these patients are probably due to lytic factors created by proximate proliferative activity of tumor tissue. It is possible that the generalized osteoporosis occurring in other patients may be due to these local factors operating in a more uniformly disseminated form of the disease, while the lack of bone lesions in still other patients with multiple myeloma may signify a less advanced stage of tumor infiltration.

Summary. Determinations of calcium ion activities by potentiometric measurements using permselective sulfonated polystyrene-collodion membranes indicate that calcium is not very strongly bound by Bence-Jones protein. It is concluded that bone destruction frequently associated with plasma cell proliferation in patients who have multiple myeloma cannot be due to a direct chemical interaction of bone calcium with the Bence-Jones proteins.

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Antibody Response in Hematologic Patients. (26432)

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Previous studies from this laboratory(1) demonstrated that antibody response to subcutaneous injection of phenolized tularemia vaccine in 92 of 105 splenectomized patients was similar to that observed in normal controls. Failure of the remaining 13 patients to exhibit antibodies was attributed to underlying disease rather than absence of spleen. As a correlative study, antibody response of patients with hematologic diseases and intact spleens was studied. Killed tularemia vaccine (Foshay) was employed because the incidence of naturally-occurring tularemia in this area is low, and the vaccine is not generally available. Thus it could be assumed that any response would be due to a primary antigenic stimulus.

Materials and methods. The subjects used in the study were selected at random from patients visiting the hematology clinics at University Hospital. "Normal" controls were selected from presumably healthy volunteers (medical students and employees). All received a single 0.5 ml subcutaneous injection of Foshay killed tularemia vaccine. Blood for serologic studies was obtained before immunization and 3-6 weeks after. Antibody titers were determined by the bacterial agglutination test described earlier(1).

Results. The response of 162 hematologic patients and 48 control subjects to a single injection of tularemia vaccine is presented in Table I. Antibody titers varying from 1:20 to 1:640 were detected in 45 of 48 (93.7%) controls. In contrast (Table I) only 67 of 162 (41.4%) patients with hematologic disorders showed agglutination titers varying from 1:10 to 1:640. The lowest incidence of antibody response was seen in chronic lymphatic leukemia where only 2 of 25 (8.0%) had titers of 1:10 and 1:640, respectively. Similarly only 5 of 20 (25.0%) lymphosarcoma patients showed titers varying from 1:10 to 1:320. A total of 15 of 37 (40.5%) Hodgkin's patients exhibited titers from 1:10 to 1:640. In the remaining smaller groups (Table I) antibodies were detected in 13 of 19 (68.4%) pernicious anemia and 5 of 12 (41.7%) chronic myeloid

TABLE I. Antibody Response of Hematologic Patients to Tularemia Vaccine.

Diagnostic group	No. of subjects	Sex ♂	Sex ♀
Hodgkin's disease	15/37*	12/21	3/16
Lymphosarcoma	5/20	3/9	2/11
Chronic lymphatic leukemia	2/25	2/15	0/10
Acute " "	2/3	0/1	2/2
" monocytic "	3/7	0/4	3/3
Chronic myeloid "	5/12	3/5	2/7
Polycythemia rubra vera	4/5	2/3	2/2
Pernicious anemia	13/19	4/6	9/13
Iron deficiency "	2/5	—	2/5
Aplastic "	3/5	0/1	3/4
Hemolytic "	0/2	0/1	0/1
Multiple myeloma	3/6	2/3	1/3
Reticulum cell sarcoma	1/2	1/1	0/1
Myelofibrosis	2/3	0/1	2/2
Hemochromatosis	1/2	1/2	—
Miscellaneous†	6/9	3/6	3/3
Total patients	67/162	33/79	34/83
Normal subjects	45/48	24/27	21/21

* Numerator = No. showing antibodies. Denominator = Total No. vaccinated.

† Antibodies formed: Achrestic anemia, giant follicular cell lymphoblastoma, thrombocytopenia purpura, allergic purpura, disseminated lupus erythematosis with sickle cell trait, thrombocytosis. No antibodies: Sickle cell anemia, hypoplastic anemia, reticulum cell leukemia.

leukemia patients in titers of 1:20 to 1:640. Results were variable in the remaining 11 disease category groups consisting of 49 patients in which only 27 (55.1%) exhibited antibodies.

There was no good evidence that antibody response was adversely affected by the various forms of treatment. For example, only 1 of 8 chronic lymphatic leukemia patients in remission and receiving no therapy exhibited antibodies. Similarly only 11 of 23 in the lymphosarcoma-Hodgkin's group not receiving therapy showed detectable antibodies.

