

IN CONCLUSION.

My thanks are due to Major John Patterson, R.A.M.C., our pathologist who has had extensive experience of this condition in Burma, for his advice and help in the medical treatment of many of these cases, and to the D.D.M.S. Brigadier C. Scales, *M.C.*, for his permission to forward this article.

A NOTE ON SICKLING AND FLYING.

BY

G. M. FINDLAY, E. A. BOULTER, and C. B. MACGIBBON.

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DURING the past war Africans, in common with other people, found it necessary to fly. Africans served in the R.A.F. while a West African Air Corps took the place of European ground personnel for service in certain tropical areas. Examination of 5,500 West Africans showed that 12.4 per cent had red blood corpuscles which sickled *in vitro* when the oxygen tension was reduced (Findlay, Robertson and Zacharias, 1946). The question, therefore, arose whether sudden sickling would occur *in vivo* when Africans were exposed to a reduced oxygen tension by flying, thus giving rise to an acute and highly dangerous emergency which may end in death (Robertson and Findlay, 1947).

In order to examine this question experiments were carried out in West Africa in 1944 by observing the behaviour of the red cells of Africans with the sickling trait when flying at heights up to 15,000 feet above sea level.

The same problem arose in the United States of America where those of African origin also flew. Henderson and Thornell (1946) found that among negro cadets and combat pilots the incidence of sickling was 7.37 per cent. No evidence was available to suggest that there was an increased elimination of cadets because of the sickling trait. In America the effect of reduced oxygen tension was tested in a low pressure chamber on four subjects with sicklæmia. Two of these had had previous experience of the low pressure chamber. In addition one patient with active sickle-cell anæmia volunteered for a simulated flight while four negroes without sickling were used as controls. All except three subjects were given oxygen at 15,000 feet, while two, taken up to 16,000 feet in the low pressure chamber, were given oxygen after five minutes.

In the patient with sickle-cell anæmia there was a suggestive increase in intravascular sickling as the number of red cells sickled *in vivo* increased from 8 to 15 per cent but the patient himself showed no evidence of oxygen want at 15,000 feet: the three negroes with the sickle-cell trait showed no significant increase in sickling. The icterus index and the urinary urobilinogen remained normal throughout.

In the investigations carried out independently in West Africa the experimental conditions were those of an actual rather than a simulated flight.

EXPERIMENTAL INVESTIGATIONS.

Three African volunteers whose red cells sickled *in vitro* were examined during flight. Before the flight all the volunteers had total red cell counts of between 4 and 5 million per c.mm. Two of the Africans had never had symptoms suggestive of an acute sickling crisis but the third subject had had three attacks of jaundice associated with intense pain in the joints and bones; the last attack had occurred in 1940 before the patient joined the Army. None of the volunteers had ever previously been in an aeroplane so that they had had no opportunity of becoming conditioned to flying. The ground temperature was 85° F. while just above 15,000 feet, the temperature inside the aeroplane was 52° F. The flight in a transport aeroplane began at sea level. Twenty minutes were spent in arriving at 5,000 feet. About fifteen minutes were passed at each height before blood investigations were made. Oxygen was available. The volunteers' bloods were investigated for *in vivo* sickling at ground level, before and after the flight, and at 5,000, 10,000 and 15,000 feet above sea level, by removing blood from a vein in a syringe under paraffin and fixing it in 10 per cent formol saline under a paraffin seal so that the blood was never in contact with the air. In addition, a drop of blood was placed on a cleaned slide, covered with a cover glass and ringed with vaseline while the percentage of red blood corpuscles that had become sickled was noted up to six hours after removing the blood. The volunteers were observed for fourteen days after their flight.

RESULTS.

No necessity for the use of oxygen occurred but the cold caused shivering as no extra clothes beyond tropical kit were worn. Bloods drawn under paraffin and fixed in formol saline showed the following numbers of red cells sickled, 1,000 red blood corpuscles being counted.

NO. OF RED BLOOD CELLS SHOWING SICKLING *in vivo* (1,000 CELLS EXAMINED).

	Sea level	Height in feet			Sea level
	before flight	5,000	10,000	15,000	after flight
Subject A ..	0	0	0	12	4
Subject B ..	0	0	0	50	20
Subject C ..	0	0	0	8	0

It will be seen that at 15,000 ft. there was a slight degree of sickling, most marked in Subject B who in the past had suffered from what were probably acute sickling attacks. The degree of sickling, however, was in all three subjects insufficient to produce symptoms.

It is known that *in vitro* the bloods of different individuals sickle at different reduced oxygen tensions. When bloods taken at different heights were examined for *in vitro* sickling slight differences were noted in the rates at which the red blood cells underwent sickling. The relation between the rate of sickling *in vitro* and the height above sea level at which the blood was removed is shown in the table:—

PERCENTAGE OF RED BLOOD CORPUSCLES SHOWING SICKLING *in vitro* AT ONE TO SIX HOURS AFTER REMOVAL OF BLOOD AT DIFFERENT HEIGHTS ABOVE SEA LEVEL.

