may easily be done by using a slide rule or a table of reciprocals. Then any calculated difference—for example, $|Pa-Pab/b|$—may be immediately compared with the appropriate value in the table. If the calculated difference (D) is equal to or exceeds the appropriate tabulated D, then the calculated D is significant.

The actual values of Pa and of n will not usually coincide with the tabulated values of Pa and n respectively, but the actual values will each lie between two adjacent tabulated values. When this is the case, four values of D will be obtained from the table, corresponding to the two adjacent tabulated values of both Pa and n. If the calculated D is greater than or equal to the largest of these four tabulated Ds, then the difference is significant. If the calculated D is less than the smallest of the four tabulated Ds, then the difference is not significant. In practice the calculated D will seldom fall within the range of the four tabulated Ds. But when this does occur it will be necessary to interpolate. An example will make the appropriate procedure clear.

Let Pa=33.1%, Nb=21, and N=504. Thus $1/Nb-1/N=n=0.0476-0.0020=0.0456$. Now Pa lies between 30 and 35 and n lies between 0.045 and 0.050. The four values of D corresponding to these values of Pa and n are as follows: 19.1, 19.9, 20.1, and 21.0. Thus if the calculated D is equal to or greater than 21.0, then it is significant, but if D is less than 19.1, then it is not significant. But if the calculated D is 19.3, for example, then we must interpolate. To do this, take n=0.045 and note that for Pa=30%, D is 19.1, and for Pa=35%, D is 19.9. Thus for n=0.045 and Pa=33.1%, $D=19.1+\frac{33.1-30.0}{35.0-30.0}(19.9-19.1)=19.1+\frac{3.1\times0.8}{5}$ $=19.1+0.5=19.6$.

Now take n=0.050. For Pa=30%, D is now 20.1 and for Pa=35%, D is 21.0. For n=0.050 and Pa=33.1%, D therefore $=20.1+\frac{33.1-30.0}{35.0-30.0}(21.0-20.1)=20.1+\frac{3.1\times0.9}{5}=$ $20.1+0.6=20.7$. Thus for n=0.0456 and Pa=33.1%, $D=19.6+\frac{0.0456-0.0450}{0.0500-0.0450}(20.7-19.6)=19.6+\frac{0.0006\times1.1}{0.0050}=19.6+\frac{0.66}{5}=19.6+0.1=19.7$. Thus if the calculated D is equal to or greater than 19.7 it is significant at the 5% level. The figure 19.7 is the same as is obtained if the S.E. is worked out in the usual way and multiplied by 1.96.

The table should not be used if Pa or (100−Pa), whichever is smaller, multiplied by Nb or (N−Nb), whichever is smaller, is less than 500. This figure seems large, but it is really a percentage. It corresponds to an actual number of only 5. If the smallest product is less than 500, then a more accurate method of testing significance should be used (see Fisher and Yates, 1948).

I should like to thank Professor Martin Roth, professor of psychological medicine, University of Durham, for bringing this matter to my attention.

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A new feature of the Royal Society of Health's annual congress is to be a section devoted to Radiation. This will be introduced at Harrogate next April. The existing Tropical Hygiene Section will be amalgamated with the World Health Section under the new title "World Health including Tropical Hygiene." Provision has also been made for a Conference of Health Visitors in addition to a separate Conference of Domiciliary Nurses and Midwives.

HAEMOGLOBIN O (BUGINESE X) IN SULAWESI

BY

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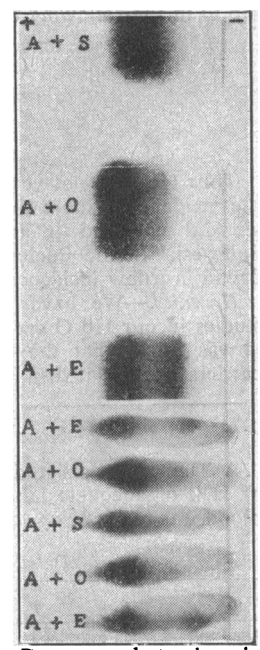
In 1956 the finding of what might be a new haemoglobin in the Buginese in Sulawesi (formerly Celebes) was reported (Lie-Injo, 1956). This report, however, did not attract any attention as it was written in the Indonesian language. In the meantime the haemoglobin has been studied more extensively by laboratories in other parts of the world, and we all agree that it is not identical with any other known haemoglobin. In this paper we record the results of further study.

