studies. Tranquilization does enhance sleep, yet does not change rumen activity.

If rumen activity does not regulate behavior, it then is either independent of behavior or, more likely, a consequence of it. First, autonomic control which is exerted over the rumen is known to be affected by the state of alertness. Rumen contraction rates are suppressed in excited animals(3), due no doubt to sympathetic activation. During rumination, the rates are accelerated, probably caused by parasympathetic activation.

Not explained by the data is why sleep and PS periods are so brief, especially when compared with other species. It is possible that these episodes are longer and more frequent at night.

Summary. This study proved that ruminants have the physiologic capacity for sleep and paradoxical sleep. Daytime ruminant sleep in goats was transient and polyphasic, averaging 5.1 ± 0.6 minutes per episode. The frequency was variable, ranging from 0 to 6 episodes during daytime. In addition, the goats exhibited paradoxical sleep, known as dreaming in man, with average durations of 5.5 ± 0.4 minutes. Rumen contraction rates apparently had no causal relation to behavioral states, but rather were a consequence of the animals' state of alertness.

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Serum Antibody Response in Sarcoidosis.* (30851)

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Although the cutaneous anergy associated with sarcoidosis has been well documented (1-3), a defect in the production of circulating antibody has not been demonstrated. Whereas decreased circulating antibody production has been reported following immunization with tetanus toxoid(4), normal levels have been observed in patients immunized with pertussis and typhoid vaccine(5), and increased titers of isoagglutinins have been noted following transfusion of mismatched blood(6).

The studies referred to have dealt with the total antibody concentration, and did not distinguish between the IgG and IgM varieties of antibody which might be present. The initial serum response to a large number of antigens has been shown to be an IgM (19S) immunoglobulin, while the predominant antibody response to secondary stimulation has been an IgG (7S) type of antibody(7-9). In the present investigation, the production of 19S and 7S antibodies by patients with sarcoidosis has been studied following primary and secondary immunization with typhoid antigens.

Methods. Five adult patients with active sarcoidosis were studied. All had biopsy evidence of non-caseating granulomas from one or more sites, and all were found to be anergic at the beginning of the study when injected intracutaneously with the following

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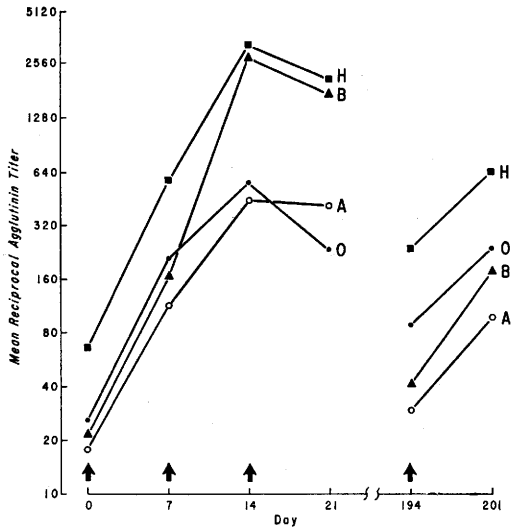


FIG. 1. Average primary and secondary agglutinin response in whole serum of 5 patients with active sarcoidosis following immunization with typhoid O and H, and paratyphoid A and B antigens. Arrows (↑) indicate times of injection.

antigens: intermediate strength PPD; scotochromogen, 1:1000; photochromogen, 1:1000; nonchromogen, 1:1000; histoplasmin, and mumps skin test antigen. One patient was taking 20 mg of prednisolone daily. None had a history of prior immunization with the typhoid antigens used, and all clinical histories were negative for episodes of Salmonellosis.

Each patient was injected intramuscularly 3 times at weekly intervals with 0.5 ml of mixed typhoid-paratyphoid vaccine (Cutter). Blood was drawn prior to immunization and weekly up to and including one week following the third injection. Six months following the third injection, the patients were again bled and given another intramuscular injection of vaccine and bled one week later. Serum was stored at −20°C.

