INFORMATION TO USERS

This manuscript has been reproduced from the microfilm master. UMI films the text directly from the original or copy submitted. Thus, some thesis and dissertation copies are in typewriter face, while others may be from any type of computer printer.

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleedthrough, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send UMI a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

Oversize materials (e.g., maps, drawings, charts) are reproduced by sectioning the original, beginning at the upper left-hand corner and continuing from left to right in equal sections with small overlaps.

ProQuest Information and Learning
300 North Zeeb Road, Ann Arbor, MI 48106-1346 USA
800-521-0600

UNIVERSITY OF CINCINNATI

May 31, 1935 19

I hereby recommend that the thesis prepared under my supervision by Henry Lee, M. D.

entitled "A Study of the Physiologic Effects of Silicon and of its Role in Health and Disease."

be accepted as fulfilling this part of the requirements for the degree of Doctor of Philosophy

Approved by:

Ulmer R. Reid

Robert A. Kehoe

Form 668—G. S. and Ed.—1M—7-31

A STUDY OF THE PHYSIOLOGIC EFFECTS OF SILICON AND OF ITS ROLE IN HEALTH AND DISEASE

A dissertation submitted to the

Graduate School
of the University of Cincinnati

in partial fulfillment of the
requirements for the degree of

DOCTOR OF PHILOSOPHY

1935

by

Henry Lee

A.B. Washington and Lee University 1926
M.D. Johns Hopkins Medical School 1930

TABLE OF CONTENTS

A STUDY OF THE PHYSIOLOGIC EFFECTS OF THE SILICON AND OF ITS ROLE IN HEALTH AND DISEASE

Henry Lee, M. D.

I

Introduction

Although silicon has a widespread and bountiful distribution over the earth, little evidence has been adduced to emphasize its probable importance in the organic world. Its presence in the ash of all plants and animals has been repeatedly demonstrated and this is certainly suggestive that its role is more than that of an accidental contaminant. This element has been much neglected in physiologic studies for many reasons. The technical difficulties encountered in chemical analyses make impossible the isolation of the different compounds containing silicon which must of necessity exist in living tissues. Thus one resorts to the expedient of expressing the silicon content of tissues in terms of silicon dioxide in the ash. This gives no information as to the chemical form of silicon in the normal, functioning structures. The well-nigh impossible feat of excluding silicon in any feeding experiment bars this mode of approach. The customary concept of the inertness of silica within the living body is contradicted by numerous facts and these will be introduced. The therapeutic possibilities of the silicates have also been little investigated and merit a thorough study.

The unravelling of the role of the silicates in the causation of silicosis of the lungs has been the principle source of our information on the physiologic effects of the different compounds of silicon. The more recent and exact technical procedures for the quantitative determination of silica have served to upset many of the former views of the significance of silicon in the animal organism, but, as yet permit no final conclusions to be drawn.

Folk remedies have pointed the way for many advances in scientific medicine, and none should be carelessly tossed aside without an exhaustive investigation of their clinical value and an attempt to evolve a rationale for any apparent beneficial effect which may follow their use. There exists a practice among the mountaineers of the state of Virginia which on first thought provokes mirth, yet, demands a close scrutiny. "Ulcers of the stomach" are treated by the oral ingestion of "fine river sand", and strangely enough the results are gratifying both to the mountaineer and his more highly educated neighbor who resort to the same remedy for the same ailment after the usual medical treatment with diet and alkalies fails to give the desired result. An attempt to offer a rational explanation for this strange phenomenon was the incentive for this investigation.

A consideration will be given only to those compounds of silicon which are known to exert a definite effect in the living organism. Silicon dioxide and silicic acid will be discussed. These two compounds must not represent all the compounds of silicon of physiologic importance, yet, our knowledge of the other compounds is

negligible in comparison.

II

Occurrence of Silicon in Nature

Silicon next to oxygen is the most abundant element and represents 27 percent of the earth's lithosphere. Silicon does not exist in the free state. Silicon dioxide is one of the most common minerals in the earth's crust, and also, silicon is the characteristic element of all important rocks with the exception of the carbonates (Mellor).

Deposits of a friable powder, known as diatomaceous earth, are found in many places. These represent the fossil remains of diatoms, organisms which abound in sea-water and from which silicon is extracted to form their skeletal framework. Many of these deposits represent almost pure silicon dioxide. The skeletal framework of sponges are also made up of spicules of hydrated silica. The work of Richter revealed the necessity for the inclusion of a soluble silicate in an artificial nutrient media which would be suitable for the cultivation of diatoms. This has also been confirmed by King and Davidson. Experimental evidence is lacking of the essential quality of silicon in the growth of any other plants and animals.

Silicon in Plants: The presence of silica in the ash of all plants has been often demonstrated. These analyses have shown an amazing diversity in the capacity of the different types of plants to

assimilate the silica from the soil. The silica content of the soil is also of influence on the quantity taken up, and Vogel found amorphous silica was more abundantly assimilated than the crystalline variety. The ash of grasses are particularly rich in silica and the highest content is found in the equisetaceae and gramineae. Siliceous concretions, tabasheer, are found in the nodes of certain bamboos and its ash is almost pure silicon dioxide. The older a plant the greater is its content of silica. Von Swiecicki, Kall, and Struve made the earliest extensive studies on the silicon content of various plants.

Vogel was able to demonstrate a definite selective localization of silica within plants. The roots contained the least, then followed the stem and leaves, and the greatest amount was found in the husks of seeds. Abshagen made transverse sections through plants and found a progressive increase in the content of silica proceeding from within outwards.

The chemical nature of silicon as it is taken up by the roots is not known. The presence of minute quantities of silicon in all river, well, and spring water makes probable the existance of colloidal silica in the soil. Thus one is not forced to search for a process through which the roots would render soluble the silica in the soil. The colloidal silica probably passes into the roots along with the water in which it is in solution.

The chemical compounds in which silicon exist in plants are

imperfectly known. Lange believed that he could demonstrate the colloidal form in plants. Ladenburg thought silicon was in an organic compound. The relation of silicon to cellulose is summarized thus, by Samec: "Silicic acid cannot be wholly removed by the strongest reagent and apparently has a definite influence on certain properties of cellulose. Malfitano supposes the structure of a colloid generally to consist of the nucleus of an electrolyte ion (SiO_2 in the case of cellulose) around which are arranged the polymers of an organic element similar to a true Werner Complex". Balch and Paine believe organic compounds of silicon to be present in the juice of cane sugar and these give rise to the silica containing precipitates in cane syrup. In starches "Maltifano considers that in the arrangement of the building stones in the starch micelles, polymers of an anhydrous saccharide are stratified around a phosphate or silicate ion. Silicic acid is likewise in partial esterfication as well as fatty acids." (Samec) Pfeiffer demonstrated the presence of silica sol in cells by means of a very complicated technical procedure which is dependent on refraction. He discussed the deposiyion of silica in the membranes and cell protoplasm, which process was accelerated in dead cells.

Hall and Morrison concluded that the presence of silica in soil influenced the assimilation of phosphoric acid. Lemmerman and Weisman believed colloidal silicic acid could replace the phosphates in the absence of the latter and the importance and function of the silica in soil has been ably discussed by Gordon.

The role of silicon in plants has never been satisfactorily evaluated. It is questionable whether it contributes to the rigidity of plants as von Swiecicki believed. Sachs grew straw in soil with a low content of silica. As a result, the ash contained little silicon dioxide, yet, the rigidity of the straw was not affected. Jodin grew wheat in soil containing little silicon and found a lessened resistance to rust and parasites after several generations.

Silicon in Animals: Herrera believes silica can be demonstrated in all animal and vegetable cells which have been slowly incinerated. The great majority of silica in animals gains entry through the gastro-intestinal tract. The amount which is resorbed depends on the type and quantity of the ingested food. This can be easily verified by a study of the silica excretion in the urine of humans and laboratory animals on varying diets. Much more silica is ordinarily found in the urine of the herbivora than in the carnivora and this corresponds with the relative content of silica in the two types of food. However, Heffernann noted a uniformity in the silicon content of the organs of dogs and rabbits despite the differences in their diets. The particles of silica which are inhaled and deposited in the lung tissue undergo at least partial dissolution and must contribute relatively little to the total silica which is excreted in the urine. The chemical form in which silicon is taken up from the gastro-intestinal tract is not known. It is difficult to conceive of the simple colloidal silicic acid being resorbed without first

undergoing some change as this substance possesses marked toxic properties following either subcutaneous or intravenous injection. However, the oral administration of silicic acid is followed by no toxic sequelae despite a great resorption of this material from the intestines. The chemical nature of the compound into which it must have become transformed has not been ascertained.

Silica appears to be excreted chiefly in the urine. The chemical compound in which it is excreted is not known and the quantity of silicon is usually expressed in terms of silicon dioxide. King, Stantial and Dolan found the daily urinary output of silica in the normal adult on the usual refined diet ranged from 15 to 20 milligrams per day. The higher content of silica in the urine of the herbivora has been held responsible for the presence in cattle of urinary calculi containing a high content of silica (Dammann). Attempts have been made to implicate the large intestine in the excretion of silica but the evidence is most unconvincing. Studies on the concentration of silica in the urine of humans using the colorometric method described by King and Stantial revealed wide variations, depending on the quantity of silicic acid which had been ingested. In Fig.11 may be seen the results of an average of the excretion in eight patients and in whom a range of 9 mgs to 34 mgs of silica per liter of urine was found. The normal value promptly returned following the discontinuance of silicic acid by mouth and this is suggestive that no storage of this material took place in the body.

A pathologic condition of the kidneys in the human has not been found to be definitely related to the excretion of silica. Collis found the incidence of chronic nephritis among the miners of South Africa to be greater than in the general male population of the same age. Hackmann reported an increase in the silica content of the liver and spleen in three cases of silicosis of the lungs, but found no elevation in the kidneys. Burge's report of the presence of silica in cataracts of India and none in those from America is of interest, and he believes the differences in the diets are responsible.

