient evidence for the trait. It has been pointed out that there is a close similarity between the haemoglobin electrophoretic patterns in the sickle-cell trait and in some cases of sickle-cell β-thalassaemia. However, the concentration of Hb A in sickle-cell β-thalassaemia uncommonly exceeds 30%, whereas in the sickle-cell trait it is usually above 60%. In short, the Hb S band is more prominent in sickle-cell β-thalassaemia and the Hb A band is more prominent in the sickle-cell trait. The strict diagnostic criteria adopted by Dr. Konotey-Ahulu (15 January, p. 177) for the sickle-cell trait are admirable, and with these in mind we would like to consider the following case reports. Smith and Conley[5] reviewed the haemoglobin electrophoretic pattern in 15 cases of splenic infarction occurring in flight. In 11 of these they noted two bands, and particularly commented that "the amount of normal hemoglobin exceeded the amount of sickle hemoglobin. This is the pattern in the sickle-cell trait." Rotter *et al.*[6] described three cases of splenic infarction in which investigation indicated Hb A levels of 56%, 56·2%, and 57·5% respectively. Thompson[7] reported a case of splenic infarction in which the AS pattern was present with 40% Hb S.

It appears to us that these 15 cases are acceptable as examples of the sickle-cell trait and we feel that there is no reason to entertain any other diagnosis. We consider that the association between the sickle-cell trait and splenic infarction at high altitude is established, and it is against this background that we were surprised at the incredulity surrounding Case 1 of our article (the Ghanaian sickle-cell trait case who developed an infarctive crisis during flight in an unpressurized aircraft). However, in this case we must agree that the available haematological investigations have not excluded a diagnosis of sickle-cell disease. The surgeon in charge of this case (Wing Commander Keiller) has forwarded all available details to Lieutenant-Colonel R. O. Addae as requested (1 January, p. 53), and we share his interests in further investigations to establish the genotype in this patient.

It was also suggested that the four fatal cases reported by Jones *et al.*[8] at 4060 feet (1234 m) were possibly not sickle-cell trait carriers. Elsewhere Binder and Jones[9] stated that three of the four cases had haemoglobins A and S present on electrophoresis with "an obvious predominance of Hb A in each case." As stated earlier, we consider this is good evidence for the sickle-cell trait. At this time, however, it is impossible to relate the significance of these fatalities to members of the general population with sickle-cell trait.

At this stage we would like to restate the purpose of our original communication which was to draw attention to the fact that even in pressurized aircraft, cases of sickle-cell haemoglobin C disease and sickle-cell β-thalassaemia are at some risk. As Dr. Konotey-Ahulu has pointed out, these cases may have normal haemoglobin levels and it follows that they may escape detection unless adequate screening is applied. An association between the sickle-cell trait and splenic infarction in unpressurized aircraft at high altitude appears to us to be established, but no cases have been reported in pressurized aircraft.

Finally, with regard to aircrew we wish to reiterate our comment that "It would seem most important that a firm, lasting, and internationally acceptable policy be defined on this subject by the authorities responsible for aircrew licensing."

The relationship of the sickle-cell trait to altitude is but one aspect of the much wider issue relating to the possible pathogenetic significance of the sickle-cell trait. There is much ignorance in this field at present, and we are sure that all workers would join in the hope that future studies will serve to clarify the situation, not only in respect to altitude, but also to other areas.—We are, etc.,

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Mercury Poisoning from Wheat

SIR,—We would like to draw attention to an outbreak of poisoning from the mercurial compound Granosan M (ethyl mercury p-toluene sulphonanilide), which has ravaged Iraq in the last two months. The poisoning occurred among farmers whose wheat grain had been dressed with the fungicide. The number of hospital-admitted cases exceeded 5,500, and the deaths reached 280.

A similar outbreak on a smaller scale occurred in this country in 1961 and has been reported.[1 2] The present outbreak is being thoroughly studied and will be reported in due course.

It will be greatly appreciated if doctors from other countries with experience in this field, particularly as regards treatment, would correspond with the undersigned.—We are, etc.,

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The Haemoglobinopathies

SIR,—My old friend Professor H. Lehmann (26 February, p. 571) is quite correct. True sickling is no doubt a property of Hbs S and C Harlem/Georgetown, in which valine replaces glutamic acid in position 6 of the β-chains. However, according to Harris and Kellermeyer,[1] Hb Memphis, an α-chain variant in which glycine replaces glutamic acid in position 23, may produce sickling by the same mechanism. These authors also state that Hbs F Alexandra (not F as stated in Professor Lehmann's letter), Barts, I, and Porto Alegre can induce a sickle shape-change.—I am, etc.,

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