on the nature of the sugar moiety, nor on the presence of either thymine or uracil among the nucleic acid bases.

Inactivation of single-stranded DNA phage, S13, as well as of double-stranded DNA phages T2 and P22, suggests that alkylating agents can link not only across complementary strands (interstrand cross-linkage), but also across reactive sites on a single strand (intrastrand cross-linkage). The relatively faster rate of inactivation of the double-stranded, as compared with single-stranded phages, may indicate that both types of cross-linkage are possible in the double-stranded DNA phage. The spatial arrangements of DNA in the double-stranded T2 and P22, as well as that in the single-stranded spherical S13, are unknown. It is conceivable that intrastrand cross linking might occur across sections brought close together by folding. However, this would not be true for rod-shaped f1 phage, which seemingly exists as a single, straight helix, similar to the RNA of tobacco mosaic virus.

With a double-stranded DNA phage P22, a single-stranded DNA phage S13, and RNA phage MS2, there are short lag periods occurring during the initial 1 to 2 minutes of the reaction. This may represent either the time necessary to complete a two-stage reaction or a delay in the alkylating agent's penetrating the protein coat of the phage particle. Commings and Kozloff (*8*) reported that raising *p*H increases the permeability of phage protein coat. They showed that at high *p*H large molecules such as methylene blue can penetrate the protein coat and gain access to DNA. In our experiment at high *p*H the inactivation rate by nitrogen mustard was accelerated for all phages. Moreover, raising *p*H decreases the initial lag period (*9*). This observation suggests that the initial lag period of inactivation is dependent on the permeability of the protein coat.

That other mechanisms, such as an alkylation of amino acids in the protein coat, participate in phage inactivation, cannot be ruled out. Two amino acids, histidine and lysine, are highly reactive with alkylating agents (*10*). However, at *p*H 7.0, under the conditions of these investigations, lysine is not reactive (*10*), and the protein coat of phage MS2 does not contain histidine (*11*). From the above information the reaction between amino acids of protein coat and nitrogen mustard does not seem to play an important role in the inactivation of phage.

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Susceptibility of the Gibbon Hylobates lar to Falciparum Malaria

Abstract. *The splenectomized juvenile gibbon,* Hylobates lar, *is susceptible to infection with trophozoites of* Plasmodium falciparum. *All subjects in a group of six animals that were injected with freshly collected blood from four infected humans in Saraburi Province, Thailand, developed parasitemia 2 to 20 days later; infections were transmitted from one of these subjects to three clean gibbons.*

The white-handed gibbon (*Hylobates lar*) is a potential laboratory tool for the study of *Plasmodium falciparum* infections. Although the splenectomized chimpanzee (*Pan satyrus*) can be readily infected with falciparum malaria (*1, 2*), rapid decimation of chimpanzee populations, problems of animal management, and common parasitism with three species of malarial parasites indicate that another animal might better serve as an experimental host for this parasite.

Young gibbons (weighing 1.75 to 2.75 kg) were splenectomized by SEATO Medical Research Laboratory personnel between 16 April and 10 June. For radical cure of possible latent malarial infections, these animals were placed on a chloroquine and primaquine regimen (*3*). During the period of experimental work the gibbons were housed in mosquito-proof quarters.

Six splenectomized gibbons (P-1, P-3, P-7, P-8, P-11, and P-13) were inoculated with samples of blood from patients at the Prabuddahbet Malaria Clinic with *Plasmodium falciparum* in-

Table 1. Infection of gibbons, *Hylobates lar,* with asexual *Plasmodium falciparum.* All animals except P-12 were splenectomized prior to inoculation.

Gibbon No.	Prepatent period (days)	Day of peak parasitemia	Days of continual parasitemia	Highest No. parasites per mm³ of blood
P-1	5	35	22 to 39 +	143,500
P-2	5	12	5 to 22 +	241,800
P-3	17	25	25 to 26	11,750
P-7	20	35	23 to 46 +	38,000
P-8	2	37	28 to 39 +	15,600
P-11	4	18	18 to 19	310
P-12	5	14	5 to 6	1,400
P-13	2	17	2 to 54 +	57,000
S-2	4	12	4 to 22 +	45,200

fections. Each gibbon received 6.3 × 10^7 to 9.9 × 10^8 trophozoites by the intraperitoneal or the intravenous route. After a prepatent period of 2 to 20 days all animals had small ring forms in their erythrocytes (Table 1). These were followed by the larger trophozoites characteristic of falciparum malaria infections. The number of trophozoites increased rapidly and peaks were attained 1 to 5 weeks after the infections became patent. Asexual parasites were in the peripheral blood of most animals throughout the observation period but declined to approximately 1000 per cubic millimeter 2 to 3 weeks after reaching the height of parasitemia. All animals except P-11 had gametocytes in the peripheral circulation 4 to 25 days after inoculation. Peaks in the number of gametocytes usually paralleled the equivalent number of trophozoites but were of lesser magnitude. Most gibbons had approximately 1000 gametocytes per cubic millimeter of blood at varying intervals. P-1, with 9500 gametocytes per cubic millimeter of blood, had the highest number of sexual parasites in this series. In virtually all instances the gametocytes were immature. This was similar to the development of the parasite in the chimpanzee.

