acrosome reaction when Ca^{2+} was added (Fig. 1D). Unlike the bivalent V-IgG, V-Fab was not inhibitory (data not shown); SV-IgG (5 mg/ml) was not inhibitory (Fig. 1D).

In the guinea pig, the acrosome-reacted spermatozoon attaches to the zona pellucida of the ovum (*19*). This is followed by zona penetration, fusion with the ovum, and swelling of the sperm head in the vitellus (*20*). We placed acrosome-reacted spermatozoa in K-MCM containing antibody. Fifteen minutes later, we introduced either zona-intact or zona-free guinea pig ova. Zona attachment of spermatozoa was completely inhibited by V-IgG, but not by the SV-IgG control; V-Fab showed a 57 percent inhibition (Table 1).

Bivalent V-IgG, but not V-Fab, effectively blocks sperm-ovum fusion (Table 1). The different effects of these reagents indicate that cross-linking or some modulation of surface autoantigens on the spermatozoon prevents fusion with the ovum. The lack of inhibition by the control SV-IgG rules out a significant effect through the Fc portion of the V-IgG molecule.

The effects of autoantibodies on agglutination and on the acrosome reaction of spermatozoa may be important when considering a possible immunological basis of male infertility. Exposure of spermatozoa within the male reproductive tract to antibodies would result in binding of antibody to the plasma membrane of the sperm head. This would result in the prevention of the acrosome reaction which is an essential preliminary to both sperm penetration through the zona pellucida and fusion with the ovum (*21*). It has been shown that V-IgG can gain access to spermatozoa in the male reproductive tract and can be detected in the seminal plasma of vasectomized men (*4*). It remains to be determined whether spermatozoa treated in vitro with V-IgG can subsequently fertilize ova in vivo after artificial insemination.

THOMAS T. F. HUANG, JR.
Department of Anatomy and Reproductive Biology, University of Hawaii School of Medicine, Honolulu 96822
KENNETH S. K. TUNG
Department of Pathology, University of New Mexico School of Medicine, Albuquerque 87131
RYUZO YANAGIMACHI
Department of Anatomy and Reproductive Biology, University of Hawaii School of Medicine

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Glucose Transfer from Male to Female Schistosomes

Abstract. *The rate of glucose assimilation by male and female* Schistosoma mansoni *was significantly greater in copulating than separated flukes, especially in copulating females. In the three medically important schistosome species, glycogen content was greater in unpaired males than in copulating males, suggesting that the female depletes glycogen stored in the male. Transfer of [^{14}C]glucose from the male to the copulating female was demonstrated over a period of minutes. A considerable portion of the glucose utilized by the female during her life may be supplied by the male.*

Schistosomiasis afflicts more than 200 million people worldwide. It is caused by permanently copulating pairs of male and female blood flukes living in afferent tributaries of the portal veins (*Schistosoma mansoni* and *S. japonicum*) and the vesicular venous plexus of the bladder and colon (*S. haematobium*) of man and animals (*1*). Tissue reactions resulting from the deposition of eggs are primarily responsible for the disease state (*2*).

Male and female schistosomes are interdependent. In experiments in which the male is separated from the female, the female does not grow to adult size

Table 1. Comparison of hexose assimilation in copulating and separated male and female *Schistosoma mansoni*. Each value is the mean (± the standard deviation) for 5 to 12 schistosomes. Ages of schistosomes were 68 days (D-glucose), 101 days (3-*O*-methylglucose), and 103 days (2-deoxy-D-glucose).

^{14}C-Labeled hexose	Time exposed to isotopic medium (min)	Tissue uptake index (*7*)			
		Unpaired males	Paired males	Unpaired females	Paired females
D-Glucose	3.5	175.6 ± 12.3	188.2 ± 28.0	109.1* ± 40.1	208.1 ± 53.5
3-*O*-Methyl-glucose	4.0	41.9† ± 6.7	59.9 ± 4.8	24.4 ± 16.5	71.7 ± 4.4
2-Deoxy-D-glucose	3.0	154.4† ± 22.0	213.9 ± 33.5	109.8* ± 61.5	170.2 ± 49.4
	4.0	181.3† ± 51.7	368.3 ± 98.1	126.8* ± 48.9	252.7 ± 47.1
	5.0	307.4 ± 17.6	352.9 ± 81.1	171.6* ± 47.3	277.5 ± 37.3

*Significantly different from corresponding value for paired females ($P < .01$, Student's *t*-test). †Significantly different from corresponding value for paired males ($P < .01$).

