in the present paper in animals with the celiac plexus decentralized and the intestine transected, can be explained most satisfactorily as true reflex reactions. Abolition of these responses by application of a nicotine solution to the decentralized celiac ganglia also supports the assumption that the neural mechanisms employed include synaptic connections in these ganglia.

By what mechanism the flow of bile is inhibited has not been determined. Vasomotor reactions in the liver undoubtedly play a rôle in this response. The formation of bile, according to Tanturi and Ivy,[4] is influenced by intrahepatic vascular pressure. In their experiments, stimulation of the sympathetic nerves to the liver resulted in decreased bile formation, probably due to vascular or mechanical changes. True inhibitory secretory nerves to the liver have not been demonstrated. Inhibition of intestinal motility, as demonstrated in our experiments, probably is effected by impulses reaching the intestinal musculature through its sympathetic innervation

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Effect of Sulfanilamide and Sulfapyridine on the Avian Malarias.*

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The effect of sulfanilamide and sulfapyridine on some of the bacterial infections has been so striking that these drugs have been tried on many others, including some of the malarias, both of man and of animals. The results obtained have been of considerable interest, and not the less so because they have varied a great deal with the species. Coggeshall,[1] for example, found that sulfanilamide was effective in eradicating *Plasmodium knowlesi* infection in monkeys, but was apparently without any action on *Plasmodium inui* in the same host. He suggested that the difference might be due to the much more rapid metabolism of the former species. This seems probable in view of the generally accepted idea that sulfanilamide is effective because oxidation products are formed from it which destroy catalase, and hence interfere with the metabolic activities of the cell.

[4] Tanturi, C. A., and Ivy, A. C., *Am. J. Physiol.*, 1938, **121**, 61.

* Aided by a grant-in-aid from the American Philosophical Society.

[1] Coggeshall, L. T., *J. Exp. Med.*, 1940, **71**, 13.

Since the malaria parasites are present in the blood stream they are presumably more exposed to this effect than if they were segregated somewhere in the tissues.

Against the malaria parasites of man sulfanilamide and its derivatives appear not to be of great value, although the reports are conflicting, and there seems to be but one report of its use in avian malaria. Coggeshall[2] states that when administered to chicks infected with *Plasmodium lophuræ* and canaries infected with *Plasmodium cathemerium* it was without noticeable influence. It has also been used on *Hemoproteus columbæ*, but failed to exert any effect (Durand and Villain[3]).

Since it is well-recognized that the various species of malaria plasmodia react quite differently to even the same drug, trial of sulfapyridine and sulfanilamide on some of the other species of avian malaria has been undertaken. So far all the tests have been made on blood-induced infections because such infections are more easily produced in the numbers required for extensive experimenting, and also because mosquitoes have not been available. And in the case of one of the species used, *Plasmodium nucleophilum*, nothing is yet known as to the natural vector.

Up to the present, we have used these drugs against 3 species of avian malaria, *Plasmodium circumflexum* (Strain E; Manwell and Goldstein[4]), *relictum* var. *matutinum*, and *nucleophilum*. The second of these 3 species was isolated from an English sparrow in December, 1938, and the third is the original type strain, isolated from a catbird in April, 1934. All experiments were carried out with female canaries.

Because of the relatively low solubility of the drugs both the sulfanilamide (Prontylin, Winthrop) and the sulfapyridine (furnished through the courtesy of E. R. Squibb and Sons) were given in suspension. Treatments were given daily (the dosage being 0.02 g in 100 mg of physiological saline) by intraperitoneal or intramuscular injection. This amount represented about 1/5 the M.L.D. The duration of treatment varied considerably, particularly in the experiments involving sulfapyridine and *Plasmodium circumflexum*, because it was desired to evaluate the effects of the drugs as accurately as possible. Details are given in Table I.

In summary, it may be said that only one of the species was affected by either drug. This was *Plasmodium circumflexum*, which

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2 Coggeshall, L. T., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 768.

3 Durand, P., and Villain, *Arch. Inst. Pasteur de Tunis*, 1939, **28**, 94.

4 Manwell, R. D., and Goldstein, F., *Am. J. Hyg.*, 1939, **30**, 115.

TABLE I.
Effect of Sulfapyridine and Sulfanilamide on Three Species of Avian Malaria.*

Species	Treatment: When given	Treatment: Duration, days	Sulfapyridine: Exp. cases	Sulfapyridine: Con-trols	Sulfapyridine: Effect†	Sulfanilamide: Exp. cases	Sulfanilamide: Con-trols	Sulfanilamide: Effect
Plasmodium circumflexum (Strain E)	B + I	13-26‡	8	5	+++	10	7	—
	I	9	6	5	++	0	—	—
	A	5	6	5	+	0	—	—
Plasmodium var. matutinum	B + I	11-17‡	6	3	—	6	4	—
Plasmodium nucleophilum	B + I	12	6	2	—	4	2	—
Totals			32	20§		20	13§	

*Abbreviations used as follows:
B = before inoculation
I = during incubation period
A = during acute stage
Drugs given by intraperitoneal or intramuscular injection.
†This is indicated by plus signs which have the following meaning:
+++ no parasites or very few, but subinoculation showed that no birds were sterilized.
++ a few parasites seen in some cases, but duration of infection short.
+ mild infections, but heavier than those indicated with a double plus.
‡Birds were matched with controls and treated until parasites began to diminish in latter. Hence some were treated for longer periods than others.
§The total number of controls was 22; totals given are larger because some birds served as controls in series in which some birds received one drug and some the other.

was markedly susceptible to sulfapyridine. This drug was capable of aborting the appearance of parasites in the peripheral blood, and of causing their rapid disappearance after the infection becomes patent. But it is less effective than plasmochin, atebrine, or quinine.

Visible changes in the parasites were noticed only in this one species, and were especially evident in the older schizonts. These forms no longer stained normally, and the division process also seemed abnormal.

It is interesting that *Plasmodium relictum* var. *matutinum*, which is a relatively large and rapidly reproducing species (and hence of presumably high metabolic rate), appears to be entirely unaffected by either drug. It is also noteworthy that *nucleophilum* was not influenced, although it is one of the small species, several of which have previously been found especially susceptible to other antimalarial drugs. (Manwell,[5] Manwell and Haring[6].)

[5] Manwell, R. D., *Am. J. Trop. Med.*, 1932, **12**, 123; *Ibid.*, PROC. SOC. EXP. BIOL. AND MED., 1933, **31**, 198.

[6] Manwell, R. D., and Haring, Ann T., *Riv. d. Parasit.*, 1938, **2**, 209.