Chromatographic separation of the serum into 4 fractions was carried out on diethylaminoethyl (DEAE) cellulose columns as described by LoSpalluto and Ziff(10). Whole serum, the combined eluates of peak I, containing 7S gamma globulin, and the combined eluates of peak IV, containing 19S gamma globulin, were tested for antibodies to typhoid O and H and paratyphoid A and B antigens using standard methods(11). In all instances, the completeness of separation of 19S and 7S immunoglobulins by the chromatographic technique was checked by sucrose density gradient ultracentrifugation (12). In all cases, the titers of the more rapidly sedimenting antibodies in the macroglobulin region were approximately equal to the titers eluted in peak IV, and the titers of the more slowly sedimenting antibodies in the 7S region corresponded to the titers eluted in peak I. The completeness of separation of 19S and 7S immunoglobulins was also checked by addition of an equal volume of 0.1 M 2-mercaptoethanol to the chromatographic fractions. This compound destroys the activity of 19S but not 7S antibodies(13). Agglutinating activity of the peak IV fractions was uniformly abolished by this treatment, while the activity of the peak I fractions was relatively unchanged.

Results. The average antibody response of 5 patients with active sarcoidosis following primary and secondary immunization with mixed typhoid-paratyphoid antigens is shown in Fig. 1. Maximum mean titers were observed 14 days after the initial injection (Table I). Even though the mixed vaccine was injected a third time on day 14, no further increase in antibody levels was observed, while a slight decrease in the mean titers of all agglutinins was detected one week later. Six months after the primary immunization, the mean whole serum titers had decreased markedly from their peak levels. One week following an injection of mixed vaccine, however, increased whole serum antibody titers to all antigens were again detected.

The sera obtained on day 14, representing the maximum primary antibody response, were individually fractionated on DEAE cellulose into 19S and 7S components. The mean titers of these two immunoglobulin components are shown in Fig. 2. It is seen that the predominant agglutinating activity is in the 19S fraction, eluted as peak IV with 0.3 M phosphate buffer, pH 5.0. The 7S component, eluted as peak I with 0.01 M phosphate buffer, pH 7.0, constituted the smaller fraction of all 4 antibodies.

The sera obtained on day 201, representing the secondary antibody response, were simi-

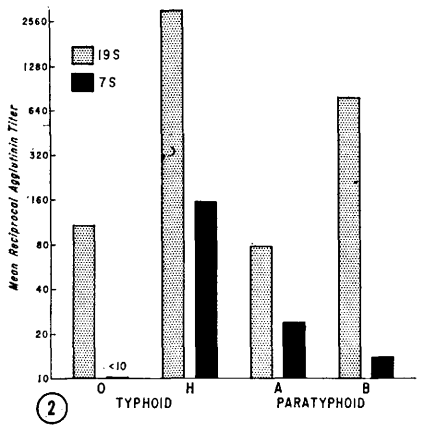
larly fractionated (Fig. 3). The predominant antibody response at this time is seen in the 7S fraction with the exception of typhoid O antibodies which have, as previously noted(8, 14), remained in the 19S form.