The chemical forms in which silicon exist within the living body are not known. King and Stantial report the total and soluble silicates in the blood are always equal and this renders unlikely the occurrence of particulate silica. Drechsel found evidence of an ortho-silicic acid ester of a di-valent alcohol ($Si(O.C_{34}H_{59}O)_4$) in the blood and liver. Silicon is thought to be present as calcium silicate in calcified tuberculous lymph nodes. The chemical combinations of silica in boneand in the various concretions of the biliary and urinary tract have not been ascertained.

Gorup Besanez (1862) considered silicon an essential element in animal protoplasm without, however, advancing any satisfactory proof for his contention. Very complete analytical studies of the occurrence of silicon in the various tissues of the body were reported by Schulz in 1901 and 1902. These reports stimulated a great interest in the silicates and his speculations furnished a field for further work.

Schulz was of the opinion that the silicates were concerned in all the defensive mechanisms of the body and based his claim on the presence of a high content of silica in connective and granulation tissue. In the light of more recent and exact quantitative determinations of the silica content of connective tissues as reported by King and Stantial, this view cannot be substantiated. The silicon content of bone has been considered as contributing markedly to its strength and rigidity. The significance of silicon in the animal organism remains problematical, yet probably has a function other than that of an accidental contaminant. The widely varying results in the numerous analyses for silicon in tissues can be explained on the basis of the technical difficulties involved in the quantitative determinations. Kraut spoke of a normal blood level of silicon with the individual and with different pathological conditions and also with the diet. An average of 1.74% of the ash of blood was found to be silicon dioxide in twenty-three normal individuals. The values ranged from 1.16% to 3.02% of the ash. Re-examination after a period of four weeks of thirteen of the subjects showed only a maximum variation of four percent from the original findings. King and Stantial found only a tenth as much silica in the blood as Kraut.

Bibliography

1. Abshagen, U.: Untersuchungen uber den Kieselgehalt von Arundinariajaponica. Kiel. 1912.

2. Balch, R. T. and Paine, H. S.: Colloid chemistry in sugar industry. Alesander's Colloid Chemistry, Vol. IV, p. 148.

3. Burge, W. E.: Analyses of the ash of the normal and the cataractous lens. Arch. Ophth. 38:435, 1909.

4. Collis, E. L.: The statistical characteristics of Dust Phthisis. Jour. Ind. Hyg. 8:457, 1926.

5. Dammann: Eine Massenerkrankung von Ochsen durch Kieselsaure-Harnsteine und deren Vorbeuge. Deut. tierztl. Wchnschr. 5:435, 1897.

6. Drechsel, E.: Vorlaufige Mitteilung uber einen Naturlich vorkommenden Kieselsaureester. Zentralbl. f. Physiol. 11:361, 1897.

7. Gordon, N. C.: Theory of adsorption and soil gels. Holmes' Colloid Symposium Monographs, Vol. II, p.

8. Gorup Besanez, E. F.: Lehrbuch der Physiologischen Chemie. 3:600, 1862. Braunschweig.

9. Hackmann, C.: Ueber den Kieselsauregehalt pneumokoniotischen Lungen. Beitr. z. Path. Anat. u. z. Allg. Path. 90:623, 1933.

Hall, A. D. and Morrison, A.: Cited by Mellor.

10. Heffernann, P.: Some Notes on the biophysics of silica. Brit. Med. Jour. 2:489, 1929.

11. Herrera, A. L.: Plasmogeny. Alexander's Colloid Chem. Vol. II, page 82.

12. Jodin, M. V.: Du role de la silice dans la végétation du mais. Ann. Chim. Phys. 30:485, 1883.

13. Kall, F.: Die Kieselsaure im tierischen und menschlichen Organismus. Inaug. Diss. 1898.

14. King, E. J. and Davidson, V.: The biochemistry of silicic acid. IV. Relation of Silica to the growth of Phytoplankton. Biochemical Journal. 27:1015, 1933.

15. King, E. J. and Stantial, H.: The biochemistry of silicic acid I. Micro-determination of silica. Ibid: 27:990, 1933.

16. King, E. J. and Stantial H. and Dolan, M.: The biochemistry of silicic acid.
II. The presence of silica in the tissues.
Ibid: 27: 1002, 1933.
III. The excretion of administered silica.
Ibid. 27:1007, 1933.

17. Kraut, H.: Über den Kieselsäuregehalt des menschlichen Blutes und seine Veränderung durch Kieselsäurezufuhr.
Ztschr. f. Physiol. Chem. 194, 81, 1931.

18. Ladenburg, A.: Ueber die Natur der in den Pflanzen vorkommenden Silicumverbindungen. Ber. d. duetsch. chem. Gesellsch. 5:568, 1872.

19. Lange, W.: Ueber die Natur der in den Pflanzen vorkommenden Silicumverbindungen. Ber. d. Chem. Gesell. 11:822, 1878.

20. Lemmerman, O.:and Wiesman, H.: Cited by Mellor.

21. Mellor, J. W.: A comprehensive treatise on inorganic and theoretical chemistry. Vol. VI.

22. Pfeiffer, H.: Uber Methoden zum Studium der Verkieselungsprozesse innerhalblebendenpflanzlicher Zellen.
Arch. f. exp. Zellforsch. 6:418, 1928.

23. Richter, O.: Ueber Reinkulturen von Diatomeen und die Notwendigkeit von Kieselsaure fur die Diatomee Nitzschia Palea. Verhandl. Ges. duetsch. Naturforsch. Ärzte. 2:249, 1904.

24. Sachs, F.: Cited by Mellor.

25. Samec, M.: Colloid chemistry of cellulose.
Alexander's Colloid Chemistry, Vol. IV, page 10.

A summary of the colloid chemistry of starches.
Ibid. Vol. IV, page 168.

26. Schulz, H.: Ueber den Kieselsauregehalt Menschlichen und Thierischer Gewebe.
Pfluger's Arch. ges. Physiol. 84: 67, 1901.

Einige Bemerkungen uber Kieselsaure.
Muench. Med. Wchnschr. 49:440, 1902.

27. Struve, G. A.: De silicia in Plantis Nonnullis, 1835, Dresden.

28. von Sweicicki, V.: Die Bedeutung der Kieselsaure als Bestandtheil der Pflanzen und Ihre Beziehung zum Lagern des Getreides. Inaug. Diss. 1896.

29. Vogel, A.: Die Aufnahme der Kieselerde durch Vegatabilien, 1882.

III

Physiologic Effects of Silica

(Silicon dioxide, SiO_2)

Inhalation of dust containing silica: Arnold (1885) observed the difference in the reaction of the tissues of the lung to the various types of dust which were inhaled in the course of many occupations. Gardner's work showed that particles of coal, marble or carborundum incite little reaction in the lung. The phagocytes engorge themselves with the particles to such an extent as to obscure even the nucleus. Furthermore, the great majority of the phagocytes remain in the alveoli and are subsequently expectorated. Relatively few particles are carried back into the parenchyma, and these provoke only a minimal reaction. Even a suspension of iron oxide, aluminum oxide, marble, coal, or carborundum (SiC) may be injected subcutaneously without exciting any more than a minimal response (Nicholson, Kettle, Gardner.)

The particles of silica lead to a very different reaction on the part of the tissues. The phagocytes of the lung do not engorge themselves, but take up only a few particles. Neither do these phagocytic cells remain in the alveoli, but assume a marked amoeboid activity and pass into the parenchyma of the lung where a reaction takes place which leads to the formation of connective tissue (Gardner and Cummings).

The fate of the particles of silica after their deposition in the lungs has been the object of intensive study because of its intimate relationship to silicosis. Moir found the average diameter

of the phagocytized particle of silica to be one micron, and none larger than ten micra were encountered. Two rather divergent explanations have been advanced to explain the fibrosis of the lungs. The physical characteristics of the particles, namely, their sharp edges and insolubility have been held responsible by many authors (Moore, Peissachowitsch and Gottlieb, et als). On the contrary a slow liberation of colloidal silicic acid under the influence of the alkaline medium of the tissues has been considered by Schulz, Kettle, Mavrogardato, Collis and others as the factor which provokes the formation of connective tissue. This process can be greatly accelerated by the simultaneous inhalation of particles of alkali and silica as occurs in the manufacture of abrasive soaps (Chapman; Heffernan). Gardner believes the fine size of the particles of silica rather than the accompanying alkali is responsible. Bohme found the degree of induration in a silicotic lung followed closely its content of silicon dioxide.

The body apparently possesses a rather efficient mechanism for the elimination of the particles of silica which gain access to the lungs. Sladden estimated 10 to 25 grams of silica found its way into the parenchyma of the lung of coal miners. He found an average content of 4.1 grams of silica in the lungs of 24 miners and he believed the remainder had been dissolved before the lungs had been damaged to any great extent.

It is to be expected that any disease process as silicosis of

the lungs with its attendant extensive formation of connective tissue would injure the lung directly and also lessen its resistance to other infections. Moreover, silicosis of the lungs appears to be accompanied by a general decrease in the resistance of the body. Collis and Yule have compiled extensive mortality records to illustrate the effect of the human body following the inhalation of silica dust. Those individuals exposed to silica dust were found to be more liable to contract diseases of the circulatory system, the nervous system, the digestive organs, the kidneys and the liver, and more especially the respiratory system.

It is rather generally considered that particles of silica are solely responsible for silicosis of the lungs. However, Jones advanced the view that seracite, a hydrous silicate of aluminum and potassium, is responsible and bases his contention on the results of the analyses of rocks whose dust have caused silicosis and the high content of seracite in the lungs of three individuals who had died as a result of extensive fibrosis of the lungs.

