the blood urea nitrogen dropped to 150 mg %.

The electrolyte solution was prepared from sterile concentrates† and had the following standard composition as expressed in g %. Dextrose 1, NaCl .610, $NaHCO_3$ .220, KCl .0360, $CaCl_2$. $6H_2O$ .0450, $MgCl_2$. $6H_2O$ .0107, $NaH_2PO_4H_2O$ .0058.

Summary. An efficient and safe dialyzer‡ suitable for continuous operation under sterile conditions is described. It is made up of a variable number of component channels according to surface area desired. Sterility is accomplished by autoclaving as a whole and optional controlled ultrafiltration is possible.

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Chemotherapeutic Effectiveness of Alloxan in Murine Bartonellosis.* (18528)

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Alloxan, an oxidation product of uric acid, is present in combined form in several compounds which are of importance in mammalian physiology, and there is some evidence for its occurrence in the free state in blood and other animal tissues(1). It has been extensively studied in recent years because of its specific toxic action on the beta cells of the pancreatic islands, resulting, when suitable dosages are used, in the experimental production of diabetes(2,3). There is evidence that its diabetogenic effect is caused by reaction with SH groups in enzyme systems(4). Alloxan, as far as we can learn, has not previously been tested for chemotherapeutic activity in any infectious disease.

Material and methods. Latently infected (carrier) rats of the St. Louis University strain were used. Previous work with several hundred rats of this strain has shown that splenectomy is invariably followed by severe bartonellosis. The organisms appear in the erythrocytes on the 2nd or 3rd day after removal of the spleen (occasionally on the 1st day), reach a maximum on the 5th or 6th day, and disappear, in surviving animals, by the 9th or 10th day. The highest daily bartonella counts are rarely below 100 per 100 erythrocytes, and the mortality is usually about 50%.

All rats in the experiments to be reported here were maintained throughout the observation periods on a low sulfur diet (LSD) with the following composition: casein 6%, salt mixture 4%, sucrose 15%, corn starch 48%, lard 22%, cod liver oil 3%, and debitterized brewers yeast powder 2%.

In Exp. 1, 20 rats, previously maintained for 10 days on LSD, were splenectomized. Ten of these served as controls. The remaining 10 were given daily intraperitoneal injections (40 mg per kilo) of freshly prepared solutions of alloxan in distilled water for 13 days, starting 4 days before splenectomy.

In Exp. 2, 14 rats, previously maintained for 3 days on LSD, were splenectomized. Four rats served as controls. The remaining 10 were given daily intraperitoneal injections

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TABLE I. (Exp. 1). Effect of Alloxan on Murine Bartonellosis in Splenectomized Carrier Rats.

Rat No.	Treatment	Lowest hemoglobin level, mg	Highest bartonella count (per 100 rbc)	Outcome
1	Control	5.5	252	S*
2	,,	4.5	214	,,
3	,,	5.0	293	,,
4	,,	4.0	188	,,
5	,,	4.0	90	,,
6	,,	6.0	273	Died 6th day
7	,,	5.5	315	S
8	,,	5.5	252	,,
9	,,	6.0	218	,,
10	,,	5.5	162	Died 6th day
11	Alloxan	16.5	0	S
12	40 mg/kg	16.5	0	,,
13	daily	17.0	0	,,
14	,,	17.0	0	,,
15	,,	16.5	0	,,
16	,,	16.5	0	Died 5th day†
17	,,	15.5	0	S
18	,,	16.0	0	,,
19	,,	16.5	0	,,
20	,,	16.5	0	,,

* Survived.
† Splenectomy wound broken down. No hematological evidence of bartonellosis.

TABLE II. (Exp. 2). Effect of Alloxan on Murine Bartonellosis in Splenectomized Carrier Rats.

Rat No.	Dosage	Treatment started	Highest bartonella count	Outcome
1	—	Control	182	S
2	—	,,	299	Died 6th day
3	—	,,	249	,,
4	—	,,	301	,,
5	40 mg/kg	1 day p.s.*	0	S
6	,,	1 day p.s.	0	,,
7	,,	day of spl.	0	,,
8	,,	day of spl.	0	,,
9	,,	1 day a.s.†	0	,,
10	,,	1 day a.s.	0	,,
11	,,	2 days a.s.	0	,,
12	,,	2 days a.s.	0	,,
13	,,	3 days a.s.	0	,,
14	,,	3 days a.s.	0	,,

* p.s. = After splenectomy.
† a.s. = Before splenectomy.

of alloxan at various intervals before the expected appearance of organisms in the blood. Treatment was stopped on the 8th day after splenectomy.