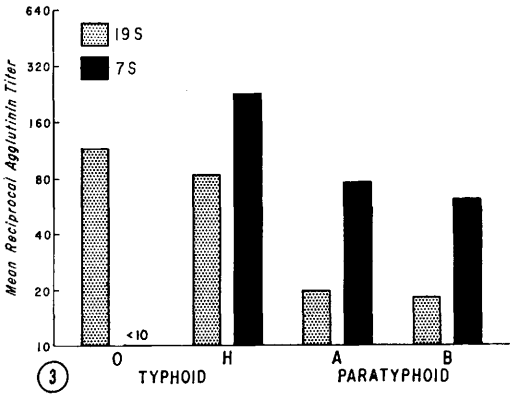
The findings in the sarcoid group were

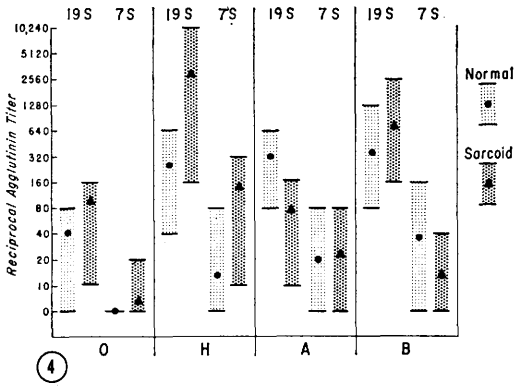
TABLE I. Primary and Secondary Antibody Responses to Typhoid O and H, and Paratyphoid A and B Antigens in 5 Patients with Sarcoidosis.*

	Primary response†				Secondary response‡			
Fraction	O	H	A	B	O	H	A	B
Whole serum	568 (40–1280)	3200 (640–5120)	448 (10–1280)	2816 (640–5120)	240 (160–320)	640 (320–1280)	100 (40–160)	180 (80–320)
Peak IV (19S)	106 (20–160)	2976 (160–10240)	78 (10–160)	768 (160–2560)	112 (10–320)	82 (10–160)	20 (10–40)	18 (10–40)
Peak I (7S)	4 (0–20)	154 (10–320)	24 (0–80)	14 (0–40)	0 (0)	220 (80–320)	75 (20–160)	60 (40–80)

* The mean reciprocal antibody titer of 5 patients is shown followed by the range (in parentheses).
† Maximum values, measured on day 14.
‡ Measured 7 days after booster injection.







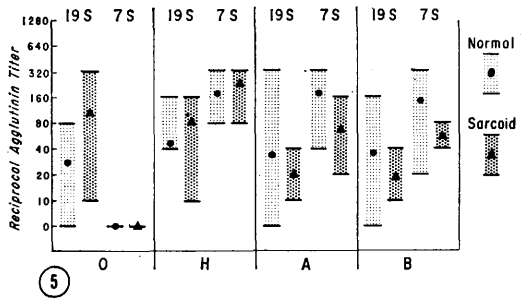


FIG. 2. 19S and 7S antibody response to primary immunization of sarcoidosis patients with typhoid-paratyphoid antigens. Average titers of 5 patients are represented.

FIG. 3. 19S and 7S antibody response to booster immunization of sarcoidosis patients with typhoid-paratyphoid antigens. Average titers of 5 patients are represented.

FIG. 4. Comparison of the 19S and 7S antibody responses of sarcoidosis patients (▲) with those of 9 normal subjects (●) following primary immunization.

FIG. 5. Comparison of the 19S and 7S antibody of sarcoidosis patients (▲) with those of 11 normal subjects (●) following secondary immunization.

compared with those obtained by LoSpalluto and coworkers(8) in this laboratory in a group of normal subjects immunized by the same schedule. It is seen (Fig. 4) that the antibody response is predominantly 19S in both groups following primary immunization and that the ranges of agglutinin titers in the sarcoid group correspond with those of the normal group. This is noted for both the 19S and 7S fractions. Although the immunization schedule in the sarcoid patients was identical to that used in the normal group, the serum fractionated for analysis of the primary response in the normal individuals was the 21-day sample, whereas that of the sarcoid group was obtained on day 14, the date of maximum antibody response. This difference may account for the increased titer observed in the sarcoid group in the case of the anti-H antibody following primary immunization. The similarity of the antibody response in sarcoidosis to that of normal individuals is also evident following booster immunization (Fig. 5). Serum was obtained one week after booster injection from both the normal and the sarcoid subjects. The antibody response was predominantly 7S in type in both the sarcoid and normal groups.

Discussion. The immunoglobulin character of agglutinating antibodies following immunization of a normal population with typhoid-paratyphoid antigens has been clearly defined previously in this laboratory(8). This demonstrated that the antibodies normally elaborated following initial immunization were principally in the high molecular weight or 19S form. After booster injection following an interval of 3 to 15 months, the antibodies to typhoid H and to paratyphoid A and B were principally in the low molecular weight or 7S fraction, and anti-typhoid O antibodies remained predominantly 19S.