The development of the silicotic nodule has been followed in the lung after the inhalation of dust containing silica and also has been studied in the subcutaneous tissue following the injection of a suspension of particles of silica. Excellent descriptions of this process have been given by Lemon and Higgins and also by Benecke. The mononuclear cells phagocytize the particles of silica and pass back into the lung tissue. A primary exudative reaction of polymorphonuclear cells occurs and this is

succeeded in thirty-six hours by a marked mononuclear cell reaction. A proliferation of fibroblasts is next observed. The nodule either advances to a stage of encapsulation or else the particles of silica are disintegrated and there would then result a return of the involved tissues to their approximate normal state. Mills was able to demonstrate a partial disintegration of the spicules of a sponge which had been injected into animals. These spicules are composed largely of silica and excited the typical proliferation of fibroblasts.

Injection of a fine suspension of silica into the subcutaneous tissue or muscle of the thigh in dogs leads to the development of an indurated area at the site of the injection. Subsequently, histologic evidence of a rather extensive fibrosis can be demonstrated and similar changes are present in the iliac lymph nodes, which is evidence of the transport of particles of silica through the lymphatic vessels. No changes are demonstrated in the internal organs. Cummings and Sladden showed that particles of silica passed through the lymphatic channels from the hilus of the lung to the lymph nodes beneath the diaphragm. Gardner and Cummings investigated the fate of particles of silica of different sizes which had been injected intravenously. The large particles, 6 to 12 micra, were screened out by the lungs, the intermediate sizes were largely deposited in the spleen, and the smallest, one micra, were found in the liver. This latter organ gave the picture of a coarse nodular cirrhosis. A proliferation of fibrous tissue was noted in the spleen,

and many cells, indistinguishable from Langhan's giant cell of tuberculosis were present. The kidneys were not involved.

The regular ingestion of 200 mesh diatomaceous earth by five adult males for more than a year has not lead to any untoward sequelae. Oral administration of 40 grams of this material was found to increase the urinary output of silica only 2 milligrams. The presence of the silica in the alkaline medium of the small intestine would lead to the formation of a minute quantity of colloidal silicic acid, a portion of which is then resorbed.

Bibliography

Arnold: Cited by Borchardt.

Benecke, E.: Uber die Reaktion des Unterhaut - und Bauchfellbindegewebes auf die Zufuhr silizium haltigem Gesteinstaube. Beitrage z. Path. Anat. u. z. Allg. Path. 91:503, 1933.

Borchardt, H.: Ueber die Einatmung verschiedener Kohlenstaubarten. Virch. Arch. f. path. Anat. 271:366, 1929.

Bohme, A.: Chemische Untersuchungen an pneumonokoniotischen Bergarbeiterlungen. Klin. Wchnschr. 1909, 1924.

Chapman, E. M.: Acute silicosis, J.A.M.A. 98:1439, 1932.

Collis, E. L.: The influence of dust inhalation upon the incidence of phthisis. Public Health. 34:97, 1920-21.

Cummings, S. L. and Sladden, A. F.: Coal Miner's Lung. Jour. Path. and Bact. 33, 1095, 1930.

Gardner, L. U.: Studies on experimental pneumonokoniosis. VIII. Inhalation of quartz dust. Jour. Ind. Hyg. 14:18, 1932.

Gardner, L. U.; and Cummings, D. E.: The reaction to fine and medium-sized quartz and aluminum oxide particles. Silicotic cirrhosis of the liver. Amer. Jour. Path. 9:751, 1933.

Heffernan, P.: Some Notes on the biophysics of silica. Brit. Med. Jour. 2:489, 1929.

Jones, W. R.: Silicotic lungs: the minerals they contain. Jour. Hyg. 33:307, 1933.

Kettle, E. H.: Experimental silicosis. Jour. Ind. Hyg. 8:491, 1926.

Lemon, W. S.; and Higgins, G. M.: The development of the pulmonary silicotic nodule in the experimental animal. Am. Rev. of Tuberc. 28:470, 1933.

Mavrogardato, A.: Experiments on the effects of dusts and inhalations. Jour. Hyg. 17:439, 1918.

Mills, R. G.: The effect of prolonged exposure of the siliceous spicules of a fresh water sponge (Spongilla Fragilis) to the action of animal tissues. Amer. Jour. Hyg. 13:224, 1931.

Moir, J.: Report on a specimen of dust from a silicotic lung. General report of the miners phthisis prevention committee. Pretoria. Appendix 9, page 138. 1916.

Moore, B.: The incidence of industrial tuberculosis. Proc. Royal Soc. Med. 11:145, 1918.

Nicholson, B. S.: The dust lung with special reference to the inhalation of silica dust and its relation to pulmonary tuberculosis. Jour. Ind. Hyg. 5:220, 1923-24.

Peissachowitsch, I. M.; and Gottlieb, E. S.: Die Pathologie des Staubes. Virch. Arch. f. Path. Anat. 279:295 and 315, 1930.

Sladden, A. F.: The silica content of lungs. Lancet. 2:123, 1933.

IV
Physiologic Effects of Silicic Acid ($Si(OH)_4$)

The intravenous injection of a small quantity of freshly prepared colloidal silicic acid acts as a violent poison. Kramer noted the immediate death of a dog weighing 4.5 kg. after the injection of 70 mgs. Similarly, a 1400 gram rabbit was killed by 28 mgs. The toxicity of the solution decreases as it ages and gelation appears. Also, larger quantities of a more dilute solution are required to kill. Autopsy reveals the right heart and pulmonary vessels to be filled with a clot. Gye and Purdy believed the endothelial lining of the blood vessels are principally affected by colloidal silica. However, they found this material had no influence on the extravascular clotting of blood.

Gye and Purdy gave daily intravenous injections of 5 mgs. of freshly prepared colloidal silica to rabbits and produced a fibrosis of the liver, an enlargement of the spleen, and changes in the kidneys resembling interstitial nephritis. Apparently, particles of silica formed after the gelation of the colloidal silicic acid by the serum were engulfed by the phagocytes of the affected organs and then provoked the connective tissue proliferation.

Zuckmayer injected colloidal silicic acid (0.005 to 0.01 gm.) subcutaneously and intramuscularly in humans and dogs. There resulted an elevation of temperature after a few hours to 40.5°C and above.

This elevation would be maintained for five to fifteen hours and would then return to normal. The height and duration of the elevation of temperature were dependent on the quantity of silicic acid which had been injected. The colloidal solutions near gelation had no effect. The simultaneous injection of a calcium salt along with silicic acid caused a marked lessening of the severity of the reaction, apparently the result of an immediate gelation of the silicic acid.

No toxic sequelae are observed following the oral administration of colloidal silicic acid. Gye and Purdy fed this material to rats, mice, guinea pigs and monkeys in large quantities over as long a period as a year and found no pathologic changes in the internal organs. Bruhns believed silicic acid administered by mouth had a decided anthelmintic effect. Colloidal silicic acid is readily resorbed from the gastro-intestinal tract in contrast to the barely appreciable quantity of diatomaceous earth which is taken up. The composite chart (Fig. 1) illustrates the great extent of the resorption of colloidal silicic acid and the immediate excretion of the excess which has gained entry into the body. Kochmann and Maier did not demonstrate an increased growth in rats kept on a diet rich in silica. However, the amount of silica in their bodies was increased. Excised portions of skin of mice showed a greater elasticity provided the animals had received an injection of 2.5 mgs. of colloidal silica from eight to eighteen days prior to the test.

A piece of skin left in Ringer's solution to which a small quantity of colloidal silicic acid had been added was more elastic than one left in plain Ringer's solution.

Liebermann noted the agglutination of washed red blood corpuscles by silicic acid and found agglutination was always accompanied by hemolysis and the latter increased with the quantity of silicic acid up to a certain optimum. Beyond this point an increase of the silicic acid caused a precipitation of the hemoglobin. Cummins believes a gel is formed in the serum of whole blood on the addition of silicic acid and this prevents agglutination. Bechold believed lecithin linked the silicic acid and red blood corpuscles and brought about agglutination. Hirschfeld found the ability of silicic acid to precipitate red blood corpuscles was shared by many of the salts of the heavy metals and this property was dependent on the cations and was independent of the anions. Kramer referred to the precipitation of a suspension of washed sheep red blood cells on the addition of a minute quantity of silicic acid to a strength of one part in 500,000. The prior addition of a solution of one percent peptone in physiologic salt solution prevented the agglutination and precipitation. However, the addition of still greater quantities of colloidal silicic acid overcame the influence of the peptone solution.

Kramer found the addition of colloidal silicic acid in the ration of 1 to 10,000 to a young broth culture of colon bacilli would cause a prompt agglutination and precipitation of the bacilli.

This does not occur if the culture is several days old and neither will a suspension of young colon bacilli suspended in physiologic salt solution be affected.

Colloidal silica was found by Cummins to interfere with the bactericidal quality of blood in a marked degree. Cummins and Weatherall showed that the addition of silicic acid preserved typhoid bacilli from lysis in human blood or serum. Similarly, type I pneumococci did not undergo lysis in ox bile to which colloidal silicic acid had been added. The peptic and tryptic digestion of albuminous substances were inhibited by silicic acid. The serological properties of colloidal silica as recorded by Nathan are quite extensive and their true significance and practical application remain uncertain.

Bechold, H.: Colloids in Biology and Medicine.
Translated by J. G. M. Bullowa, 1919.

Bruhns. Cited by Kuhn.

Cummins, S. L.: The anti-bactericidal properties of colloidal silica.
Brit. Jour. Exp. Path. 3:237, 1922.

Cummins, S. L. and Weatherall, C.: The retardation of lytic processes by colloidal silica.
Brit. Jour. Exp. Path. 12:239, 1931.

Gye, W. E., and Purdy, W. J.: The poisonous properties of colloidal silica.
I. The effects of the parenteral administration of large doses. Brit. Jour. Exp. Path. 3:75, 1922.
II. The effects of repeated intravenous injections on rabbits - fibrosis of the liver. Ibid. 3:86, 1922.
III. The poisonous properties of colloidal silica.
Ibid. 5:238, 1924.