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Table 2. Glycogen and protein content of adult male and female schistosomes. Each value is the mean ± standard deviation for 18 or more schistosomes.

Species and age	Sex and status	Protein content per fluke (μg)	Glycogen content per fluke (μg)	Ratio of glycogen to protein
S. mansoni, 86 days	Female, paired	1.56 ± 1.32	3.05 ± 1.70	1.81 ± 0.84
	Male, paired	18.80 ± 2.90	21.06 ± 5.58	1.12 ± 0.24
	Male, unpaired	22.68 ± 1.92	30.35 ± 1.60	1.33 ± 0.11
S. haematobium, 123 days	Female, paired	6.92 ± 1.78	6.99 ± 1.05	1.09 ± 0.24
	Male, paired	25.97 ± 4.93	41.04 ± 6.08	1.43 ± 0.33
	Male, unpaired	16.23 ± 8.71	26.82 ± 13.40	1.54 ± 0.59
S. japonicum, 68 days	Female, paired	13.85 ± 4.03	2.64 ± 0.89	0.22 ± 0.14
	Male, paired	36.43 ± 4.39	19.57 ± 1.04	0.54 ± 0.07
	Male, unpaired	36.92 ± 12.85	41.90 ± 11.72	1.18 ± 0.27

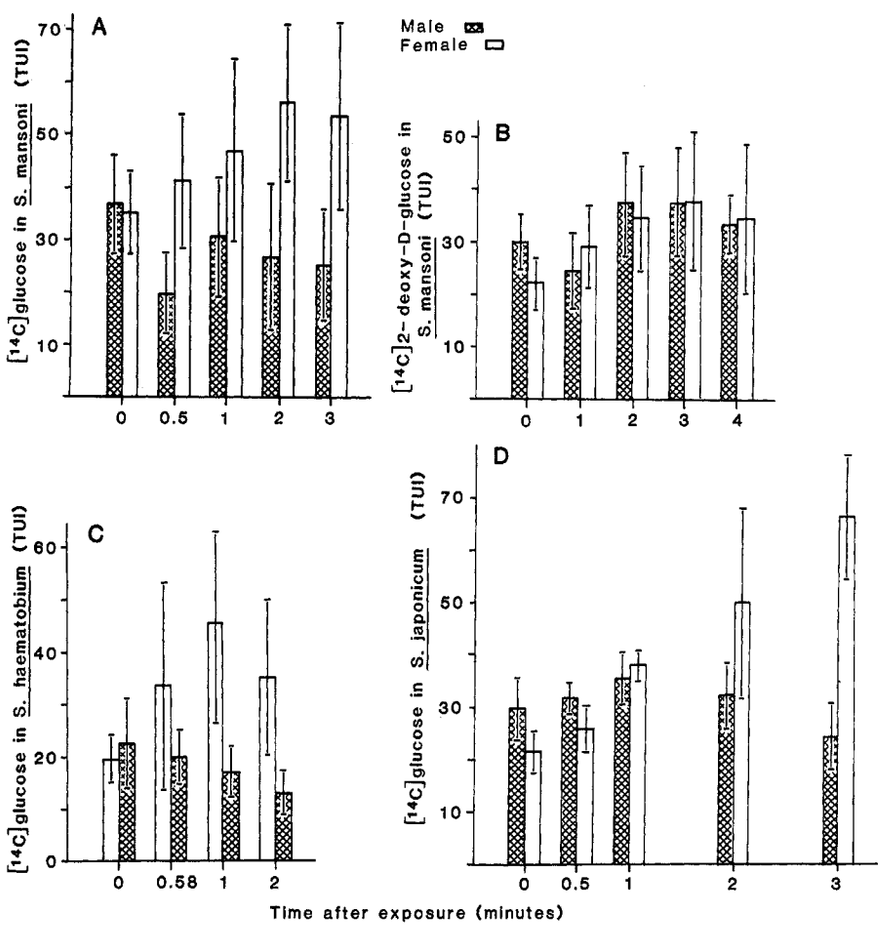

Fig. 1. Transfer of hexose from the male to the female schistosome in copulating pairs. Values are tissue uptake indices (*TUI*) (*7*). (A) Uptake of [^{14}C]glucose in 55-day-old male and female *Schistosoma mansoni* 0 to 3 minutes after a 5-second exposure in the radioactive medium. Significant differences ($P < .05$) between the sexes were observed at 0.5, 2, and 3 minutes. Linear regression analysis indicates a slope of 6.6 percent per minute for the females ($R = .91$, $P < .05$). The same phenomenon was observed in studies of 60- and 73-day-old schistosomes. ($N = 8$ to 10 pairs for each mean.) (B) Uptake of [^{14}C]2-deoxy-D-glucose in 87-day-old male and female *S. mansoni* 0 to 4 minutes after labeling. Linear regression analysis indicates a positive correlation for the females only. The slope over the first 3 minutes (5.2 percent per minute, $R = .89$, $P < .05$) compares favorably with that obtained for D-glucose (A). This phenomenon was confirmed in studies of 61-day-old schistosomes. ($N = 9$ to 11 pairs for each mean.) (C) Uptake of [^{14}C]glucose in 88-day-old male and female *S. haematobium* 0 to 2 minutes after labeling. Significant male-female differences ($P < .05$) were observed at 1 and 2 minutes. There was a positive correlation for the females (slope = 12.5 percent per minute, $P < .05$) and a negative correlation for the males (slope = −5.8 percent per minute, $P < .05$). ($N = 8$ to 14 pairs for each mean.) (D) Uptake of [^{14}C]glucose in male and female *S. japonicum* 0 to 3 minutes after labeling. Male-female differences at 1 and 2 minutes are significant at $P < .01$ and $P < .05$, respectively. There is a significant increase over time in the glucose content of the female ($R = .995$, $P < .001$, slope = 15 percent per minute). In the period 1 to 3 minutes after exposure, males lost glucose at a rate of 6 percent per minute, suggesting that the rate of exchange is greatest in this species.

