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INDUCED MALARIA IN YUGOSLAVIA TRANSMITTED ACCIDENTALLY
BY BLOOD TRANSFUSION

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Induced malaria, transmitted accidentally by blood transfusion, has been known since 1911 and has been reported frequently in medical literature. This subject has drawn recently an increased attention in view of its importance for malaria eradication.

Most of the authors agree on the methods for prevention of accidentally induced malaria and on the difficulties involved in tracing and investigating the blood donors. Thus, Atienza (1955), reported from the Philippines, that between 1948-1954, 83 378 bottles of blood were transfused into 53 138 patients of whom 38 developed malaria and of these, 21 were confirmed as P. vivax infections. The incubation period varied between 6-28 days. The blood had been kept before transfusion for an average of five days at 4-6°C. The author points out that most of the donors gave no history of malaria, or previous malaria infection, apart from a few who admitted attacks 20-25 years ago. Similarly Black (1960), reported four cases of induced malaria following blood transfusion in Australia from 217 948 bottles of blood used. Of these four cases, two were caused by P. vivax with incubation periods of seven and nine days, one by P. falciparum after seven days and one by P. malariae with an incubation period of 43 days. Tigano et al. (1951), studying the problem of induced malaria, described two infections caused by P. malariae with an estimated incubation period of two weeks, the donors having had attacks of malaria 16 and 19 years before donating the blood.

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Studying the morphological changes of plasmodia in blood stored at 4-6°C, Morcqs (1961) found that the late trophozoites and gametocytes were mostly affected, fewer changes being observed on the ring stages and schizonts. The author pointed out that the maximum period of persistence of the different stages of P. vivax and P. malariae in the stored blood could be accepted as 12 days.

Regarding the methods of prevention of malaria transmission through blood transfusion, Carrescia (1960) pointed out that when infected donors, used in malaria therapy of patients suffering from general paralysis, were given 1 g of chloroquine 24 hours before bleeding, they have/^{still}been able to produce malaria attacks in two-thirds of the patients. Out of nine patients given such blood, four developed infections with P. vivax, one each with P. falciparum and P. malariae, and three patients were not infected. Thus even 1 g of chloroquine given 24 hours before bleeding would not prevent malaria induced by blood transfusion.

As the world-wide malaria eradication programme progresses, induced malaria following blood transfusion is becoming more important. Although, generally speaking, the epidemiological importance of induced malaria should not be over-emphasized, the occurrence of it in a given area shows the persistence of an unrecognized parasite reservoir. Furthermore, in the countries in which the system of blood donation is on a voluntary basis involving a large proportion of the population, induced malaria cases may even serve as an index of persisting parasite reservoirs, during the consolidation or maintenance phase of the malaria eradication programme.

Induced malaria cases by accidental blood transfusion in Yugoslavia

Widespread control of malaria in Yugoslavia started actually in 1947 covering a population of some 5 200 000 exposed to the risk of infection. This programme was converted to eradication in 1959, protecting 2 240 000 inhabitants: it was successfully pursued and by 31 December 1962 all areas were under consolidation phase. During these four years, more than 40 induced cases were notified to the National Malaria Eradication Service, of which only 36 were fully investigated and will be discussed.

In Table 1, cases are classified according to the species of parasite, number of blood transfusions received and the incubation period estimated from the date of receiving the suspect blood to the date of appearance of clinical symptoms.

TABLE 1. CASES OF INDUCED MALARIA IN YUGOSLAVIA DURING 1959-1962

Species of parasites	Number of blood transfusions received	Incubation period										Total	
		5-10 days	11-20 days	21-30 days	31-40 days	41-50 days	51-60 days	61-70 days	71-80 days	81-90 days			
<u>P. vivax</u>	1	-	-	1	-	1	-	-	-	-	-	-	1
	2	-	-	-	-	1	-	-	-	-	-	-	1
	3	-	1	-	1	-	-	-	-	-	-	-	4
	4	-	-	-	-	1	-	-	-	-	-	-	1
	5	-	-	-	-	-	-	-	-	-	-	-	-
	6	-	-	-	1	-	-	-	-	-	-	-	1
	Total	-	1	1	2	3	-	2	-	-	1	-	10
<u>P. malariae</u>	1	3	2	2	-	-	-	-	-	-	-	-	8
	2	-	1	-	1	1	-	-	-	-	-	-	3
	3	-	1	1	-	2	-	-	-	-	-	-	4
	4	1	-	1	-	-	3	-	-	-	-	-	6
	5	-	-	1	-	-	-	-	-	-	-	-	1
	6	-	-	-	-	-	-	-	-	-	-	-	-
	More than 6	-	-	-	-	-	-	-	-	-	1	-	1
Total	4	3	5	1	3	1	6	-	-	-	-	23	

