curative effect in a blood-induced infection of lophurae malaria in the duck. Quinine, quinacrine and chloroquine are not curative, while pamaquine appears to cure a fair percentage of ducks. When treatment is started 24 hours after infection, pamaquine is still curative. However, when treatment is started 48 hours after infection a much smaller per cent of cures is produced. In the table the criterion of "cure" is interpreted as 2 negative subinoculations, the last taken at least 26 days after infection. In our experience a small percentage of ducks having 2 negative subinoculations will prove to be infected if further subinoculations are done; however, this percentage is so small that it would not significantly change these data.

In addition to the drugs listed in Table I, we have found that SN 6911, 7-chloro-4-(4-diethylamino-1-methylbutylamino) - 3-methyl quinoline; SN 1796, α-(diamylaminomethyl)-1,2,3,4 - tetrahydro-9-phenanthrene-methanol; SN 187, 3',5'-dibromosulfanilanilide; SN 6520, 2 - (dimethylaminomethyl)-1-naphthol; SN 901, 6-chloro-2-methoxy-9-[3-(6-methoxy-8-quinolylamino)-propylamino] acridine; SN 475, 2,2',3,3'-tetramethyl-1,1'-diphenyl-4,4'-bi-3-pyrazoline-5,5'-dione; SN 11,426, 5-(*p*-chlorophenyl) - 1-isopropyl-1-methylbiguanide, salt with acetic acid; are not curative when given in maximal tolerated dosage for 6 days. However, SN 5241, α-(dinonylaminomethyl)-1,2,3,4-tetrahydro-9-phenanthrene methanol appears to cure a certain per cent of ducks when given in the maximal tolerated dosage. With the exception of SN 5241, pamaquine is the only drug examined which appears to cure lophurae malaria in a moderate percentage of ducks.

Summary. A number of drugs have been examined for their curative action in lophurae malaria in the duck. Pamaquine appears to cure a fair percentage of the birds, while quinine, quinacrine, chloroquine and a number of other drugs do not.

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Filtrable Agents Lethal for Ducks.*

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In studying the curative activity of drugs against lophurae malaria in ducks it was found that approximately half the birds died with no demonstrable malaria before it could be established that they were cured. Extensive studies indicated that the deaths were not due to living conditions or to the various experimental procedures to which the birds were subjected. It appeared that the causative agent was in the blood injected to produce the malarial infection. Injection of blood from normal ducks did not produce deaths.

It seemed unlikely that the lethal agent was a toxin since the deaths were delayed 15 to 30 days after infection and since the causative agent was transferable by blood passage. It also seemed unlikely that it was a form of malaria since the birds which died had no detectable erythrocytic forms of the parasite and since studies in this and other laboratories[1] had failed to reveal any large number of exoerythrocytic forms of *P. lophurae* in the duck. Bacteriologic studies indicated that none of the common bacteria was responsible for the deaths. In view of these data it seemed likely that the lethal agent might be a filtrable organism. Subse-

* This investigation was done under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and The Johns Hopkins University.

[1] Porter, R. J., personal communication.

quent experiments showed that if plasma from ducks with lophurae malaria were filtered through a Seitz filter impervious to *Serratia marcessans* the filtrate produced no growth in broth at 38°C but was lethal for ducks when given intravenously.

This filtrable agent associated with *P. lophurae* caused the deaths of about 50% of the birds in 12 to 30 days. Twelve to 72 hours prior to death the birds became lethargic, anorexic and weak. These symptoms became progressively more severe and terminated in convulsions followed by death. This agent was serially passed 5 times by blood transfer. In addition, it was carried with the lophurae malaria through biweekly blood transfer for at least 2 years. Passage of the malarial parasite through mosquitoes, chicks, canaries or turkeys† failed to eliminate the filtrable agent. Washing of the parasitized erythrocytes with normal duck plasma or glucose-Ringer's solution, hemolysis with 0.05% saponin and rewashing of the parasite-containing residue with normal plasma or glucose-Ringer's solution failed to eliminate the filtrable agent. This lethal effect was also associated with *P. lophurae* in ducks obtained from other laboratories. Various attempts to obtain malaria parasites, free of the filtrable agent, from ducks which had survived an infection with both also failed. A number of drugs which were tried for their curative effect in malaria had no detectable effect on the filtrable agent. Decreasing the dose of this agent decreased the percent of ducks which die. This agent was not lethal to white mice when given intravenously, intraperitoneally or intracerebrally, and it was not lethal to dogs when given in large doses intravenously.

A lethal filtrate was obtained by filtration of plasma from ducks infected with *P. cathemerium*. It was serially transferred 35 times by blood inoculation. When first obtained this agent was 100% fatal in 3 to 5 days. Its lethality was unaffected by sulfaguanidine, penicillin, sulfadiazine and a number of potent antimalarial drugs. This rapidly lethal strain was lost; however, the agent was obtained again but it was only lethal in 10 to 20 days. Various attempts to increase its virulence failed. This agent could not be washed from the parasitized erythrocytes either before or after hemolysis. Administration of the filtrate by various routes had no effect on the time of death. Apparently ducks which had survived infection with both *P. cathemerium* and this filtrable agent possessed some degree of immunity to reinfection with the filtrable agent.

Filtrates which were lethal for ducks were also obtained by Seitz filtration of plasma from ducks infected with *P. relictum* or *P. elongatum*. The former was lethal in 30 to 40 days while the latter required only 3 to 6 days. The agent associated with elongatum malaria was transferred serially 5 times by blood passage. A quantity of pooled plasma from several birds infected with this filtrate was stored at the temperature of solid carbon dioxide.

Summary. Filtrable agents, lethal for ducks, were obtained by Seitz filtration of plasma from ducks with lophurae, cathemerium, relictum or elongatum malaria. Attempts to free the malaria of the filtrable agent were unsuccessful.

† We wish to thank Dr. R. J. Porter of the University of Michigan for passing the parasites through mosquitoes, canaries, and turkeys.