(*3*). The differences between the sexes in enzyme activities and other biochemical parameters (*4*) may be circumstantial evidence for metabolic interdependence between copulating schistosomes. A recent study indicates that a protein synthesized by the male mansonian schistosome is transferred to the female over a 20-hour period (*5*). These findings point to an obligatory continuous relationship between the pair.

In the present study we measured surface assimilation (*6*, *7*) of three different ^{14}C-labeled hexoses in the male and female schistosome. Uptake rates were measured in vitro in *S. mansoni* pairs and compared with uptake rates in experimentally separated males and females from the same infected animals. As shown in Table 1, uptake rates were higher in copulating schistosomes than in separated flukes for all three hexoses used (2-deoxy-D-glucose, 3-*O*-methylglucose, and D-glucose). The differences were all highly significant among females ($P < .01$, Student's *t*-test) but not always among males. Furthermore, when schistosomes were not in copula, hexose uptake rates in males exceeded those in females. Conversely, in copulating pairs the uptake rates for glucose and methylglucose were maximal in the female, exceeding those in the male (*8*). These data suggest that the energy requirement of a copulating pair is greater than that of an unpaired male and female.

The relatively high uptake rates in the copulating female might be explained by transfer of glucose from the male to the female or stimulation of the female by the male. If the male is simply providing a stimulus, then the biochemical composition of unpaired males should be the same as that of paired males. We measured the glycogen and protein content (*9*) of the three major schistosome species infecting man, comparing copulating adult females, copulating adult males, and noncopulating adult males. The latter are found only in experimental animals that have been exposed to an excess proportion of male cercariae, and are morphologically indistinguishable from the paired males. The protein content of schistosomes (Table 2) is an indicator of size (*S. japonicum* > *S. haematobium* > *S. mansoni*).

In all three species, the protein content of unpaired males was not significantly different from that of paired males. Glycogen content was lower in females than in males and significantly higher in unpaired males than in copulating males. Glycogen-to-protein ratios normalize for any slight mass differences that may exist between paired and un-

paired male schistosomes. These ratios clearly show that greater glycogen reserves are present in unpaired males in all three schistosome species (Table 2). It appears that the glycogen or glucose reserves of a male schistosome are depleted by the presence of a female in the gynecophoral canal.