Analysis of the serologic data in relation to age of patients which ranged from 13 to 82 years, revealed no association between age and antibody production. However there was an association between sex and antibody production in the lymphosarcoma-Hodgkin's group wherein 15 of 30 males as compared to only 5 of 27 females demonstrated antibodies. It is also of interest that the 2 of 25 showing antibodies in the chronic lymphatic leukemia group were males.

Discussion. To assess further the role of the spleen in antibody formation, patients with similar disease processes and intact spleens should be studied as previously described(1). However, since splenectomy is usually performed in this institution when various manifestations of hypersplenism are evident, such patients were not available. Since it was felt that the underlying disease rather than absence of the spleen was responsible for lack of antibody response in 13 of 105 splenectomized patients, other patients with blood dyscrasias were studied. The antibody response in hematologic disorders has been reviewed(2). The results obtained in our study are in agreement with the earlier reports(2-5) that antibody formation in chronic lymphatic leukemia is poor. There has not been general agreement on antibody response in Hodgkin's disease(4-9). Our studies demonstrated that in Hodgkin's and lymphosarcomas antibody response to a single injection of tularemia vaccine was detectable in only 20 of 57 patients. The numbers of persons studied in each of the other disease categories were too small to make definite conclusions other than that as a group, patients with hematologic disease processes did not form antibodies as well as normal individuals. Under the conditions of this study a sub-optimal single antigenic stimulus was used rather than the 3 daily injections routinely employed with Foshay vaccine. However, the difference between these 2 regimes was not great in our previous studies in which 39 of 48 (81.3%) and 52 of 57 (91.2%) demonstrated antibodies following 1 and 3 vaccine injections, respectively.

Of additional interest is the observation that only 5 of 27 female patients with lymphomas showed antibodies as compared to 15 of 30 males. Previous studies(1) from this laboratory in splenectomized persons showed that 11 of 70 females as compared to 2 of 35 males showed no antibody response after immunization. Also, properdin levels(10) were significantly lower in females than males. It is also of interest that the 2 of 25 patients showing antibodies in the chronic lymphatic leukemia group in this study were males. Further studies to elucidate these factors are in progress.

Summary. A single injection of 0.5 ml of phenolized tularemia vaccine elicited detectable agglutinating antibodies in 67 of 162 (41.4%) patients with hematologic disorders as compared to 45 of 48 (93.7%) in normal controls. Particularly significant was the lack of response in 23 of 25 chronic lymphatic leukemia and in 37 of 57 lymphoma patients. In the latter group only 5 of 27 females as compared to 15 of 30 males exhibited antibodies.

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Acute and Subacute Toxicity of Amino-Hexose-Reductones. (26433)

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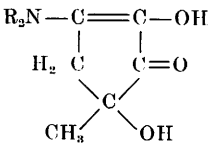
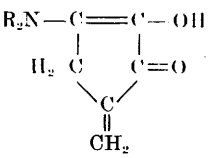
The well-known Maillard reaction, responsible for browning discoloration in many foods, involves combination of reducing sugars with amino groups of amino acids, peptides, and proteins, with subsequent enolization and dehydration of the sugar radical(1, 2). In studies on the sugar rearrangement and dehydration reactions, Hodge and collaborators(3,4) isolated new "amino-hexose-reductones," $R_2N \cdot C_6H_7O_3$ (I), and "anhydro-amino-hexose-reductones," $R_2N \cdot C_6H_5O_2$ (II), from reactions of hexoses with secondary amine salts and determined their structure(4). Because these reductones showed excellent antioxidant properties in fats and oils(5,6), toxicity studies were undertaken to determine their suitability for food use.



(I)



(II)

The present report presents data on the acute and subacute toxicity of 5 reductones, namely, dimethylamino - hexose - reductone (DMA) and its anhydro derivative (ADMA), piperidino-hexose-reductone (PIP) and its anhydro derivative (APIP), and morpholino-hexose-reductone (MORPH).

Methods. Aqueous propylene glycol was used as solvent for DMA and MORPH in acute toxicity studies employing oral and intraperitoneal administration. Because of lack of a suitable solvent of low toxicity for PIP, APIP, and ADMA toxicity determination of these reductones was limited to single oral administration of a suspension in 20% gum acacia. The limited amount of material available for determination of acute toxicity necessitated the use of mice (weighing 15 to 20 g each) except in the case of DMA for which an approximate determination of the toxicity was made by single intraperitoneal injection in rats (weighing 125 to 150 g) as well. In addition 2 groups of 5 mice each were given daily oral doses of 25

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