Hirschfeld, L.: Untersuchungen uber die Hemagglutination und ihre physikalischen Grundlagen. Arch. f. Hyg. 63:237, 1907.

Kochmann, and Maier, L.: Beitrage zur Biochemie der Kieselsaure.
I. Einfluss der Kieselsaure auf das Korpergewicht wachsenden Ratten. Biochem. Ztschr. 223:228, 1930.
II. Retention der Kieselsaure im Organismus der Ratten.
Ibid. 223; 231, 1930.
III. Einfluss der Kieselsaure auf die Elastizitat des Bindegewebe. Ibid. 223:243, 1930.

Kramer, S. P.: The colloidal solutions of silicic acid.
N. Y. Med. Jour. 103:680, 1916.

Liebermann, L. and P.: Ueber die Wirkung von Kieselsaure auf rote Blutkorperchen. Arch. f. Hyg. 62:297, 1907.

Nathan, E.: Ueber die Wirkung kolloidaler Kieselsaure auf die roten Blutkorperchen. Ztschr. f. Immunitatsforsch.
19:216, 1913.

Zuckmayer, F.: Ueber die Ausscheidung der Kieselsäure durch den Harn nach Eingabe verschiedener Kieselsäurepräparate.
Ther. d. Gegenw. 61:344, 1920.
Ueber parenteral Kieselsäurezufuhr.
Ibid. 62:376, 1921.

V

Radiation and the Silicates

Herrera in his interesting speculations on the origin of life referred prominently to the influence of radium emanations in the production of colloidal silica and its significance in plasmageny or the origin of life.

No study has been devoted to the effect of radiations of different types on the silicon which is contained in the body. No in vivo experiments have been recorded. These seem to be warranted in view of the enormous physiologic activity possessed by minute quantities of colloidal silica. Possibly, the favorable effect observed after radiation of tumors may in some way be related to the chemical transformation of the silicates contained in the tissues.

Sosman gives an excellent review of the effects on the silicates of the different types of radiation. "Vitreous silica shows a faint green fluoresence under the direct action of x-rays, the light ceasing when the x-rays are cut off. It is succeeded by an actinic phosphoresence, invisible, but capable of acting on a photographic plate and this persists for three to four weeks. It can be destroyed by heating the glass to redness for two minutes. (page 758)". Again, "Pyro-luminesence is a phenonomen exhibited by many specimens of natural quartz. It consists in the production of light when the specimen is heated to a temperature about 150°C. This natural phosphoresence is not reproducible, lasting only a few seconds, and not returning on subsequent heating.

The power of pyro-luminesence is restored to the quartz only by exposure to the radiations from radium. Sunlight, the electric spark, the electric arc and x-rays are all without effect in restoring it. (page 761)". Also, "when placed in contact with a burning jet of hydrogen, certain substances including silica in some of its forms, emit a visible radiation, called flame luminesence, which is very different from the radiation due to temperature alone". Doelter mentioned the production of colloidal silica following the radiation of silica with radium. The colorless quartz becomes smoky and the discoloration penetrates to a depth of one centimeter following the exposure of colorless quartz to the emanations of radium for a period of seven days (Mellor, page 130). The radio-activity of native quartz is ascribed to the inclusion of radium, uranium, helium or argon. Quartz does not become luminescent after exposure to radium. However, it does become brittle. Doelter and Sick found colorless rock crystal was colored brown after exposure to radium or X-rays and this was due to the action of the gamma and beta rays. The color is removed by exposure to ultra-violet rays or by heating to 200°C. Other workers found quartz was made pleochroic by the emanations of radium.

Bibliography

Doelter: Cited by Mellor.

Doelter, and Sick: Cited by Mellor.

Herrera, A. L.: Plasmogeny. Alexander's Colloid Chemistry. Vol. II, page 82 and 87.

Mellor, J. W.: A Comprehensive Treatise on Inorganic and Theoretical Chemistry. Vol. VI.

Sosman, R. B.: The Properties of Silica. 1927.

VI

History of Silicon in Medicine

Cohn and Siegfried have traced the use of silicon in medicine to the period of the ancient Greeks and Romans. The ash of siliceous concretions, tabasheer, found in the nodes of certain bamboos, is almost pure silicon dioxide and was prized as a tonic. Also, it had extensive use in dyssentery, jaundice, lung diseases and leprosy. According to Schulz, Avicenna and Gerardus von Cremona advocated the use of tabasheer. Paracelsus recommended sodium silicate in several diseased conditions. Socquet (1858) advised sodium silicate by mouth in gout, rheumatism and neuralgia. Dubreuil (1872) irrigated the bladder with a weak solution of sodium silicate in patients with a severe cystitis and obtained good results. Pirot (1872) used the same preparation per os in diabetes mellitus. Rabuteau and Papillon (1872) and Löwenhaupt (1889) found that sodium silicate inhibited putrefaction and fermentation.

The osteopaths have made extensive use of preparations containing silicon and number them among their sovereign remedies. These preparations are reported to be particularly efficacious in gastric disturbances, wart growths, blood tumors, tuberculosis and all inflammatory processes. Sodium silicate and powdered silica are the compounds usually prescribed (Kent, Pierce, and Pharm. Instit. Homeo.) Historical reference in greater detail is made under the separate diseased conditions which are discussed.

Bibliography

Cohn, F.: Ueber Tabaschir.
Beitr. z. Bio. der Pflanzen. 4:365, 1887.

Kent, J. T.: Materia Medica. Third edition, page 890, 1923.

Pharmacopeia of the Amer. Institute of Homeopathy. Page 522, 1897.

Pierce, W. I.: Plain Talks on Materia Medica. Page 726, 1911.

Schulz, H.: Ueber den Kieselsäuregehalt menschlichen und thierischer Gewebe.
Pfluger's Arch. ges. Physiol. 84: 67, 1901.

Siegfried, A.: Ein Beitrag zur Kenntnis der Physiologischchemischen und Pharmakologischen Verhaltens des Kieselsauren Natrium, etc.
Arch. Internat. de Pharmacodynamie et de Therapie.
9: 225, 1901.

VII

The Role of Silicon in Tuberculosis (With a Study of the Excretion of Silicon in the Urine of Tuberculous Patients)

Preparations containing silicon have been used for centuries in the treatment of the many manifestations of tuberculous infections. The folk remedies for tuberculosis were herbs whose ash is extremely rich in silicon dioxide (J.A.M.A.). Recent years have witnessed a revival in this mode of therapy and many attempts have been made to establish a rational basis for its use. The evidence is not conclusive but is suggestive of possibilities for therapeutic use and also for a more thorough understanding of the healing process in tuberculosis.

The imprisonment of silicon is said to be responsible for the relatively large amount of this element found on examination of tuberculous lymph nodes. The analysis of Kahle revealed the silicon dioxide content of a normal lymph node to be 0.14 gm. per kilo of the dried substance, while that of the calcareous lymph node of a child and of an ox were found to be 1.6 and 1.54 gm. per kilo respectively. Zickgraf found the ash of calcified bronchial lymph nodes to contain from 5 to 12 per cent silica. However, Maver and Wells reported no silica in a calcified mesenteric lymph node and believed silicon played no role in the healing of tuberculosis. Gerhartz and Stiegel did not always find silica in calcified bronchial lymph nodes. Kraut has found the average silicon dioxide content of the ash of normal blood to be 1.75 per cent while the average was 1.99 in 55 tuberculous patients.

Kramer believes the tubercle bacillus is similar to many plants in its tendency to extract silicon from its environment. The studies of de Schweinitz and Dorset showed the ash of tubercle bacilli to contain 0.57 per cent silica. Kramer draws an interesting analogy between the changes which can be produced by chemical means in an oil emulsion of silicic acid and the processes which accompany the growth of the tubercle bacillus in the body. A permanent oil emulsion is formed by the addition of a minute quantity of sodium silicate to olive oil. This is said to represent fatty degeneration. The addition of lime water will cause this emulsion to "caseate" and the bubbling of carbon dioxide through this caseous mass will induce a further change. According to his concept fatty degeneration represents the effect of large quantities of free silicic acid, liberated by the growth of the tubercle bacilli, on the surrounding tissues. Caseation results from the deposition of lime in this focus, and calcification follows the breakdown of the calcium silicate to form calcium carbonate, under the influence of carbon dioxide.

Schulz reports the connective tissues to be extremely rich in silica, while McNally describes the lungs of tuberculous subjects as containing somewhat more silicon dioxide than those of normal persons. Kahle ascribes the exacerbation of pulmonary tuberculosis in pregnancy to the demands made by the fetus for a bountiful supply of silicon. This would extract silicon from the tissues and thus lead to a weakening of the wall of fibrous tissue which serves to keep the

tuberculous focus in check. Robin thinks silica is withdrawn principally from the bones in pulmonary tuberculosis.

The influence of silicon on the growth of the tubercle bacillus in the body is obscured by conflicting reports. Kettle found a greater growth of tubercle bacilli in abscesses produced by the injection of silica sol than in those caused by the injection of turpentine or calcium chloride. Moreover, he found that a much greater growth of the organisms was found at the site of the injection if a suspension of silicon dioxide were injected subcutaneously and subsequently tubercle bacilli were injected intravenously. Cummins and Weatherall observed a greater local reaction following the experimental inoculation of silica sol and tubercle bacilli, without, however, an earlier or a more general dissemination. They did not find that the addition of silica sol to human blood influenced the growth of the tubercle bacillus in this media outside the body. Price has reported that the addition of a minute quantity of sodium silicate to a modified Dorset's egg medium will stimulate the growth of the tubercle bacillus. Gardner showed that the inhalation of quartz dust would cause a reactivation of experimental pulmonary tuberculosis in guinea pigs. Kahle fed guinea pigs affected by tuberculosis an organic silicon preparation and these animals showed a much greater connective tissue proliferation than the controls. An instructive example of the influence of silicon on tuberculosis of pigs has been reported by Kobert. Pigs fed on roots which contained only minute

quantities of silicon were found to suffer severely from tuberculosis, while the addition of mineral powders containing silicon to their diets served to eradicate the disease.