In Exp. 1, the effectiveness of the agent was judged by counting the number of organisms in giemsa-stained blood films, and by hemoglobin determinations. These observations were made daily for 12 days, starting on the day after splenectomy. The bartonella counts were based on the examination of 400 erythrocytes, and were recorded as organisms per 100 erythrocytes. Hemoglobin was determined directly by the Dare method. In Exp. 2, bartonella counts only were made, and the observation period was 14 days.

Results. In Exp. 1 (Table I) the 10 controls showed the expected severe anemia and parasitization of erythrocytes, while the rats given alloxan showed no evidence of anemia or bartonella infection.

The results of Exp. 2 (Table II) again showed complete suppression of the infection by daily injections of 40 mg per kg of alloxan, even when started the day after splenectomy, when multiplication of the organisms had probably already begun.

The animals surviving in these experiments, as well as in other similar experiments, were observed daily for several weeks after bartonella counts were discontinued, and no clinical evidence of delayed bartonellosis was noted. It seems probable, though not yet proved, that rats given alloxan at this dosage level were rendered bartonella-free. In another series of rats, not included in the tables, daily injections of 20 mg per kg for 12 days completely suppressed the infection, but typical bartonellosis occurred in several animals 4 to 5 days after cessation of therapy.

Discussion. The diabetogenic action of alloxan may be inhibited by BAL, glutathione, cysteine, and related compounds containing the SH group, but only if the protective substance is given almost simultaneously with the alloxan. For this reason, it has been assumed that the pancreatic injury results from inactivation of thiol groups(4). It will be of interest to determine whether the therapeutic action of alloxan can be neutralized by the compounds mentioned above.

The dosage of alloxan used in these experiments is well below that required for the production of diabetes. It has been shown, however, that a diminution in glucose toler-

ance is caused in rats by the intravenous injection of as little as 25 mg per kg every other day for 4 weeks, although blood sugar levels remain normal while the rats are on a normal diet(5).

Inhibition of bartonella multiplication is effected physiologically by the presence of the intact spleen, and artificially by arsenicals(6), by aureomycin and terramycin(7), and by alloxan. Arsenicals and alloxan are known to inactivate thiol groups. In spite of extensive study, the mechanism by which the spleen inhibits the growth of *Haemobartonella muris* has not been discovered(8).

In future work, the possibility that alloxan may have chemotherapeutic activity in infections other than bartonellosis will be explored, and a variety of closely related compounds will be tested. The observation reported here suggests the possibility that compounds formed naturally in the course of nucleic acid metabolism may be chemotherapeutically effective.

Conclusions. Alloxan in relatively low and presumably nondiabetogenic dosages was found to be effective in preventing the development of murine bartonellosis, which invariably follows splenectomy in untreated carrier rats. The activity of this agent probably depends on its reaction with SH groups.

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Factors Influencing Effect of Radioactive Colloidal Gold on Free Tumor Cells in Peritoneal Fluid.* (18529)

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In a previous note(1) a method has been outlined for screening quantitatively the effect of radioactive isotopes on tumor cells in mice: cells of Sarcoma 37 were grown serially as free cells in the peritoneal fluid of CFW mice and tested for their resistance to various doses of a radioactive isotope injected intraperitoneally. Using this technic in experiments with radioactive colloidal gold(2) it has been found that sarcoma cells grown in the peritoneal fluid of a CFW mouse 2 to 5 days after inoculation of 10,000 cells, disintegrated and completely disappeared within 48 hours after i.p injection of 0.3 to 0.42 mc of radioactive colloidal gold. In a new series of experiments with several groups of mice, we have analysed this radiotherapeutic effect† by varying in each group of mice one of the conditions of the experiment.

Material and methods. Two strains of tumors were used in this work: (1) Sarcoma 37 was grown in 2 strains of mice—CFW and dba; (2) malignant lymphoma (isolated originally from the thymus of a dba mouse) in dba mice. Thus, dba mice were used for carrying 2 different tumors. Both tumors were propagated in serial transfers in the peritoneal fluid. The technic of inoculation with a requisite number of tumor cells and the method for estimating the therapeutic results

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