The present study has demonstrated that elaboration of typhoid and paratyphoid antibody immunoglobulins in patients with active sarcoidosis follows a normal pattern when compared with the earlier study using an identical immunization schedule. Primary stimulation was followed by the appearance mainly of 19S antibodies. After an interval of 6 months, these patients reacted to a booster stimulation with the production of agglutinins predominantly of the 7S type except for typhoid O agglutinins which remained 19S.

Cellular or delayed hypersensitivity has been demonstrated by many studies to be diminished in patients with active sarcoidosis (1-3). Although one study has demonstrated a diminished serum antibody response in this disease(4), others have found this response normal(5) or even increased(6). In the present investigation, it has been shown that not only are the whole serum titers produced in response to typhoid and paratyphoid antigens normal in magnitude, but that the sequence of formation of 19S and 7S immunoglobulins in the primary and secondary responses is also normal in pattern.

Summary. Five patients with active sarcoidosis were immunized with typhoid-paratyphoid mixed vaccine. Antibody levels were determined after primary and secondary stimulation. When compared with the response of an identically immunized group of normal subjects, the sarcoid group responded in a normal fashion. They produced similar levels of 19S or macroglobulin antibodies after primary immunization, and subsequently of 7S antibodies following secondary immunization.

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Cardiac Tamponade: Fluid and Pressure Effects on Electrocardiographic Changes.* (30852)

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The production of cardiac tamponade by the introduction of gas or liquid into the pericardial space results in both hemodynamic(1, 2,3) and electrocardiographic changes(4,5,6, 7). The electrocardiographic changes are of interest since they are used empirically as criteria for the diagnosis of cardiac tamponade or pericarditis. Among the changes involved are decreased QRS voltage(6,7), elevated RS-T segment and inverted T wave(5, 6). The decreased QRS voltage currently is attributed to decreased conduction through the pericardial space(6,7); whereas, the other electrocardiographic changes are thought to result from mechanical injury of the sub-epicardial muscle layers(8).

This study was undertaken to evaluate these explanations of the empirical observations. Studies performed included the effect of a) increased fluid volume in the pericardial sac, b) altered volume conduction, c) positional changes of the heart, and d) diminution of right atrial inflow on electrocardiographic recordings and on arterial and venous pressures.

Methods. Mongrel dogs, used without regard to age, sex, or weight, were anesthetized with sodium pentobarbital (30 mg/kg body weight) by intravenous injection. A tracheostomy and thoracotomy were performed. After the midsternal thoracotomy was begun the dogs were ventilated by a Harvard 607 positive pressure respirator using ambient air. Standard limb leads were recorded in all procedures by the use of needle electrodes.

Central venous pressure was recorded with a polyethylene catheter (Clay-Adams PE 240) inserted through the right external jugular vein. The open end of the catheter was positioned in the superior vena cava approximately 3 cm cephalad to the right atrium. Arterial pressure was recorded from the arch of the aorta by a catheter inserted through the left femoral artery. Intrapericardial pressure was measured by a cannula sewn through the pericardial sac (Fig. 1). All pressures were transmitted through P23AC Statham strain gauges to a Grass model 5 polygraph as were the electrocardiographic findings. The recordings were obtained at a paper speed of 25 mm/sec. The data were analyzed by the "t" test for paired samples (9). A "P" at the 0.05 level was considered to be significant.

Procedures. In all instances a control record of at least 15-minute duration was obtained prior to any of the following procedures. Data were collected for at least 2 minutes after initiation of the experimental procedure. Each animal served as its own control.

Series A. An increase in pericardial pressure was imposed on 4 dogs using nitrogen gas under a maintained pressure head of 55 mm of Hg.

Series B. An increase in pericardial pressure was imposed on 7 dogs using a high-conductance liquid (Ringer's solution or serum) under a maintained pressure head of 55 mm of Hg. Conductance of these liquids was between 1.16×10^{-2} and 1.25×10^{-2} mhos,

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