The evidence leads one to believe the apparent beneficial influence which silicon may exert in some instances on a tuberculous infection results from the stimulation of connective tissue proliferation, and not from any effect on the tubercle bacillus per se. Kessler observed an enormous connective tissue proliferation in a suicide suffering from pulmonary tuberculosis, who had been treated by the oral administration of large quantities of a preparation containing silicon. Roth also reports autopsy findings to support the above view. Kobert believes the ingestion of silicates induces a hyperaemia in the involved area and also promotes the formation of connective tissue.

The many clinical reports on the use of silicon in tuberculosis are for the most part enthusiastic. Kuhn observed favorable results using an infusion prepared from the herbs, Caleopsis, Equisetum and Polygonum. The silicates contained therein are in the form of alkaline silicates. Junker reports untoward complications arising from the alkaloid content of these infusions and from the alkalies liberated in the gastro-intestinal tract. Bauer recommended a concentrated infusion of Equisetum and believed it promoted the formation of fibrous connective tissue. Ladendorf gave tuberculous patients mineral water containing large quantities of silica and noted clinical improvement.

Due to the great variations in the amount of silicon contained in the herbs and, also, the uncertainty of its resorption

from the gastro-intestinal tract, attempts have been made to substitute other more suitable preparations. Sodium silicate has been used extensively by the homeopaths in the treatment of tuberculosis (Zimmer). Various organic preparations said to contain silica in its active form as silicic acid have been used. Helwig employed "Silternum", and was struck by the manner in which it brought the disease to a standstill even in cases with bacilli in the sputum and cavities already existent. Klare and Budde, and Zeller have reported excellent results in the more proliferating forms of pulmonary tuberculosis in children after the use of "Silistren", the orthotetraglycolic ester of silicic acid. Junker recommends the oral administration of a preparation, "silcasin", consisting of 96 per cent casein and 4 per cent sodium meta silicate. Zimmer advises intravenous and intramuscular injections of suitable preparations containing silicon and has also seen good results following oral administration. Forster also recommends several proprietary drugs containing silicon in the treatment of pulmonary tuberculosis. Scheffler, Sartory and Pellissier gave repeated courses of intravenous injections of sodium silicate (2 c.c. of a 0.5% sol.) for ten injections every day for the same disease. Stein observed clinical improvement and a striking deposition of calcium in the hilus lymph nodes of children after the oral administration of a proprietary drug containing iron, calcium and silicon. Helbach used "silcasin" in the treatment of fifteen children with active pulmonary tuberculosis and noted excellent results. Rosenstingl and

Salomon recommended a proprietary preparation containing silicon in pulmonary tuberculosis on the basis of their clinical experience. Freund obtained remarkable clinical results with "silistren."

Thoma reported definite exacerbations of pulmonary tuberculosis in patients treated by intravenous injections of a solution of colloidal silicic acid, "siliquid," containing 0.3 per cent silicon dioxide. Frank treated 71 cases of tuberculosis in children involving different regions of the body with "teas" and others with "silistren," but could observe no improvement. He was unable to note any favorable effect on experimental tuberculosis of guinea pigs treated with a silicon preparation.

The relation of silicosis to tuberculosis has been the subject of numerous reports. The incidence of tuberculosis in association with silicosis is often given as 20 to 30 percent. Hayhurst et als, examined 912 workers in a sandstone quarry and found evidence of silicosis in 28.5 per cent and tuberculosis in 1.9 per cent. Five per cent of those with silicosis had an associated pulmonary tuberculosis. Moore reports a higher incidence of tuberculosis among workers exposed to silica dust than in coal miners and Hoffman found the death rate from phthisis to be uniformly low in coal miners. Hackman analyzed the lungs of 37 miners for the silica content and could find no relation between the quantity present and an accompanying tuberculous infection. Greenburg determined a close correlation between the mortality rate from tuberculosis and the quantity of silica inhaled by industrial workers. Selkirk found the incidence of

tuberculosis among lime workers to be relatively low. Thus the evidence shows that an excess of silica in the lung tissue does not decrease the incidence of pulmonary tuberculosis. Probably those afflicted with silicosis are more liable to contract tuberculosis as the damaged tissue hinders the reparative process.

Excretion of Silicon in the Urine

No quantitative determinations of silica in the urine of tuberculous subjects have been reported. Such analyses might show the retention of this substance in the body and would make probable its use in connective tissue for the encapsulation of the diseased focus. The metabolism of silicon is but poorly understood. The factors which influence its absorption from the gastro-intestinal tract and its elimination through the kidney, and possibly, the large intestine, are not clear. The output of silica in the urine of an adult on the usual refined diet was found to range from 15 to 20 mgm. per day by King, Stantial and Dolan. A low value for its excretion in the urine might signify either a poor resorption of this substance from the gastro-intestinal tract or its retention within the body. Silica has been demonstrated in the ash of all animal tissues and has usually been considered an accidental contaminant.

Determinations of the content of silica in the urine were made in three groups of patients: (1) those with active pulmonary tuberculosis, (2) those with tuberculosis of bone, and (3) convalescent patients with no evidence of a tuberculous infection. All these

patients were taking the regular ward diet, with extra nourishment for those with tuberculosis. The colorimetric method described by King and Stantial was employed in these determinations. The urine samples were collected in paraffin-lined flasks.

The mean silica content of 68 twenty-four-hour samples of the urine of eighteen patients with active pulmonary tuberculosis was 9.15 ± 0.32 in contrast with the mean value of 11.48 ± 0.24 mgm. yielded by 142 similar samples from 9 patients with tuberculosis of the bone. The mean 24 hour urinary excretion of 16 patients with no evidence of a recent tuberculous infection was 15.92 ± 0.25 mgm. as determined from the analysis of 153 samples. A further study of the results on 51 samples from three of the patients with tuberculosis of bone, whose lesions were clinically quiescent, revealed a mean excretion of 13.35 ± 0.46 mgm., while the mean of the findings on 42 samples from three patients with quite active bone lesions, was 9.05 ± 0.30 mgm.

CONCLUSIONS

The comparison of these mean values, taking into account their respective probable errors, demonstrate the following:

(1) The daily urinary output of silica by convalescent non-tuberculous patients was significantly higher than that of patients with either pulmonary tuberculosis or tuberculosis of bone.

(2) The daily urinary output of silica on the part of patients with active tuberculosis of bone did not differ significantly from that

of patients suffering from active pulmonary tuberculosis.

(3) A significant and progressive decrease in the magnitude of urinary silica excretion was demonstrated by groups of patients representing respectively, quiescent, moderately active, and rapidly progressive tuberculosis of bone.

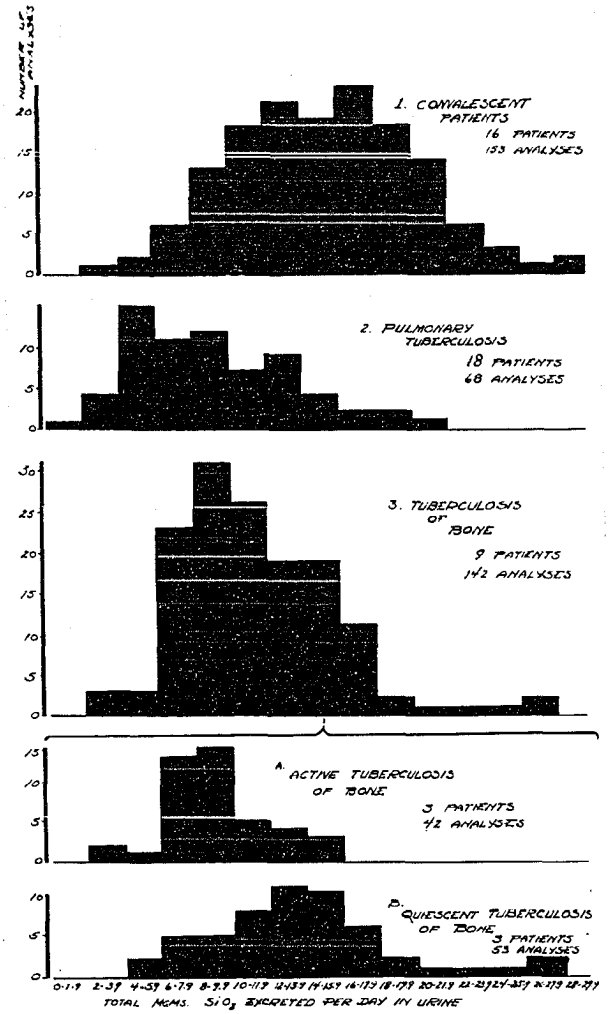

Fig. 1. Excretion of silicon dioxide in urine.

Bibliography

Cummins, S. L., and Weatherall, C.: Effects of Colloidal Silica Upon the Growth of Tubercle Bacilli in Blood. Brit. Jour. Exp. Path., XII, 245, 1931.

Cummins, S. L., and Weatherall, C.: The Effects of Colloidal Silica on Experimental Tuberculosis in Guinea Pigs. Hyg., XXXIII, 295, 1933.

Forster, J.: Die Kieselsauretherapie die Lungentuberkulose. Tuberkulose, 9:118, 1929.

Frank, A.: Klinische und experimentelle Beiträge zur Frage der Kieselsäuretherapie bei Tuberkulose. Beitr. z. klin. d. Tuberk. 55:470, 1923.

Freund, A.: Zur Kieselsäure behandlung der Lungen tuberkulose. Ther. de Gegenw. 65:107, 1924.

Gardner, L. U.: Reactivation of Healing Primary Tubercles in Lung by Inhalation of Silica, etc. Amer. Rev. Tuberc., XX, 833, 1929.

