and the Utah Industrial Commission has begun a study of occupational disease under the direction of State Health Commissioner John L. Jones, of Salt Lake City, who has leave of absence for two years. The state legislature has appropriated $25,000, which will be used for the conduct of the study with a view to developing a permanent occupational disease service. The federal public health service will participate in the first six months of the investigation, the major problems of which will be exposure to silicious dusts and dusts in bituminous coal mines, lead and other metallic dusts and fumes and certain gases. Later, health hazards in other industries will be investigated.

A NEW siderite, or iron meteorite, to be called the Mapleton meteorite, has been acquired by Field Museum of Natural History from Mr. Harvey Meevers, Mapleton, Iowa. This is the first iron meteorite to be reported from that state. Previous to the discovery of this iron, four other meteorites were known from Iowa, three of which were aerolites or stone meteorites, and one a meso-siderite or variety of iron-stone meteorite. No conclusive evidence is at hand regarding the date and time of the fall of the meteorite, which probably does not represent much more than half of the original mass. It weighs 49 kilograms (108 pounds). Its greatest length, breadth and height are 17½ inches, 9⅞ inches and 6 5/16 inches, respectively.

THE Committee on Sedimentation of the Division of Geology and Geography of the National Research Council has prepared a symposium on recent marine sediments. This consists of thirty-four papers by specialists in different fields of this subject. Emphasis has been placed upon the processes affecting the deposition of sediments. Because of the bearing of this subject on petroleum geology, the symposium has been published by the American Association of Petroleum Geologists. Dr. Parker D. Trask, associate geologist of the U. S. Geological Survey, became chairman of the committee four years ago. At that time he proposed the assembling in a single volume of the large amount of information that had been obtained in the previous ten or fifteen years by investigators of conditions in the oceanographical, geological, biological and other publications in many parts of the world. This idea received favorable reception, and a book of 740 pages, which is now about ready for distribution, is the result.

The E. W. Scripps, the research vessel of the Scripps Institution of Oceanography of the University of California, sailed from San Diego early in August for a study of ocean currents and undersea strata from San Diego to Santa Barbara. Samples of undersea strata will be taken about thirty miles off shore. Dr. Roger Revelle, member of the institution, is in charge of the cruise. Dr. R. T. Young, physicist of the Worcester Polytechnic Institute, will make a special study of the transmission of light in sea water. *The E. W. Scripps* returned recently after a cruise of 1,200 miles of the Pacific from the Oregon border to Cedros Islands in Mexico. The cruise, which lasted two months, was made in cooperation with the Federal Bureau of Fisheries, which was interested in studying the distribution of sardine eggs off the California coast. General hydrographic conditions were observed at a number of stations from just off shore to as far as 360 miles at sea.

DISCUSSION

THE MODE OF ACTION OF SULFANILAMIDE

DR. PHILIP SHAFFER'S communication on this subject in the issue of SCIENCE[1] for June 16 suggests that both the therapeutic and toxic actions of sulfanilamide may be exerted through a "mechanism by which the sterilizing oxidation intensity of molecular oxygen is applied nearly at its maximum to bacteria and unavoidably also to some extent to host cells."

The undersigned are in agreement with this conception to the extent that it indicates a source of sulfanilamide toxicity. They do not find the available evidence compatible with a concept of identity between the mechanisms producing the known toxic and therapeutic effects nor with an explanation of the therapeutic usefulness of sulfanilamide in terms of capacity to act as a reservoir for an intermediate substance of high oxidizing intensity.

[1] P. 547.

The Shaffer premises: Ingested sulfanilamide is assumed to become (1) converted by a process of biologically mediated oxidation into derivatives which act, in turn, as oxidizing agents; (2) producing injuries to the cellular reducing systems; (3) less easily tolerated by the invading pathogen than by the resisting host.

The acting derivatives are assumed to form a reversible electrode couple (as do ferrous and ferric iron) composed of p-hydroxylamino and p-nitroso benzene sulfonamide "or the corresponding semiquinone free radicals."

The cell components mentioned as especially susceptible to injury by this oxidizing combination are: catalase, hemoglobin, glutathione and ascorbic acid. The injuries are presumed to be more readily tolerated by the host than by the invader because of "the relative immunity of host tissues to toxic effects . . . due

to their lower oxygen tension, their higher metabolism and to higher catalase content."