It will be observed from Table 1 that the average duration of the incubation period appears to be a prolonged one. This is doubtless due to the low density of parasites in the blood of donors. This low density causes considerable difficulties in the detection of infected donors, particularly when as frequently happens several donors are involved for one induced case. It should be pointed out that careful and repeated investigation of all donors involved in induced cases of malaria had been made and had failed to detect a parasitaemia in their blood.

The epidemiological importance of the asymptomatic parasite carriers with such a low density of parasites in their blood, particularly when P. malariae is involved, is illustrated by the observation that between 1959-1962, only six late relapses of P. malariae were detected, but none of them had had any epidemiological relation either with donors or with recipients involved in induced cases of malaria. Similar observations were also made for induced cases caused by P. vivax and their lack of relation epidemiologically to late P. vivax relapses. Where the area is under total coverage by residual insecticides, the epidemiological importance of such asymptomatic parasitaemias is eliminated as the vector control subsequent to the use of insecticides prevents secondary or introduced cases occurring. However, it should not be forgotten that induced cases discussed in this paper occurred not only in areas under the attack phase, but also in those areas in consolidation or maintenance phases.

As may be seen from Table 1, there appears to be no direct relation between the species of parasite and the duration of incubation, nor between the number of blood transfusions and the duration of incubation. Presenting these data according to the age-groups, it will be observed that clinical symptoms develop more rapidly in the younger age-groups than in adults. This is shown in Table 2 below.

Insufficient information is available to discuss the immunological aspects of the earlier development of the clinical attack in the younger age-groups compared with adults but there is most probably some non-specific tolerance by the adult group.

It has already been mentioned that the number of blood transfusions does not seem to influence, either the development or the duration of the incubation period. Evidence is also available on the size of inoculum and its apparent lack of influence on the period before development of the clinical attack.

TABLE 2. AGE-GROUP DISTRIBUTION OF CASES
OF INDUCED MALARIA BY TRANSFUSION

Age-group (years)	Incubation period in days								
	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90
0-1	3 P.m.	2 P.m.	2 P.m.	-	-	-	-	-	-
1-4	1 P.m.	-	-	-	-	-	1 P.m.	-	-
5-15	-	1 P.m.	1 P.m.	-	-	-	1 P.v.	-	-
Adults	-	1 P.m.	3 (2 P.m. 1 P.v.)	3 (2 P.v. 1 P.m.)	6 (3 P.m. 3 P.v.)	1 P.m.	6 (4 P.m. 2 P.v.)	-	1 P.v.

The amount of blood given at one time to adults generally ranged between 250-350 ml, in most of the cases being 300 ml. However, one of the cases discussed in this paper received a single transfusion of 600 ml, and in this case, the clinical attack due to P. vivax developed within 24 days. As several other patients developed clinical attacks within a shorter period although given only 300 ml of blood, the size of inoculum can not be considered to have much influence on the duration of the incubation period.

Amongst cases discussed, there is a group of induced cases of particular interest. These are five infants aged between three and five months who, on 24 January 1961 were given 80 cc of blood each, from one single bottle. The donor was a woman, who came from an area which had been malarious many years ago. The woman denied any history of malaria, nevertheless all five children developed clinical attacks of malaria. Out of the five, three of the children developed clinical symptoms after seven days, one after 15 and one after 23 days.

In addition to the 33 cases shown in Tables 1 and 2, there were three others, which did not lend themselves to easy classification within the tables.

One P. malariae infection in a child of four years who received 13 blood transfusions and in whom the incubation period could be estimated as between 37-86 days.

One P. malariae infection in an adult male, 38 years of age who received eight blood transfusions and in whom the incubation was between 18-46 days.

One P. vivax infection in an adult male, 64 years of age, who received six blood transfusions and in whom the incubation could be estimated as between 33-59 days.

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