Gerhartz, H., and Stiegel: Uber Lungensteine und Kieselsaurebehandlung. Brauers Beitr. 3. Klin. d. Tuberk. 10:33, 1908.

Greenburg, L.: Dust, Fumes and Smoke and Their Relation to Health. Alexander's Colloid Chemistry. Vol. I, p. 865.

Hackmann, C.: Über den Kieselsäuregehalt pneumokoniotischen Lungen. Geitr. z. Path. Anat. u. z. Allg. Path. 90:623, 1933.

Hayhurst, E. R., and Kindel, D. J., Neiswander, B. E., and Bennett, C. D.: Silicosis with Low Incidence of Tuberculosis. J. Indust. Hyg., 11:228, 1929.

Helwig: Die Bedeutung der Kieselsäure für Phagocytose und Wundherlung. Ztschr. f. Balneol. 7 Jahrg. 303, 1914.

Helbach, H.: Das Silcasin in der Behandlung der offenen Kindertuberkulose. Ztschr. f. Tuberk. 49:33, 1927.

Hoffman, F. L.: Mortality from Respiratory Diseases in Dusty Trades. U. S. Bur. Labor Statistics. Bull. 231, Wash., D. C., 1918.

Editorial: Does Silicon Have a Physiologic Significance.
J.A.M.A., 73:1770, 1919.

Junker, F.: Kieselsäurebehandlung der Lungentuberkulose mit Silcasin.
Med. Klin. 23:21, 1927.

Kahle, H.: Einiges über den Kieselsäurestoffwechsel bei Krebs und Tuberkulose und Seine Bedentung für die Therapie der Tuberkulose.
München Med. Wchnschr. 61:752, 1914.

Kessler, A.: Zur Frage der Kieselsäuretherapie bei Lungentuberkulose.
Deutsche med. Wchnschr., 46:239, 1920.

Kettle, E. H.: The Demonstration by the Fixation Abscess of the Influence of Silica in Determining B. Tuberculosis Infection.
Brit. J. of Exp. Path. 5:158, 1924.

Kettle, E. H.: Experimental Silicosis.
J. of Indust. Hyg. 8:491, 1926.

King, E. J., and Stantial, H.: Micro-determination of Silica.
Biochemical. J. 27:990, 1933.

King, Stantial and Dolan, M.: Presences of Silica in Tissues.
Ibid. 27, 1002, 1933.

Klare, K. and Budde, O.: Zur Kieselsäuretherapie Der Kindlichen Tuberkulose.
München Med. Wchnschr. 69:741, 1922.

Kobert: Cited by Zimmer.

Kramer, S. P.: Uber die Herstellung von Oelemulsionen mit Hilfe Kolloider Kieselsäure und deren Beziehungen zu Tuberkulösen Processen.
Kolloid Ztschr. 31:149, 1922.

Kraut, H.: Über den Kieselsäuregehalt des menschlichen Blutes und seine Veränderung durch Kieselsäurezufuhr.
Ztschr. f. Physiol. Chem., 194:81, 1931.

Kühn, A.: Zur Behandlung der Lungentuberkulose mit Kieselsäure.
Munch. Med. Wchnschr. 65:1459, 1918.

Ladendorff: Über Änderungen des Blutdruckes bei Lungentuberkulösen. Ztschr. f. Belneol. 5:159, 1912.

Maver, M. E., and Wells, H. G.: The Chemical Composition of Calcified Tuberculous Lesions. Am. Rev. Tuberc., 6:649, 1922.

Moore, B.: The Incidence of Industrial Tuberculosis. Proc. R. Soc. Med., 11:145, 1918.

McNally, W. D.: Silicon Dioxide Content of Lungs in Health and Disease. J.A.M.A., 101:584, 1933.

Price, R. M.: Effect of Silica on Growth of Tubercle Bacillus. Proc. Soc. Exp. Biol. and Med., 28:819, 1931.

Rosenstingl, A.: Zur Bewertung der Kieselsäurezufuhr in der Phthiseotherapie. Beitr. z. Klin. Tuberk., 73:110, 1929.

Rössle, R.: Zur Siliziumbehandlung der Tuberkulose. München Med. Wchnschr., 61:756, 1914.

Roth, M.: Zur Frage der Kieselsaürebehandlung bei Lungentuberkulose. Ther. d. Gegenw. 62:369, 1921.

Scheffler, L., Sartory, A., and Pellissier, O.: Les Injections Intraveineuses de silicate de soude. Presse Méd., 28:806, 1920.

Selkirk, W. J. B.: Tuberculosis in Limeworkers. Brit. Med. Jour., 2:1493, 1908.

Schulz, H.: Über den Kieselsäuregahalt menschlichen und thierischer Gewebe. Pfluger's Arch Ges. Physiol. 84:67, 1901.

de Schweinitz, E. A., and Dorset, M.: The Mineral Constituents of the Tubercle Bacillus. Centralblatt f. Bacteriologie, 23:993, 1898.

Salomon, P.: Beitrag zur Kieselsauretherapie. Zertzl. Rundschau., 37:212, 1927.

Stein, W.: Zur Kieselsäuretherapie der Bronchialdrüsentuberkulose. Ztschr. f. Tuberk., 51:377, 1928.

Thoma, E.: Experimentelle und klinische Beobachtungen zur Kieselsauretherapie bei Akuten und Chronischen Infektionskrangheiten. München Med. Wchnschr., 69:1603, 1922.

Zeller, H.: Erfahrungen mit Silistren. Ther. d. Gegenw., 63:38, 1922.

Zimmer, G.: Silicum als Reizmittel. München Med. Wchnschr., 70:233, 1923.

Zickgraf. Ueber die therapeutische Verwendung des Kieselsäure an der Bildung von Lungenstein. Beitr. z. Klin. d. Tuberk., 5:399, 1906.

VIII

SILICON DIOXIDE IN THE TREATMENT OF PEPTIC AND MARGINAL ULCERS.*

"Fine river sand" has long been used as a folk remedy in the treatment of "ulcers of the stomach" among the mountaineers of the state of Virginia. The use of finely powdered silica or sand for this same diseased condition in the era of the Civil War was reported by Kent. Sodium silicate and powdered silica have also been employed as a homeopathic remedy in all gastric disturbances. However, this mode of therapy has not been subjected to a critical study and no attempt has been made to explain its rationale.

Our interest in silicon dioxide was prompted by an account of a most interesting case seen in the general practice of Doctor W. T. Chitwood, of Rocky Mount, Va. His patient, residing in the Blue Ridge mountains of the southwestern portion of the state of Virginia was treated for an ulcer near the pylorus. All the classical signs and symptoms of an active ulceration, including roentgenologic confirmation, were present. A Sippy regime was instituted and faithfully tried with no relief. In desperation the patient resorted to the folk remedy, namely, the ingestion of "fine river sand". This was followed by a prompt improvement and a rapid gain in weight and strength.

An analysis of the effect of finely powdered sand or diatomaceous earth must take into consideration its adsorptive capacity. This is best exemplified in its ability to remove the last trace of protein from urine

*From the Department of Surgery and the Kettering Laboratory of Applied Physiology, of the College of Medicine, University of Cincinnati.

(Bechold). Unna ascribed a beneficial effect following the use of finely powdered diatomaceous earth on chronic leg ulcers and decubitus ulcers to a mechanical cleansing and adsorption of the products of the wound secretion. He also observed an increased proliferation of granulation tissue lining the base of the ulcers. In this regard it is well to consider the specific local stimulation of the amoeboid activity of the phagocytes of the lung following the inhalation and deposition of silica particles in the lung tissue (Gardner). Other types of dusts as coal, marble, and carborundum fail to excite any unusual activity of the phagocytes. Doubtless, a similar process may be re-enacted in peptic and marginal ulcers following the ingestion of a fine suspension of silica or diatomaceous earth.

Adsorption of the products of wound secretion and the local stimulation of the silica particles on the ulcer itself are the more likely effects exerted by silica, if a truly beneficial effect is exerted at all. This explanation is substantiated by a study of the total daily excretion of silica in the urine before and after the daily ingestion of known quantities of silicious material in which the colorimetric method described by King and Stantial was employed. The normal silica excretion was found to average 14.2 mgs. in the group of six patients chosen for this study. The output was only increased to 16 mgs. after the daily ingestion of 40 grams of 200 mesh diatomaceous earth. No significant difference in the excretion could be observed between those patients with peptic ulcers and those with no gastric-intestinal complaints. This behavior of diatomaceous earth is in marked contrast to the great

absorption of a freshly prepared colloidal preparation of silicic acid given orally in 200 mgm. quantities for a period of three days. The results are shown in the composite chart of eight convalescent patients who had no evidence of any diseased condition of the gastro-intestinal tract. (Fig. 2) The slight absorption of powdered silica as well as the immediate excretion of any excess that may gain entrance into the body relieves one of the fear of any toxic sequelae as a result of its oral administration.