Association of the oxidizing potentialities of the postulated intermediate with the nitroso and not with the hydroxylamine component: Nitrous acid, in the orientation present in p-nitroso benzene sulfonamide, is an effective oxidizing agent, producing damage to the capacity of hemoglobin to transport oxygen and to the capacity of the body to maintain circulation. Hydroxylamine is not an oxidizing agent at the pH of the blood, excepting toward substances of unusually powerful reducing capacity or under conditions of catalytic mediation. *In vitro,* it reduces Fehling's solution much as glucose does. *In vivo,* it becomes converted into nitrite[2,3]—again acting as a reducing, not an oxidizing agent. The point is emphasized because hydroxylamine is known to block catalase action in concentrations as small as M/100,000.[4]

Insusceptibility of catalase to oxidative injury of the type postulated: The oxidizing potentialities of p-nitroso benzene sulfonamide would be a source of injury to hemoglobin, glutathione and ascorbic acid, but not to catalase. Keilin and Hartree[5] and K. G. Stern,[6] authorities on the properties of catalase, report it to be so extraordinarily resistant to oxidation as to suggest that the iron content of that enzyme may be in the ferric condition, passing fleetingly into the ferrous condition only after *reduction* by hydrogen peroxide.

Successful chemotherapeutic action is directed against a type of vulnerability, in the pathogen, not shared by the host: Oxidizing actions against hemoglobin, glutathione and ascorbic acid are directed against oxygen-carrying power and against capacity to sustain circulation. They are highly toxic because they strike at the host where he is most vulnerable in his defense against oxygen want. The pathogens responsive to sulfanilamide are less vulnerable to oxygen want[7] and more vulnerable to peroxide.[8] The maximum chemotherapeutic possibilities are obviously not to be sought in an action striking at the defenses against oxygen want but in an action striking at the defenses against peroxide, namely, against catalase.[9,11] For this action, the reducing, hydroxylamine derivative of sulfanilamide is definitely available[9,11] *not* the oxidizing nitroso derivative, which is a source of toxicity.

Alternative suggestion: There can be no question but that p-hydroxylamino and p-nitroso benzene sulfonamide are obtainable from sulfanilamide by biologically feasible types of oxidation. They may not, however, be produced together but, rather, stepwise: the hydroxylamine derivative being formed within the locus of infection[9,11] by the metabolic process which *yields* peroxide, and the nitroso derivative being formed following diffusion of the hydroxylamine from the areas vicinal to the cell substance of the pathogen, into the blood.

This stepwise production, first of the therapeutically active derivative and, secondly, of the toxic derivative, is possible in the manner outlined. It would not be possible as a result of the peroxide-mediated type of oxidation postulated by Shaffer. The latter type of oxidation is, however, not indicated: (1) because the pathogens most responsive to sulfanilamide are not those producing the most peroxide and permitting accumulation of peroxide to highest levels—as is demanded by a hypothesis of conversion mediated by peroxide—and (2) because such a type of oxidation contains no factor of self-limitation. (Production of active intermediate as a function of available peroxide concentration would increase progressively with increasing peroxide concentration until the pathogen was destroyed. Sulfanilamide does not act, *in vivo,* in any such drastic fashion. It produces only a degree of growth retardation, in infections responsive to its action, sufficient to hold down the *numbers* of the pathogen to be disposed of, by the host, to levels within possibility of control.[10,11]

An assumption of stepwise production of the therapeutically active and toxic agents opens up the possibility of using, in place of sulfanilamide, an agent making hydroxylamine available, within the locus of infection, in a form not so readily oxidized to a nitrous acid derivative as is p-hydroxylamino benzene sulfonamide. The comparative anti-catalase and anti-hemoglobin potentialities of hydroxylamine linked to the sulfon group, following blockade of the p-amino group against oxidation, should be explored in this connection.

Adjuvant measures should be taken, during sulfanilamide therapy, to counteract toxic actions on hemoglobin and on circulatory capacity so as to permit full realization of therapeutic effect.[10,11]

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[4] M. G. Sevag and L. Maiweg, *Biochem. Zeitschr.,* 288: 41, 1936.

[5] *Proc. Roy. Soc. (London),* B124: 397, 1938.

[6] *Jour. Gen. Physiol.,* 20: 631, 1937.

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