The morphological and cultural characteristics of the organism are described, and are compared with those reported by other workers.

A morphologically similar organism found in the normal vagina, which must not be mistaken for fusiformis, is briefly mentioned.

With suitable antibiotic treatment, and surgical drainage where indicated, the prognosis in infection with these organisms is regarded as good.

I wish to thank both Dr. J. L. Pinniger, of St. Thomas's Hospital, London, in whose laboratory this work was done, and Dr. Mary Barber, of the Department of Bacteriology, St. Thomas's Hospital Medical School, for their helpful criticism and advice.

BIBLIOGRAPHY

- Beveridge, W. I. B. (1934). *J. Path. Bact.*, **38**, 467.
 Chandler, F. A., and Breaks, V. M. (1941). *J. Amer. med. Ass.*, **116**, 2390.
 Dack, G. M., Dragstedt, L. R., and Heinz, T. E. (1936). *Ibid.*, **106**, 7.
 ——— (1937). *J. Infect. Dis.*, **60**, 335.
 ——— Johnson, R., and McCullough, N. B. (1938). *Ibid.*, **62**, 169.
 ——— and Kirsner, J. B. (1941). *Ann. Surg.*, **114**, 653.
 Forbes, G. B., and Goligher, J. C. (1944). *Lancet*, **1**, 399.
 Franklin, A. W. (1933). *Ibid.*, **2**, 645.
 Harris, J. W., and Brown, J. H. (1927). *Bull. Johns Hopk. Hosp.*, **40**, 203.
 Jones, H. P. (1944). *Lancet*, **2**, 824.
 ——— (1944). *Ibid.*, **1**, 409.
 Lemierre, A. (1936). *Lancet*, **1**, 701.
 Owen, G. D., and Spink, M. S. (1948). *Ibid.*, **1**, 402.
 Schwabacher, Herta, and Mitchison, D. A. (1947). *J. clin. Path.*, **1**, 39.
 Topley, W. W. C., Wilson, G. S., and Miles, A. A. (1948). *Principles of Bacteriology and Immunity*. London.

EXPERIMENT TO DETERMINE IF A PROGUANIL-RESISTANT STRAIN OF *P. FALCIPARUM* WOULD RESPOND TO LARGE DOSES OF PYRIMETHAMINE

BY

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This experiment was undertaken to find out if a proguanil-resistant strain of malaria also showed partial or absolute resistance to pyrimethamine ("daraprim"). I was both subject and experimenter. By the co-operation of Dr. G. I. Robertson, of the I.C.I. laboratory, Nairobi, I received 10 bites by five mosquitoes (*A. gambiae*) infected with a proguanil-resistant strain of malaria parasite imported from the Tampin area in Malaya.

The biting took place on August 21, 1952. All mosquitoes showed sporozoites on dissection. Parasites appeared in the blood on September 1 (Day No. 1) (see Table).

Course of the Infection

Day No.	Maximum Parasitaemia	Ring/Leucocyte Ratio	Treatment	Time of Treatment
1	38/50 leucocytes	0.7:1	50 mg. pyrimethamine	Noon
2	53/50 "	1:1	50 " "	"
3	94/50 "	2:1	100 " "	"
			100 " "	2 p.m.
			50 " "	10 "
4	625/50 "	12:1	10 gr. quinine i.v., 7 tab. chloroquine in divided doses	1 "
5	763/50 "	15:1	10 gr. quinine i.v. and 10 gr. by mouth, 6 tab. chloroquine in divided doses	1 "
6	58/50 "	1:1	4 tab. chloroquine and 20 gr. quinine in divided doses	

On the third and fourth days the white blood cell counts were 4,100 and 4,500 per c.mm. respectively. After the sixth day recovery was rapid, and I was able to leave hospital on the tenth day feeling fit. At no time was toxæmia profound, and mental clarity was retained throughout, though headache became very severe on the fourth day.

Discussion

I had not previously had malaria, so immunity played no part in the infection. The experiment proved that a strain of malaria resistant to proguanil can show absolute resistance to pyrimethamine. This is hardly surprising when it is realized that pyrimethamine resulted from research on the antimalarial properties of diaminopyrimidines undertaken because these compounds showed a structural analogy with proguanil and similarities of microbiological behaviour. It is probable that both drugs act upon the same enzyme system of the malaria parasite.

It is evident that medical policy in Kenya has been wise, in that the African population has not been subjected to treatment with proguanil on a large scale. Because of dispensing difficulties in Reserves this might have been given in doses small enough to allow the widespread rise of resistant strains. The same applies, in theory, to pyrimethamine, though the drug is effective in such small doses that this danger seems unlikely to occur. The sale of 5 mg. tablets for prophylaxis would be dangerous, as adult Africans would use them for treatment, with the certainty of underdosage. Perhaps only tablets of not less than 25 mg. should be allowed for sale. These are readily divisible for treating infants, and, as the drug has a very low toxicity, there seems little to fear from overdosage. Generally speaking, it is probable that the majority of people taking pyrimethamine will do so in doses that, though harmless, are far more than actually required to eradicate infection. The fact that the drug is tasteless and cheap should ensure this.

In a recent paper Wilson and Edeson (1953), as a result of work in Malaya, report no difference in response to pyrimethamine between unselected strains of malaria and those resistant to proguanil. East African strains of malaria parasites are extremely sensitive to pyrimethamine, though recently a case of subtertian malaria which did not respond to pyrimethamine has been encountered, the resistance of the infecting parasite being confirmed by subinoculation. It would be a tragedy if other resistant strains were imported. The presence of men of the King's African Rifles in Malaya creates a hazard, and it is hoped that special care will be taken that none return to East Africa with the gametocytes of Malayan strains of malaria in the blood.

I thank the Director of Medical Services, Kenya, for permission to publish this paper and Dr. B. P. Harris for undertaking treatment at the conclusion of the experiment, when intervention became necessary; thanks are also due to the senior parasitologist, Dr. R. B. Heisch, who watched the parasite rate when I was unable to do so, and to Dr. G. I. Robertson for the great help and interest shown by him in the experiment. The nursing skill and attention were beyond praise.

REFERENCE

- Wilson, T., and Edeson, J. F. B. (1953). *British Medical Journal*, **1**, 253.

This year the number of students applying for admission to American medical schools has again declined, according to a survey by the director of studies for the Association of American Medical Colleges. 3,150 fewer students applied this year than in 1951-2, 7,600 less than three years ago. Of the 16,763 persons applying last autumn only 7,778 were accepted. The survey also shows that the average pre-medical student applies to three or four medical schools, and that the geographical distribution of students is uneven, half the candidates coming from only seven States. One cautious student applied to 45 medical schools and was accepted by one.