The choice of silicon-containing compounds for use in a clinical study of their effect on peptic ulcers offers some difficulties. The most highly adsorptive product would most likely be a colloidal silicic acid gel. Its great adsorptive power is illustrated by its use in gas masks for the extraction of ammonia from the atmosphere. It is not definitely known whether the long continued ingestion of silica gel would lead to toxic changes in the organs of the body. None could be demonstrated in the liver, spleen, intestinal tract and kidneys of dogs that were given 400 mgm. of colloidal silicic acid daily, over a period of three months. In fact, these dogs gained weight and appeared to be the healthiest of all the animals in the experimental surgical laboratory. The efficient anthelmintic properties of the silica sol is the likely explanation in view of the fact that no difference was observed between those animals given neutralized sodium silicate or those given colloidal silicic acid prepared by dialysis as a result of which all the ionized salts had been removed (Bruhns). Gye and Purdy could find no pathological changes in the internal organs of rats, mice, guinea pigs and monkeys following the oral administration of silica sol and gel. It is well to bear in mind

the occurrence of urinary calculi containing a high content of silica, in cattle whose diets are extremely rich in grasses containing much silica (Dammann). One should also consider Collis' report of a higher incidence of chronic nephritis among miners suffering with silicosis. He felt this to be due to the increased excretion of silica which gained entry into the body through the slow transofmration of the solid silica particles in the lungs to a soluble form under the influence of the alkaline medium of the body cells. However, no evidence of kidney damage could be found in the two patients of this series who had been taking diatomaceous earth over a period of nineteen and sixteen months, respectively. The first had an excretion of 40% and the second 65% in one hour of 6 mgm. of phenosulphonephthalein which had been injected intravenously. The repeated intravenous injection of colloidal silicic acid in minute doses leads to a fibrosis of the liver, spleen and kidneys as described by Gye and Purdy. The fibrosis probably resulted from the gelation of the colloidal silicic acid by the blood serum and the engulfment of the particles of silica thus formed by the reticulo-endothelial cells of the affected organs. Subsequently, the slow liberation of colloidal silicic acid, as in silicosis of the lung, induces the proliferation of connective tissue.

The chemical state of silicon as it is resorbed from the gastro-intestinal tract is not known. However, there is little likelihood that it is in a chemical state injurious to the body. Similarly, the compounds of silicon which must exist in the blood and tissues have not been identified.

No evidence of any adsorption of hydrochloric acid by diatomaceous earth could be obtained by a number of in-vitro analyses. Conversely, the gastric secretions should not modify the silica. The alkaline medium of the small intestines would lead to the formation of a minute quantity of colloidal silicic acid, a portion of which would then be resorbed.

It is interesting to recall that water glass, an aqueous solution of sodium, silicate, is commonly used as a preservative of eggs. Yet, among many primitive people, moist sand and even straw, the ash of which is rich in silica, serve the same purpose. (Kramer)

Many different proprietary preparations containing silicon have been recommended in the treatment of peptic ulcer and hyperchlorhydria. These drugs are said to liberate free silicic acid under the influence of the hydrochloric acid of the stomach and also bind hydrochloric acid as well as forming a protective coating over the ulcerations.

Prominent among these preparations is Neutralon ($Al_2Si_6O_{15}$) which has been recommended by Roesnheim and Ehrmann, Schlesinger, Friedrich and Cramer. Bismoterran has been found efficacious in the treatment of peptic ulcers and hyperchlorhydria by Vas, Kadletz, Willvonseder, and Brednow. No very extensive or convincing reports have appeared for any of these drugs.

An ample supply of 200 mesh diatomaceous earth, containing 99.14% silicon dioxide, was obtained through the courtesy of Mr. P. S. McDougall, President of the Ottawa Silica Company, of Ottawa, Illinois. This material

was administered orally, after being stirred with a small amount of water, in one teaspoonful quantities at 6 A. M., 10 A. M., 2 P. M., and 9 P. M., at the start of the treatments. The dosage was decreased as clinical improvement was noted, the extent of the reduction being left largely to the discretion of the patient. One precaution need be taken. The mouth should be thoroughly rinsed following each medication and water should be swallowed to remove any silica that might have adhered to the esophagus. Failure to exercise this precaution has lead in several instances to symptoms referable to a pharyngitis and an esophagitis which were quite distressing. Occasionally a patient complained of vague discomfort in the lower back and abdomen and in the extremities. A few noted a frequency of urination with slight burning. These symptoms disappeared with a decrease in the quantity of silica ingested.

Needless to say, the presence of a marked degree of obstruction would contra-indicate the use of silica. While no instance was observed of the production of a concretion in the stomach or along the gastro-intestinal tract, yet the tendency for finely powdered silica in a moist state to become packed into a rather firm mass should be borne in mind.

Little attention is paid to the diets. A bland or soft diet was usually prescribed at the beginning of treatment to be amplified at the discretion of the patient with the improvement of symptoms.

Report of Cases.

The histories of fourteen patients treated with diatomaceous earth for peptic or marginal ulcer are abstracted. Three cases not included in this report lacked evidence of a definite ulceration and the clinical

picture was further obscured by diseased conditions of other organ systems which had no relation to the gastro-intestinal tract.

Case I, #10717. J. S., white male; age 47, was first admitted to this hospital in September, 1931, and a posterior gastro-enterostomy was required for an ulcer with obstruction at the pylorus. He was followed in the Out-Patient Clinic and symptoms of a marginal ulcer were noted in September 1932. A gastric analysis, in October, following an Ewald test meal revealed a free hydrochloric acid of 74 and a total acidity of 80. Despite a strict medical regime a perforation of a marginal ulcer on the posterior line of the anastomosis occurred in March, 1933, and was closed with considerable difficulty. His convalescence was uneventful. Constant severe burning in his mid-epigastrium and tarry stools were responsible for his re-admission to the hospital in August 1933. Roentgenograms failed to reveal any evidence of an inflammatory process in either the afferent or efferent loops of the gastro-enterostomy. No improvement was noted after eighteen days on a strict Sippy regime. Treatment with diatomaceous earth and a bland diet was then instituted. Alkalies were omitted. A complete symptomatic relief was obtained in a week and he was discharged to the Out-Patient Clinic. Diatomaceous earth was discontinued in November, 1933, and a partial return of the burning sensation in the epigastrium together with cramp-like pain occurred in February, 1934. Silica and belladonna gave relief. The dosage of silica was gradually lessened to one teaspoonful every second day and a diet suitable to his state of complete adentia was advised. He felt quite comfortable and only occasionally experienced epigastric distress. No silica was available for this patient in August 1934, and there followed a marked recurrence

of his epigastric distress which rapidly disappeared when he was again given silica. His condition remained satisfactory until December, 1934, and then burning in his epigastrium became quite severe. Roentgenograms failed to reveal any definite marginal ulceration. The stomach was rather contracted and the rugal patterns distorted. The Staff of the Medical Service felt that his symptoms warranted another Sippy regime. This only made his symptoms worse and tarry stools reappeared. Silica was resorted to and a gratifying response was obtained. Fortunately, artificial dentures were finally procured following which a mild transient epigastric distress has been noted at irregular intervals. He continues to take a teaspoonful of diatomaceous earth every second day. His weight has remained practically unchanged, being 120 pounds in August, 1933, and 125 pounds in April, 1935.

Case II, #13802. G. N.; white male, age 50, had a posterior gastro-enterostomy performed in 1919 for the relief of a duodenal ulcer which had not been amenable to medical therapy. A return of epigastric burning and distress after meals occurred in 1930 and he then began attending the Out-Patient Clinic. Hospitalization was necessary in September, 1933, because of a continuous pain in his epigastrium, nausea and tarry stools. The roentgenological examination revealed a rapid emptying of the stomach through the gastro-enterostomy stoma with evidence of an inflammatory process in this region. The afferent loop was somewhat dilated. A strict Sippy regime gave a satisfactory response. However, re-admission to the hospital the latter part of October, 1933, was required because of a return of all his previous symptoms. A strict Sippy regime was followed until the middle of December, 1933, and as no improvement was noted he was transferred to surgery for operative interference. A trial of silica and a bland diet gave almost complete relief in ten days. He has remained almost entirely free of symptoms with the exception of an occasional pain in his epigastrium. No tarry stools have been observed since his discharge from the hospital. His diet has not been limited and he has gained forty pounds in weight. This patient feels it is necessary for him to continue taking small amounts of silica at irregular intervals to prevent any epigastric distress. A roentgenologic examination March 6, 1935, showed no evidence of obstruction or inflammation in the region of the gastro-enterostomy stoma. The gastric analysis after an Ewald test meal on September 27, 1933, gave a free hydrochloric acid value of 20 and a total acidity of 37.

Case III: A patient of Doctor Marvin Menard. E. W.; white male; age 46, had a posterior gastro-enterostomy done in 1919 because of a duodenal ulcer which did not respond to a Sippy regime. This gave him almost complete relief of his symptoms until 1931, and then a return of the epigastric distress and burning necessitated an adherence to a bland diet with alkalies. Only a partial subsidence of his complaints was effected and in October, 1934, silica therapy was instituted. His symptoms disappeared entirely within a few days and he has not experienced any real discomfort despite the fact that he is taking a regular diet without any alkalies. This patient finds it is necessary for him to continue on small doses of silica in order to remain entirely free of complaints. He has gained 16 pounds in weight, feels much stronger and is able to work. No roentgenologic studies or gastric analyses were made just prior to the start of the silica therapy.

Case IV, #17585. H. R.; white male; age 33, on admission to the hospital January 18, 1934, complained of a rather constant epigastric pain, sharp in character, of two weeks duration. This followed directly after an attack of infectious mononucleosis. Symptoms of a vague epigastric distress after meals had been present for a year. The pain on admission was most severe from 1 to 4 hours after meals and was relieved by soda for a brief period. Physical examination revealed a fairly well nourished man. His teeth were in poor condition. Slight tenderness and rigidity were present in the epigastrium and the left upper quadrant. The stools contained occult blood. The urinalysis and Kahn reaction were negative. A large niche on the lesser curvature of the stomach, rather high in the pars media was found on roentgenologic examination. No evidence of improvement of his symptoms could be noted after 15 days on a strict Sippy regime. An Ewald test meal done while the patient was on this regime showed free hydrochloric acid of 18 and a total acidity of 56. He was then given silica and a bland diet. The alkalies were discontinued. An analysis of the gastric contents at this time gave free hydrochloric acid of 21 and a total acidity of 48. A complete relief of symptoms was obtained in two days and there has been no return of his symptoms. The roentgenologic examination February 26, 1934, revealed the ulcer to be practically healed. A gain of 20 pounds in weight has

occurred. He now has no symptoms (April 1935) referable to the ulceration of his stomach and is on a regular diet. He discontinued entirely the ingestion of silica two months after discharge from the Hospital, which was on February 9, 1934.