To test for transfer of ^{14}C-labeled hexoses between males and females, copulating pairs of *S. mansoni* were exposed to radioactive medium for 5 seconds and either rinsed in cold silicone oil (*10*), separated, and assayed, or maintained in warm oil for 0.5 to 4 minutes before separation and analysis. A time-dependent increase in the glucose content of the female schistosome was observed (Fig. 1A). The same phenomenon was observed in studies with the unnatural glucose analog 2-deoxy-D-glucose. Although this analog may be phosphorylated in most biological systems, it is not further degraded and remains trapped intracellularly (*11*). Thus the molecular species that is exchanged presumably is the hexose rather than some metabolite. The exchange of glucose appears to be biochemically significant because glycolysis is the major pathway for the provision of metabolic energy in schistosomes (*12*). This phenomenon was also observed in *S. haematobium* (Fig. 1C) and *S. japonicum* (Fig. 1D). Perhaps because of the greater size of male schistosomes (Table 2), concomitant reductions in the glucose content of males were not as striking as the increases in females.

Thus a considerable proportion of the energy required by the female may be indirectly supplied by the male. This represents a more immediate reason for the obligatory continuous relationship than the slow (20 hours) exchange of protein described by Atkinson and Atkinson (*5*). The inability of a female to mature and grow to full size in the absence of a male may be the result of a deficit in molecular material transferred from the partner. Thus the function of a male can be likened to that of a liver (glycogen storage and glucose regulation), and the female to a dependent gonad (*13*).

The sexually specific interdependence of blood flukes emphasizes their considerable evolutionary divergence from other free-living and parasitic flatworms. Molecular mimicry (*14*) and molecular exchange between the sexes also place schistosomes in a biologically unique position. Yet unique pharmacological vulnerability has not been discovered. In recent reviews (*15*) it is stressed that despite chemotherapeutic advances, few antischistosomal agents are completely effective and no available compound satisfies the criteria for an ideal schistosomicide. The importance of chemotherapy in controlling the disease is recognized, however (*16*), as is the need to identify molecular responses of schistosomes which are unlike those of human tissues (*17*). Many antischistosomal treatments cause a loss of glycogen in the fluke. It has been suggested that glycogen, in addition to providing energy, may help to maintain the structural and functional integrity of the schistosome (*18*). The present study would be pharmacologically significant only if a drug that safely achieves permanent interruption of male-to-female glucose transfer can be developed.

Note added in proof: Bueding (*19*) has confirmed that consistently higher glycogen levels have been observed in unpaired male schistosomes in his laboratory.

EAIN M. CORNFORD
MARIE E. HUOT
Southwest Regional VA Epilepsy Center 691-127, Veterans Administration Medical Center, Los Angeles, California 90073, and *Department of Neurology, University of California, Los Angeles 90024*

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9. Glycogen was assayed (in single flukes) as described by J. V. Passoneau and V. R. Lauderdale [*Anal. Biochem.* **60**, 405 (1974)]. Protein determinations were performed with commercially prepared reagents (Bio-Rad) by the method of M. Bradford [*ibid.* **72**, 248 (1976)].
10. We find that a silicone oil rinse removes some of the excess isotopic medium from the schistosome's surface by a sheeting action.
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Cardiac Sarcolemma: Compositional Adaptation to Exercise

Abstract. *Marked changes were observed in the lipid composition of highly purified plasma membranes isolated from the hearts of rats subjected to daily treadmill running. Compared to sedentary controls, sarcolemmal content of total phospholipid and phosphatidylserine in the trained group was increased 23 and 50 percent, respectively. This observation suggests a mechanism by which cardiac contractility may be enhanced by exercise.*

Lipid composition is an important determinant of the biological and physical characteristics of the plasma membrane, including fluidity. Membrane phospholipid acyl chain structure and the ratio of the concentrations of other lipid bilayer components influence intrinsic enzyme activity and the ability of membrane components to move within the plane of the bilayer (*1*). Plasma membrane composition undergoes alterations during the cell growth cycle and in response to events during ontogeny and transformation by viral agents (*2*). In addition, membrane composition changes in response to temperature gradients, aging, and alterations in dietary fatty acids. Thus plasma membrane composition is

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