Physico-chemical Properties

In 1956 the electrophoretic mobility of this haemoglobin at *p*H 8.6 was described as being between that of Hb S and Hb E (see Fig.). In phosphate buffer *p*H 6.5 it was slightly slower than Hb S and Hb C. It was not alkali-resistant, and the erythrocytes containing it gave negative sickling tests on repeated examinations. It occurred in addition to normal haemoglobin in the blood and was always present in a low concentration.



Paper electrophoresis showing Hb O compared with Hb A, E, and S at *p*H 8.6.

After repeated examinations it was not so easy to establish the exact electrophoretic mobility of the abnormal component. It was thought to be partly due to the low concentration (Lie-Injo, 1957). Study of this haemoglobin, which had provisionally been called Hb Buginese X, by three different well-known experts in three different countries did not make the problem easier, as all three had a different opinion regarding its electrophoretic mobility.

Recently a large amount of blood containing Hb Buginese X was obtained from the blood bank in Djakarta (Java), and large samples were again sent to different laboratories. Dr. H. Lehmann, of London, found that Hb Buginese X at *p*H 8.6 had a mobility between that of the Hb S and Hb E just as originally published by one of us in 1956 (Lie-Injo, 1956). He is of the opinion that our haemoglobin is indeed a new haemoglobin.

Dr. T. H. J. Huisman, of Holland, examined our haemoglobin by different methods and came to the conclusion that it was not identical with any other known haemoglobin. On examining Buginese X chromatographically with "amberlite IRC-50" he found that it moved faster than Hb L but was slightly slower than Hb S. Also, with his newly developed chromatographic method using carboxymethyl cellulose, he again found that our haemoglobin differed from other known haemoglobins. Dr. H. A. Itano, of Bethesda, Maryland, examined it in the Tiselius apparatus

in cacodylate buffer *p*H 6.5, and stated that it was not identical with Hb C, Hb S, Hb D, or Hb G. However, to our surprise, he said that Buginese X in this buffer moved more rapidly than Hb S and Hb D. We have found, on repeated examinations by paper electrophoresis, that Buginese X in phosphate buffer *p*H 6.5 was slower than Hb C, Hb S, and Hb D. One wonders whether the difference in findings at *p*H 6.5 was due to the different buffers or the different supporting media used.

Dr. Itano also examined our haemoglobin in the Tiselius apparatus in barbitone buffer of *p*H 8.6, ionic strength 0.1 and found that it migrated more rapidly than Hb E and C and more slowly than Hb S, in both the ascending and the descending limbs. This finding is in agreement with ours on paper electrophoresis with the same buffer of the same *p*H.

As it has been confirmed by different laboratories that Buginese X differs from all other known haemoglobins, it should be allotted a letter. N was the letter most recently used to designate haemoglobin Liberian I (personal communication by Dr. James V. Neel). So far as we know, the letter O has not yet been used, and therefore Buginese X should be called Hb O. Dr. James V. Neel agreed with this choice.

Distribution and Incidence of Hb O

Haemoglobin O has so far been found only in persons who originate from the Indonesian island of Sulawesi. The only blood specimen containing Hb O obtained in Djakarta was from a pure Buginese from Sulawesi. We have found Hb O in the following ethnic groups:

6	Hb O carriers	among	455	Buginese in South Sulawesi
3	,,	,,	136	Makassars in South Sulawesi
1	,,	,,	107	Gorontalo in North Sulawesi
1	,,	,,	77	Toradjas who originate from Central Sulawesi but who were living in Makassar.

Thus Hb O is not very rare on this island. In the south the incidence is more than 1% in the Buginese. However, we did not find it among 233 Minahassers in North Sulawesi. In the Buginese and Makassars Hb E was also found in a low incidence.

Heredity.—We have not been able to conduct family studies in our Hb O carriers. However, after close inquiry it was found that the three Makassars who were Hb O carriers were related.

