tions III and IV-1. The discrepancy between her results and ours may be due to the difference in methods used. Kirby's results suggested but did not prove that there might be a linkage between lipo- and glycoproteins. Our data do not suggest existence of major linkages of this kind and seem to indicate that the glycoproteins in the arterial wall are either deposited from serum independently rather than alongside the lipoproteins or arise from local synthesis.

Oncley also believes that lipoproteins are essentially carbohydrate-free, but stresses lack of specific methods for detection of these substances in this situation(14). It is possible that even the small amount of lipoprotein-hexosamine detected in our experiments does not reflect the presence of mucopolysaccharides. Findings similar to present data have also been reported by Heide and coworkers(15).

Our results should not be taken to indicate that there is no association whatever between lipoproteins and glycoproteins in serum or tissue. While amount of glycoprotein, expressed as hexosamine associated with lipoprotein fractions was relatively small, glyco-lipid complexes may still be of importance in certain phenomena relating to lipid transport and deposition.

Summary. The amount of glycoprotein, expressed in terms of hexosamine concentration, was determined in lipoprotein fractions of 4 human sera, separated in ultracentrifuge at various densities. On an average, no more than approximately 5% of total serum hexosamine was detected in lipoprotein fractions.

Ultracentrifugations were carried out with the help of Beverley J. Neff and Gilbert Lewis, chemical determinations by E. Nagler.

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Some Compounds Active Against Experimental Visceral Leishmaniasis.* (25080)

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In exploring further usefulness of a new 8-day method for screening compounds for activity against visceral leishmaniasis(1) we have shown that cotton rats, chinchillas, and even mice can be used equally as well as golden hamsters(2). Preliminary experiments have also shown a marked activity of amphotericin B, and its more soluble form Fungizone, against this infection in hamsters (2). That polyenes might be effective against leishmanial infections was also suggested by Grossowicz and Rasooly(3) on the basis of their powerful trypanostatic effect *in vitro* against *Herpetomonas culici-*

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darum. This report details the present status of our findings with a series of active compounds, especially 2 polyenes, in *Leishmania donovani* infections in hamsters and mice.

Materials and methods. Procedures used were those of the 8-day method(1,2). Parasites of the Khartoum strain of *L. donovani*, in saline suspensions of ground spleen of an infected donor hamster, were inoculated intravascularly [intracardically (IC) for hamster; intravenously (IV) for mouse]. Treatments were given in 6 daily doses beginning one day after inoculation. Necropsies were performed on day 8, at which time liver impression smears were made and stained with Giemsa for the parasite counts. Parasite densities were expressed, as previously described(1,2), as "total" parasites in the organ. Untreated control groups were necropsied at 1-2 hours after inoculation, to confirm establishment of infection, and at 8 days. In every experiment, one group, treated with the pentavalent antimonial, sodium stibogluconate (Pentostam†), at 94 mg/k, was included for comparison. All compounds except xerosin were administered to hamsters intraperitoneally (IP) in 0.4 or 0.5 ml/100 g body weight (b.w.). Most compounds were administered to mice IP, 0.2 ml/20 g b.w. However, Fungizone was given IV, and xerosin subcutaneously, both 0.2 ml/20 g b.w. All compounds except nystatin were given in saline. Nystatin was given in an aqueous dilution of vehicle N, N-dimethylacetamide. Maximum tolerated dose of amphotericin B in hamsters IP is 300 mg/k. Maximum tolerated doses have not been determined for other compounds under these treatment procedures in these hosts.

Results. Effects of compounds tested on visceral leishmaniasis in hamster and mouse appear in Tables I and II. Uniformity of response from experiment to experiment both in untreated controls and in animals treated with Pentostam is additional evidence of the reproducibility of results by this method(1, 2). With the amount of Pentostam administered, reproduction of parasites was nearly or completely inhibited in each experiment. The variability of response is similar to that previously reported(1) and is clearly shown here in the hamster to be a function of the level of parasitization induced by inoculation. Effect of drug administration is remarkably similar in mouse and hamster in spite of species' differences in susceptibility to this parasite(4).