Intravenous inoculations of 2.65 × 10^7 trophozoites were made from gibbon P-7 to splenectomized (P-2 and S-2) and normal (P-12) subjects. The splenectomized gibbons developed definite parasitemias and P-2 had higher parasite counts than any other animal studied in these experiments. The gibbon with intact spleen (P-12) had a transitory parasitemia.

Most animals had a slight rise in rectal temperature associated with or just prior to the onset of parasitemia. Normal body temperature for these animals is approximately 101.5°F (38.6°C) while during the "fever" period it reached 103.5° to 104.5°F (39.7° to 40.3°C). The animals had a normal appetite and were alert during the observation period. White blood counts were made twice weekly but no appreciable fluctuations were evident.

The relative ease of infecting the splenectomized gibbon with blood-induced infections of *P. falciparum* indicates that this animal may be a suitable laboratory model for immunologic and chemotherapeutic studies of falciparum malaria. The development of an animal test system for this parasite may accelerate the study of drug-resistant strains *P. falciparum*, which has been hampered by the inherent danger of studying these parasites in nonimmune human volunteers (*4*, *5*).

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Nucleic Acid and Protein Changes in Wheat Leaf Nuclei during Rust Infection

Abstract. *Microspectrophotometric measurements of DNA, RNA, histone, and total protein in the nuclei of mesophyll cells of Little Club wheat leaves were made at intervals after infection with the stem rust fungus. No change in host DNA was found within 6 days after inoculation, but there were decreases in histones and marked increases in RNA and acidic proteins as early as 2 days after inoculation.*

Modern work, especially that of Flor (*1*), has led to the view that gene-for-gene relations underlie physiological specialization in plant pathogens such as the rust fungi, although we have virtually no knowledge of the specific biochemical processes involved. The effects of infection on the structure and nucleic acid content of the host nuclei are therefore of critical interest. It has long been considered that there is often a close association between the haustoria of the rust fungi and the nuclei of invaded host cells; the enlargement and subsequent collapse of the host nuclei in rust-infected cereal leaves were first documented over 40 years ago (*2*). More recently, Person (*3*) reported that the nucleoli in the enlarged nuclei in rust-infected wheat-leaf cells stained particularly strongly for RNA. Using a microspectrophotometer, Whitney *et al.* (*4*) measured the DNA (Feulgen) and RNA (azure B) in the nuclei of mesophyll cells of rust-infected leaves of Little Club, a susceptible variety of wheat. They found no changes in DNA content until the invaded cells senesced and the nuclei collapsed, but reported a doubling of the RNA content in the enlarged host nuclei associated with infections 6 days old.

Uredospores of *Puccinia graminis tritici* Erikss. and Henn., Race 15B, were painted onto zones 1.0 to 1.5 cm long in the centers of primary leaves of seedlings of Little Club wheat, 10 days after planting. Two days after inoculation leaf segments were fixed in a mixture of ethanol and acetic acid (3 : 1) or neutral Formalin (4 percent), embedded in Paraplast, and sectioned at 10 μ. DNA (Feulgen), RNA (azure B), histone (fast green, *p*H 8.1), and total protein (fast green, *p*H 2.0) were measured in arbitrary units with the two-wavelength method (*5*). The two wavelengths chosen in each case were selected from absorption spectra of appropriately stained nuclei and are given in Tables 1 and 2. We used standard procedures to determine RNA (*6*), DNA (*7*), histones (*8*), and total protein (*9*). Sections to be stained with azure B were first treated with deoxyribonuclease to remove DNA. Staining with fast green was carried out after removal of DNA and RNA with hot 5 percent trichloroacetic acid. Fast green at *p*H 8.1 was not bound to the histones unless DNA was first removed with deoxyribonuclease. Histone staining was also prevented by extracting sections with 0.2*N* HCl before fixation. These two criteria have been used (*10*) to define histones in polytene chromosomes of *Drosophila*. Sections stained for histones were rehydrated and restained for total protein (*9*). This procedure permits measurement of histones and total proteins on the same individual nuclei. The difference between total protein and histone was termed acidic protein. The values for histone and for acidic and total protein are in arbitrary units and are not necessarily comparable in absolute