tone of the gastric blood vessels at the time that gastric secretion is depressed.

Summary. Gastric hemorrhage was produced in 93% of rats subjected to cold + restraint stress for 60 minutes. Mucosal damage was not evident and could not be induced by repeated stress periods. Anticholinergics, ganglionic blocking agents, certain central nervous system depressants and epinephrine reduced the incidence of hemorrhage. Gastric volume was reduced by cold + restraint in the pylorus-ligated and chronic gastric fistula rat, while gastric acidity was only reduced during stress in the fistula rats. The cold + restraint produced a marked hypothermic response and body temperature was depressed for 3 hours following the stress.

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Antibody Response to Brucella Antigen in Patients with Rheumatoid Arthritis.* (28556)

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Among the theories attempting to explain the presence of rheumatoid factor (RF) in the serum of patients with peripheral rheumatoid arthritis is one in which RF is considered to be a macroglobulin (19S) antibody to the patient's 7S gamma globulin(1). Relevant to this concept are reports that patients with rheumatic disease are hyperreactive in their humoral antibody response(2,3). Recently Meiselas *et al.,* noted, in rheumatoid subjects, a significant hyperreactivity to Brucella antigen which evokes a macroglobulin antibody response(4).

Because such observations have implications for the significance of rheumatoid factor, a study was made: (a) to determine whether the antibody response to Brucella antigen in patients with rheumatoid arthritis would prove to be higher than in those with osteoarthritis, a condition in which there is chronic articular disease while rheumatoid factor and other serological abnormalities are characteristically absent, and (b) to ascertain whether a relationship exists in these patients between the titer of the Brucella antibody and the titer of rheumatoid factor.

Method. The subjects were 44 ambulatory patients from the Arthritis Clinic of Univ. of California Medical Center. After physical examination and appropriate testing, they were classified according to the diagnostic criteria of the American Rheumatism Assn. Thirty-three of the patients had rheumatoid arthritis; 11 had osteoarthritis. After a sample of serum was collected, each patient was inoculated subcutaneously with 0.5 ml of Brucella vaccine (Parke-Davis) containing *Brucella abortus* and *melitensis,* 2,000 million killed bacteria per ml. Two weeks later

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serum was again drawn from each subject. This specimen and the one obtained before immunization were tested for rheumatoid factor and for the titer of Brucella antibody. The titer at the end of 2 weeks was chosen because this is usually the time of maximal antibody response to Brucella(4). Rheumatoid factor activity was measured by the F II hemagglutination test(5) at doubling dilutions carried out to 1:56,000. The antibrucella titer was measured by an agglutination technique in which the antigen (obtained from the Agricultural Research Service, U. S. Dept. of Agriculture) was incubated at 37°C for 24 hours and 22°C for 48 hours. The titers reported were the final dilutions of the sera that gave at least 50% agglutination.

Results. In only 2 patients (one with osteoarthritis and one with rheumatoid arthritis) was antibody to Brucella detectable before inoculation; in both, the titer was 1:100 or less. The titer of rheumatoid factor remained constant, having a random variation of no more than 1 tube in 41 of the 44 cases after Brucella inoculation. In all instances the higher titer was used for the analysis.

In Table I is shown the relationship between the Brucella antibody titers in the patients with rheumatoid arthritis and the titers of this antibody in the subjects with osteoarthritis. No significant difference is seen between these 2 groups (X^2 test; $p>.7$). Fig. 1 shows the relationship between the Brucella titer and the F II hemagglutination titer at the end of 2 weeks. No trend is apparent between these 2 variables.

Discussion. Brucella antigen was chosen for inoculation because (a) it has been reported by others to evoke a hyperreactive response which distinguished rheumatoid from nonrheumatoid subjects, (b) it was presumably an unfamiliar antigen, and (c) it produces an antibody which, like rheumatoid factor, has characteristics of a macroglobulin(4).

In the present study, the geometric mean of the antibrucella titers in the patients with rheumatoid arthritis (694) was slightly higher than that (555) reported by Meiselas and his colleagues for patients with this disease. However, the geometric mean for our control group, with nonrheumatoid disease (osteoarthritis) (655), was similar to that for the group with rheumatoid arthritis; whereas the mean titer for Meiselas' control group was only 80. The control group in Meiselas' study included persons with cancer, heart failure, cerebral vascular accident, or other serious disease which may have interfered with their ability to respond and could conceivably, by so doing, have caused their extremely low antibrucella titers.