Amphotericin B is poorly tolerated when administered IP into hamsters, causing extensive adhesions at high dosages. Maximum effectiveness appears at the level of com-

TABLE I. Effects of Treatment on Parasite Densities in Liver of Hamsters. Infection intravascular with *Leishmania donovani*.

Animal groups	Dosage, mg/k	Trials with hamsters, parasite density in liver (as "total" parasites) 1	2	3	4
Untreated controls					
One hr after inoc.		51	12	29	38
8 days *idem*		2307	533	854	1425
Treated					
Pentostam	94	185	8	20	142
Amphotericin B	300	354			
	60	205			
Fungizone	20		3		
	5		<4	0	
	2.5			<2	
	1.25			35	
	.675			286	
Fumagillin	30		186		
	20	1470	202		
	10		209		
	2	2571*			
Xerosin	100				843
	50				851
	25				742
TWSb	200		14		
	40		46		

"Total" parasites are shown as group medians for hamsters and group means for mice. Six to 12 animals constitute a group. All groups except the first were necropsied 8 days after inoculation. All values except those marked with asterisk are significant deviations from values of 8-day controls (p values <0.05). Values marked "less than" indicate that, for more than half the animals in group, no parasites were found on liver impression smears. A portion of data in hamster trials 1, 2 and 3 has previously been reported(2).

† We are indebted to the following for compounds used: Drs. D. W. Adamson (sodium stiboglucinate, Pentostam Wellcome), E. A. H. Friedheim (antimony dimercaptosuccinate, TWSb), V. Groupé (xerosin), G. F. Otto (fumagillin, Fumadil Abbott), and Joseph N. Pagano (amphotericin B, and Fungizone Squibb and nystatin, Mycostatin Squibb).

TABLE II. Effects of Treatment on Parasite Densities in Liver of Mice. Infection intravascular with *Leishmania donovani*.

Animal groups	Dosage, mg/k	Trials with mice, parasite density in liver (as "total" parasites) 1	2
	Untreated controls		
One hr after inoc.		29	32
8 days *idem*		276	363
	Treated		
Pentostam	94	51	135
Fungizone	2.5	<3	
	1.25	<7	
	.675	31	
	.337		103
	.168		245
Nystatin	2		152*
	1		410*
	.2		337*
	.1		394*
Xerosin	100		120
	50		154
	25		149

For additional details, see footnote, Table I.

pound where these adhesions are minimal. In the mouse treated IV with Fungizone, no toxic effects were noted, even in the highly effective range of dosages.

Xerosin, as previously reported for virus infections(5), exerts a significant effect on parasite reproduction, but inhibition is not complete even close to the maximum tolerated dose. Fumagillin acts very much like xerosin. TWSb was active at levels near the maximum tolerated dose. Although unlike the antibiotics reported here, it is included in further evaluation of the 8-day method.

Nystatin was minimally active at the highest concentration used. As seen in Table II the numbers of parasites in the liver were not unequivocally significant from the control but the numbers of parasites in the spleen were significantly reduced over those found in the controls (1.5 *vs.* 5.6 "total" Lds, respectively; P = 0.001).

The activity of amphotericin B is especially noteworthy. At 5 mg/k it produced the same effect as 188 mg/k of Pentostam; namely, no visible parasites in the sample counts of spleen or liver at 8 days.

Summary. Using an eight-day method for screening compounds against experimental visceral leishmaniasis, the following compounds showed activity in hamster or mouse infection or in both: amphotericin B (and Fungizone), fumagillin, nystatin, Sb dimercaptosuccinate and xerosin. The activity of Fungizone is especially noteworthy.

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Effect of Prior Inoculation of Packed Erythrocytes on Survival of Skin Homografts in Rats.* (25081)

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Production of a "second-set" reaction to skin homografts in rabbits following primary inoculation of whole blood or one of its fractions has been ascribable solely to the leucocytes; no such reaction was detected in response to primary inoculations of erythrocytes(1). On the other hand, erythrocytes are capable of stimulating resistance to sarcoma homografts in mice(2). In the present study, a prior inoculation of erythrocytes

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