Medicine. — *The use of plasmoquine in the prevention of malarial infections.* By S. P. JAMES, F. R. S., Lt. Col. I. M. S. (ret.). Ministry of Health, Whitehall, London. (Communicated by W. SCHÜFFNER.)

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The paper by Prof. SWELLENGREBEL and Dr. A. DE BUCK on the "prophylactic use of plasmoquine in a dosage warranting reasonable safety for routine treatment", communicated to the Royal Academy of Sciences, Amsterdam, at a meeting on the 31st October, shows clearly that the malarial infection which a person receives when he is bitten on one occasion by from 3 to 7 or more heavily infected mosquitoes cannot be prevented from developing by taking a dose of 1 cg of plasmoquine on the day before infection, three doses of 1 cg on the day of infection, and three doses of 1 cg on each of the five following days. The experiment seems in all respects to be comparable with the experiment reported in the issue of the Lancet for August 15th, 1931, page 341, in which 10 healthy volunteers were successfully protected against a similar heavy infection by taking plasmoquine in doses aggregating 6 cg daily instead of 3 cg as in Prof. SWELLENGREBEL's experiment. The conclusion which Prof. SWELLENGREBEL very properly deduces from a consideration of the results in the two experiments is that while a dosage of 6 cg daily taken in the manner and for the period described, appears to be sufficient to prevent development of the infection, a dosage of 3 cg cannot be depended upon to do so. In stating this conclusion he directs attention to two of the experimental conditions which must be taken into account if it is desired to apply these laboratory results to natural circumstances in the field. I should like to add one or two general remarks to what Prof. SWELLENGREBEL has already said on these two experimental factors, which are: 1°. the dose of sporozoites injected by the mosquito, 2°. the period during which the prophylactic drug is given. As regards the first factor, I would say in general that a chief difficulty in drawing conclusions from the results of chemoprophylactic experiments of the type with which our trials and those of Prof. SWELLENGREBEL are concerned is that existing knowledge on the sporozoite stage of the malaria parasite is unhappily very incomplete. In the first place there is no sure knowledge of what happens to sporozoites when the mosquito injects them into the blood or tissues of the person bitten, and in the second there is almost no trustworthy evidence of the comparative effect of different degrees of sporozoite infection. It has always been assumed that, when an infective mosquito bites a person, the sporozoites which it injects reach the circulation at

once and enter red blood corpuscles in which they grow to commence the parasitic asexual cycle. SCHAUDINN described the process of their penetration into red blood corpuscles in much detail but (although many have tried) no one has succeeded in repeating his observations. Thus the time has come when it must be considered whether or not our knowledge of that part of the life cycle of the malaria parasite is complete. Sporozoites are essentially parasites of tissue cells and it is possible that what happens to them when they are injected by the mosquito is that they are carried by the blood stream to reticulo-endothelial cells of the lungs and other organs and that they enter these cells and in them go through a cycle of growth and sporulation similar to the cycle of the allied bird parasite "halteridium" of which the transmitting insect is the fly *Lynchia maura*. The merozoites resulting from sporulation then escape from the cell and enter the red blood corpuscles of the circulation. The results of our further experiments in preventing malarial infection by the administration of plasmoquine lend support to the view that the action of the drug is against a subsidiary cycle of that type in tissue cells rather than that its action is simply to kill sporozoites while they are circulating in the blood. Perhaps that may be the reason why it is necessary, in order to obtain successful prophylactic results with smaller doses of plasmoquine than 6 cg daily, to begin the administration some days before infection and to prolong it for more than five days thereafter. In the series of experiments which we have in hand at the moment, daily administration of the drug is begun a week before the day of infection and is continued for ten days after infection. This series is part of a graduated series of experiments with different doses of the drug administered for different periods before and after infection. Another reason why such a series of experiments is necessary in order to ascertain what may be the smallest daily dose of plasmoquine that will prevent infection is that up to the present it is not known how quickly plasmoquine taken by the mouth is distributed through the system and tissues and how long the drug given in a single dose remains in the blood and tissues before it is all excreted. These are points about which it is hoped that further enquiry will be made. In the meantime our invariable reply to the numerous requests which we have received for a definite statement of the smallest daily dose which will effectively prevent infection is that the experiments are proceeding and that until they are completed no useful pronouncement on the subject can be made.