Haematological Study

A haematological study was difficult to carry out because of lack of adequate laboratory facilities in Sulawesi. The blood was to be flown to Djakarta directly after it had been drawn, but the persons who were to do this always failed to arrive at the time scheduled by us. We were therefore able to examine only two of the carriers. In Mrs. Sal the data obtained (see Table) were within normal limits: only the resistance of the erythrocytes to hypotonic saline solutions was increased. In Mrs. Muna there was a slight anaemia. However, her blood contained malaria parasites. In Mrs. Muna also the resistance of the erythrocytes was increased. The peripheral blood of both women did not show obvious changes, and did not resemble the picture we usually see in thalassaemia-trait carriers. Anisocytosis and poikilocytosis, when present, were very slight indeed. Target cells were very rare and no stippled cells were seen.

Details of Two Carriers

	Mrs. Sal	Mrs. Muna
Age in years when examined	35	30
Hb (g./100 ml.)	13·2	11·0
R.B.C. per c.mm.	5,230,000	4,300,000
Packed cell volume (%)	42·0	—
M.C.V. (cubic microns)	80·3	—
M.C.H. (μμg.)	24·9	—
M.C.H.C. (%)	31·4	—
Leucocytes per c.mm.	6,100	—
Differential count of W.B.C.	Normal	Normal
Poikilocytosis and anisocytosis	±	±
Target cells	Very rare	Very rare
Saline fragility: Initial at	0·44	0·44
Saline fragility: Complete at	0·20	0·20
Serum bilirubin	Not increased	Not increased
Alkali-resistant haemoglobin % of total (Singer's technique)	0·6	0·8
Hb analysis	A+O	A+O
Malaria	Negative	Positive

We are trying to get hold of the other Hb O carriers, and we hope to be able to give more details regarding them and their families in the near future.

Summary

The physico-chemical properties of Hb O (Buginese X) are described. The distribution and incidence of this haemoglobin are reported and the haematological findings in two Hb O carriers are presented.

We thank Dr. T. H. J. Huisman and Professor J. H. P. Jonxis, of Holland, Dr. H. Lehmann and Dr. J. A. M. Ager, of London, and Dr. H. A. Itano, of the U.S.A., for studying this haemoglobin and for their kind co-operation which made this publication possible. Thanks are also due to all colleagues and personnel who have helped to collect the blood specimens in Sulawesi. We are grateful to the Red Cross Blood Transfusion Service, Djakarta, especially to Miss Emmy Zachari, who sent us a large amount of blood containing haemoglobin O.

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Medical Memoranda

Unusual Reaction to Chlorpromazine

As chlorpromazine is being increasingly prescribed both in hospitals and by general practitioners, the rare toxic reaction described below seems worth reporting.

CASE REPORT

A youth of 20 attended the psychiatric clinic with the complaint that for a month he had been feeling "muddled up in his mind." As there was a strong family history of schizophrenia it was thought that he might be developing this disease. Chlorpromazine, 100 mg. thrice daily, was prescribed and he was asked to return in a fortnight. However, he was brought back to the clinic in a week by his father with the story that for the past two days he had had attacks in which—to quote the father—"he had horrible poses of his head and neck." Two attacks occurred in the clinic, each seeming to be precipitated by the stress of questioning. In the attack his head was drawn slowly backwards and to the right, and his shoulders became hunched up; the facial muscles, and to a less extent those to the neck and shoulder, underwent slow writhing movements; he was unable to speak but appeared fully conscious and was able to indicate that he understood what was said to him. The first attack lasted about 10 minutes, the second about 20 minutes. The postures were not identical in the two attacks. There was no tremor or clonic movement, nor was there difficulty in walking. In the intervals between the attacks the patient seemed quite unconcerned about them and said they caused him no anxiety or pain.

The father volunteered the information (which the patient confirmed) that two days previously the patient had taken six of his tablets at the same time—that is, 600 mg. of chlorpromazine—"in order to get some sleep." The attacks began about 12 hours after this.

The patient was admitted to hospital. He had several further attacks during the evening but then no more. Examination of his nervous system next day, and of his cerebrospinal fluid and skull x-ray film, revealed no