Although the possibility remains that patients with osteoarthritis may hyperreact to certain antigenic stimuli, it should be noted that patients with osteoarthritis were chosen for the comparison group in the present study because they resembled the subjects with rheumatoid arthritis in having a chronic joint disease but usually had no demonstrable serologic abnormalities.

TABLE I. Antibrucella Titers.

Diagnosis	No. of patients	Geometric mean antibrucella titer (2 weeks)	
Rheumatoid arthritis	33	694	(p >.7)*
Osteoarthritis	11	655	

* Chi-square.

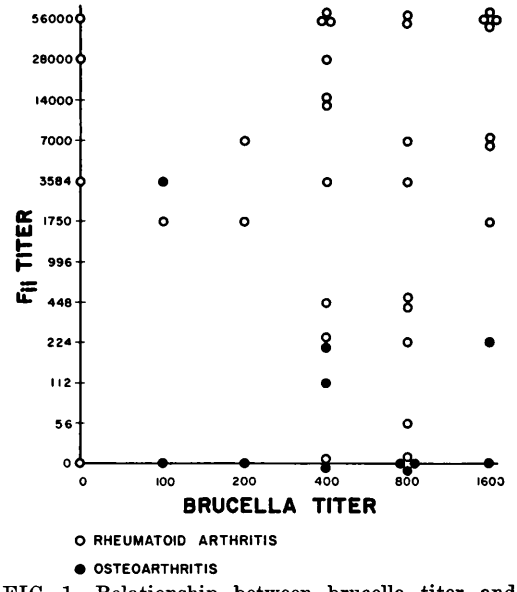

FIG. 1. Relationship between brucella titer and F II hemagglutination titer in 33 patients with rheumatoid arthritis and 11 with osteoarthritis 2 weeks after inoculation with brucella antigen.

In certain circumstances, the antigenic stimulus to RF production appears evident. It may appear in significant amounts in the presence of septicemia; when the infection clears, RF activity decreases(6). But if rheumatoid factor is an antibody, why does it persist in high titer in the serum of patients with rheumatoid arthritis in the absence of a definite antigen? If one rejects the concept of humoral hyperreactivity, then the possibility of a continuous, potent antigenic stimulus might be favored.

Humoral antibody hyperreactivity to Brucella antigen was not apparent in these patients with rheumatoid arthritis. The degree of their reactivity to other antigens not yet studied is not predictable; furthermore, no information was obtained regarding the possibility of hyperreactivity of a cellular nature.

Summary. No relationship was found between the antibody response to Brucella antigen and the F II hemagglutination titer in a series of patients with rheumatoid arthritis and osteoarthritis. Those with rheumatoid arthritis showed no greater antibody response to inoculation with Brucella antigen than did those with osteoarthritis. These observations do not confirm the report of antibody hyperreactivity in rheumatoid arthritis.

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Effect of Physical Factors on Liver Amylase Activity.* (28557)

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Other investigators(1,2) have reported that amylase is bound to particulate matter in tissue extracts and that the extracts must be subjected to additional treatment other than just normal homogenization if full measurement of amylase activity is to be obtained. Brosemer and Rutter(1) found that their rat liver homogenates and various liver fractions, particularly the microsomes, must be treated with Triton X-100 or subjected to sonication in order to demonstrate maximal amylase activity of such preparations. Grabowski and Munro(2) found that amylase activity of microsomes from pigeon pancreas was maximal only after incubation of microsomes with certain amino acids or after disintegration of microsomes with ballotini beads. Zalkin *et al.* (3) showed that inclusion of 0.2% Triton X-100 in the lysosome preparation from rabbit muscle was necessary completely to release ribonuclease, cathepsin, β-galactosidase and aryl sulfatase, and Wattiaux and deDuve (4) found that exposure of rat liver mitochondria to 0.1% Triton X-100 releases the same bound hydrolases.

To test whether conditions for eliciting maximal amylase activity of our liver preparations have been used in previous work, some of these methods mentioned above have been applied under the conditions prevailing in our experiments.

Methods. Livers were obtained fresh from white rats and dogs sacrificed under nembutal anesthesia in the laboratory. Hog liver was obtained fresh from the killing floor of the abbatoir. For preparation of homogenates from unfrozen liver, portions were removed

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