Height at which blood was removed	Subject A						Subject B						Subject C					
	Hours						Hours						Hours					
	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6
Sea level	0	0	2	8	15	21	0	0	18	52	70	76	0	0	18	26	35	42
5,000 ft. above sea level	0	3	20	32	34	42	32	55	78	94	98	100	0	4	25	38	44	56
10,000 ft. above sea level	0	18	35	46	50	54	82	94	96	98	100	100	0	22	38	54	60	68
15,000 ft. above sea level	11	28	46	54	56	60	96	100	100	100	100	100	20	38	56	74	84	88

It will be seen that the red cells of Subject B sickled more rapidly than those of A and C, thus suggesting that *in vitro* and *in vivo* sickling run parallel.

Subsequent to their flight none of the three Africans showed evidence of an increase in reticulocytes, an increased icterus index or increased urobilinogen in the urine.

DISCUSSION.

The observations here recorded made during an actual flight, together with those reported by Henderson and Thornell (1946) in the low pressure chamber, show that though reduced oxygen tension *in vitro* causes sickling of the red cells, low oxygen pressures do not necessarily cause excessive or immediate sickling of the red cells while still actually in the vessels. In both the experiments made in America and in West Africa a slight rise occurred in those with a history of sickle-cell anæmia in the number of red cells sickling *in vivo* as shown by blood drawn from the vein and fixed in formol saline in the absence of oxygen, but the degree of sickling was insufficient to cause signs of acute illness such as may occur in sickling crisis.

The factors which precipitate an acute sickling crisis are at present unknown. Hahn and Gillespie (1927) suggested that cardiac and pulmonary diseases reduced oxygen tension and were thus responsible for sickling crises. Findlay, Robertson and Zacharias (1946), however, found that Africans with pneumonia and jaundice did not show a significantly greater incidence of sickling than those with pneumonia but no jaundice. Thus consolidation of part of one lung does not tend to precipitate a sickling crisis and the icterus is probably toxic rather than hæmolytic in character. Though flying for a short time at 15,000 feet does not necessarily induce a sickling crisis through reduction of oxygen tension it may obviously cause an increased rate of sickling and as Africans vary in the reduction of oxygen tension necessary to produce sickling it is possible that sooner or later an African will be found who will sickle when flown at 10,000 or 15,000 feet for a comparatively short time. Such a sickling crisis could probably be aborted by flying at a low level. Those who have had experience of flying in the tropics will, however, be aware that owing to climatic conditions it is often impossible to come down to a low level while aerodromes are few and far between. The administration of oxygen to an African during a sickling crisis does not necessarily alleviate the pain but it does stop the *in vivo* sickling of the red cells. There is therefore an additional

incentive to see that oxygen is carried in all aeroplanes in which Africans are passengers.

CONCLUSIONS.

Experiments were carried out in West Africa to determine whether a flight up to 15,000 feet above sea level, without administration of oxygen, would induce an acute hæmolytic crisis in Africans with sicklæmia.

Three Africans with sicklæmia showed no ill-effects from such a flight, although all showed the presence of sickled red cells at 15,000 feet above sea level after ten to fifteen minutes at this height.

Differences in the rate at which sickling occurred *in vitro* in different individuals were noted and are correlated with the *in vivo* findings.

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Correspondence.

SIR,

On page 60 of the February number of this Journal, Lieutenant-Colonel R. Gwyn Evans refers to "The development during the hot summer months of a foot condition amongst tank crews in which the clinical signs consisted of pain, redness and œdema of either one or both ankles, combined with small hæmorrhages. Their interest lay in the severity of the condition after what must have been a comparatively short space of time in which crews were compelled to stand continuously in a confined and overheated space, the obvious cause of the condition."

It would be interesting to hear comments on this from medical officers with long experience of armoured warfare.

This condition gave us a lot of trouble in 9th Armoured Brigade at the Battle of El Alamein, and during the prolonged tank fights at Miteriya Ridge and Tel el Aqaqir some 70 to 80 per cent of Grant and Sherman tank commanders suffered from it; whilst Crusader tank commanders, who can sit in their tanks during battle, were rarely if ever affected. Marked œdema or brawny painful swelling extended in some cases well up the thighs; was often associated with considerable fever of which it seemed to be the only cause; and often necessitated admission to a medical unit. I personally saw no case with hæmorrhages. As the condition was much more common in officers we suspected a connexion with the rubber-soled thin "desert boots" which they wore; but the real reason for its preponderance in officers was obviously the fact that fewer other ranks were tank commanders.

The condition, as Lieutenant-Colonel Gwyn Evans says, is caused by