Case V, #9712. W. W.; white male; age 51, developed pain in his epigastrium, appearing one hour after meals, three years prior to his admission to the hospital in August, 1933. This pain was relieved by food, sodium bicarbonate or vomiting. The complaints were much more severe during the four months immediately preceding his entry in the hospital. No tarry stools were ever observed. Ambulatory treatment in the Out-Patient Clinic for months did not result in any improvement. The physical examination revealed a rather gaunt individual with no significant positive findings. The urinalysis and the Kahn reaction were negative. A gastric analysis after an Ewald test meal gave a free hydrochloric acid value of 72 and a total acidity of 96. By roentgenologic examination the duodenal bulb was found to be deformed. The pylorus was somewhat spastic but with no evidence of obstruction.

He was kept on a strict Sippy regime in the hospital for four days and then treatment with silica was started. A regular diet was allowed and sodium bicarbonate was given for the relief of any epigastric distress he might have. His symptoms were relieved within six days. Small doses of diatomaceous earth were continued until November, 1933. He was followed until March, 1934, and no return of his complaints had occurred. He had gained 28 pounds in weight. It has not been possible to follow this patient since the spring of 1934.

Cave VI, #19560. O. G.; white male; age 43, had had vague epigastric pain since 1918, appearing from two to three hours after meals. His symptoms had been more severe since 1929. Treatment for a duodenal ulcer in the hospital and in the Out-Patient Clinic by the Sippy regime resulted in only partial relief. Attempts to resume his normal activities caused a recrudescence of his symptoms. A loss of weight of 24 pounds was noted in the three years preceding the treatment with silica. No tarry stools were ever observed. The roentgenologic examination in August, 1933, revealed a saucer-shaped depression on the greater curvature of the duodenum. The gastric analysis after an Ewald test meal gave a free hydrochloric acid of 45 and a total acidity of 63. The stools contained occult blood and the Kahn reaction was negative.

The patient was last admitted to the Hospital in February, 1934, for a trial with silica therapy, to be followed if this was unsuccessful by surgical intervention. A bland diet was prescribed and sodium bicarbonate was given occasionally for the relief of epigastric distress. He became symptom free within two weeks and was followed in the Out-Patient Clinic. Often, a sense of fullness was experienced in his epigastrium, yet, without approaching the severity of his former complaints. He continued the ingestion of a teaspoonful of silica every seconddday as he said that this prevented epigastric distress. However, on April 30, 1935, a perforation of an ulcer on the greater curvature of the duodenum near the pylorus

occurred. His symptoms had been more severe for the preceding three weeks and he had taken only one teaspoonful of silica each night during this period. At operation nothing remarkable was noted in the condition of the remainder of the stomach or intestines. A simple closure was easily effected and no obstruction was present.

Case VII, #29512. F. G.; white male; age 40, complained chiefly of epigastric distress after meals which had been present since the World War. The sense of fullness and burning would occur from two to three hours after meals. Treatment in the Out-Patient Clinic since 1931 with diets and alkalies gave him some relief. The roentgenologic examination revealed a deformity on the lesser curvature of the duodenum. A gastric analysis following an Ewald test meal showed free hydrochloric acid of 61 and a total acidity of 83. He entered the hospital on September 29, 1934, because of continuous epigastric pain and tarry stools. He was given silica, a bland diet and occasionally some sodium bicarbonate. The pain disappeared and the stools became free of blood within a week. He was followed in the Out-Patient Clinic until February, 1935, and only at intervals had had slight epigastric discomfort. A regular diet was being taken, together with a small amount of silica. A gain of 10 pounds in weight was noted and he stated that he felt better since taking silica than he had felt in years.

Case VIII, #30783. E. D.; white male; age 44, was admitted to the hospital October 28, 1934, because of melena, extreme weakness and considerable epigastric distress. A typical history of a peptic ulcer of 8 years duration could be obtained. On admission, the hemoglobin was 70%. A strict Sippy regime was instituted at first and then silica therapy was substituted on November 2, 1934. A rapid improvement was noted and he was discharged to the Out-Patient Clinic on November 14, 1934. A soft diet, silica and iron ammonium citrate were prescribed in the clinic. The roentgenologic examination on November 30, 1934, revealed an "ace of clubs" deformity of the duodenum. Another examination on March 19, 1935, showed the duodenal bulb to be contracted and no apparent active ulceration.

This patient is now able to take a bland diet without any discomfort. A regular diet causes much epigastric distress. However, he has gained 9 pounds in weight and his strength is almost back to normal. He believes that he has experienced more relief on silica therapy than on any other type of medication he has taken since the onset of his symptoms eight years ago. He is comfortable as long as he does not attempt to do any physical work.

Case IX, #35239. J. M.; white male; age 50, had had symptoms referable to a duodenal ulcer for four years. In March, 1933, he began attending the Out-Patient Clinic and a bland diet with alkalies was prescribed, which gave no real relief. The roentgenologic examination on March 14, 1934, revealed an ulceration on the lesser curvature of the duodenum. A gastric analysis after an Ewald test meal on March 22, 1934, gave a free hydrochloric acid of 80 and a total acidity of 100. No tarry stools were ever observed. As no improvement was noted on ambulatory treatment he was referred to the hospital on February 2, 1935, for a strict Sippy regime. This benefited him greatly and he was discharged on February 21, 1935. A return of his symptoms was recorded on a visit to the clinic on March 15, 1935, and silica therapy was then instituted. He was told to take any diet he desired. His condition rapidly improved. At present he is on a regular diet and feels much stronger. The quantity of silica being taken has also been decreased.

Case X, #30024. C. F.; white male; age 57, was admitted to the hospital on October 11, 1934, with the complaint of a sharp, gnawing pain in his epigastrium which appeared soon after meals. This pain was first noticed three months prior to admission and had been particularly severe for the last month. No tarry stools were noted. Roentgenologic examination on October 16, 1934, revealed a large niche on the lesser curvature of the pars media of the stomach. A niche on the superior surface of the duodenal bulb about 2 cm. in width and 2 cm. in depth was also demonstrated. A gastric analysis on October 15, 1934, following an Ewald test meal gave a free hydrochloric acid of 46 and a total acidity of 62. The Kahn reaction was negative. Occult blood was present in both the stool and the gastric contents. A modified Sippy regime was carried out for eleven days with little symptomatic improvement. Silica and a bland diet were begun on October 22, 1934, and a satisfactory response was obtained. Another roentgenologic examination on November 9, 1934, showed the gastric ulcer, previously demonstrated, to have decreased about one-third to its original size. No change was noted in the duodenal deformity. At a third examination on February 12, 1935, only a small scar was present at the site of the large gastric ulcer. The duodenal deformity remained unchanged. Unfortunately, he had not been entirely relieved of his complaints when he voluntarily discontinued treatment in the latter part of February, 1935.

Case XI, #29234. W. G.; white male; age 59, had a simple closure of a perforated duodenal ulcer in February, 1933. He had had symptoms referable to this ulcer for only five weeks. His condition remained excellent despite no medication or diet until August, 1934. Then a sharp burning pain after meals appeared in his epigastrium. No tarry stools were noted and no signs of obstruction were present. On September 24, 1934, he was admitted to the hospital and silica therapy was instituted, together with a soft diet. An immediate improvement was noted and he was discharged on October 5, 1934, to the Out-Patient Clinic. Unfortunately, he did not return to the clinic and thus no rnentgenologic examination was possible. However, he did visit the Surgical Follow-Up Clinic on February 24, 1935, and his general condition at that time was excellent. He was taking a regular diet without alkalies, and had discontinued silica a week after his discharge from the hospital. No gastric analysis is recorded in his charts. One cannot be certain of the role of silica in the final result in this case.

Case XII, #9422. E. S.; white male; age 39, had had epigastric distress with seasonal variations following meals for a period of seven years. Positive roentgenologic evidence of a duodenal ulcer without obstruction was present. A gastric analysis on July 27, 1933, following an Ewald test meal revealed a free hydrochloric acid of 41 and a total acidity of 66. No satisfactory response could be obtained with diets and alkalies and he was hospitalized on August 27, 1933, for surgical intervention. Silica therapy was tried for one week without any improvement. A gastro-enterostomy was then done and as a result he has experienced almost complete relief of all his symptoms. A gain of 26 pounds in weight since his discharge from the hospital was recorded in February, 1935.

Case XIII, #15227. J. G.; white male; age 47, has been attending the Out-Patient Clinic since December, 1932, because of pain in his epigastrium which appeared one to two hours after meals and which was relieved by food and soda. The roentgenologic findings were suggestive of an ulcer in the pre-pyloric region of the stomach. A gastric analysis on December 10, 1933, following an Ewald test meal gave a free hydrochloric acid of 48 and a total acidity of 64. This patient was treated with diets and alkalies in the Out-Patient Clinic and was hospitalized for a Sippy regime from November 28, 1933, to December 22, 1933, with no noticeable improvement of his symptoms. As his complaints became much worse despite an adherence to his diet and alkalies, silica therapy was instituted on March 29, 1935. A satisfactory response was obtained and he is now on a regular diet without alkalies and has no epigastric distress. However, during the extended period of his treatment several periods of a relative remission of his complaints have occurred lasting as long as a month.

Case XIV, #31152. H. B.; white male; age 55, dates the onset of his symptoms to January, 1933, when he experienced severe epigastric distress and vomited a small amount of blood. He was admitted to the Christ Hospital and was placed on a strict Sippy regime for six weeks and was much improved. Ambulatory medical treatment for a duodenal ulcer was then instituted and this gave only partial relief. Hospitalization was again necessary in June, 1934, because of tarry stools, epigastric pain and persistent vomiting. He was discharged after five weeks on the Sippy regime and was followed in the Out-Patient Clinic where a diet with alkalies was prescribed. A roentgenologic diagnosis of duodenal ulcer without obstruction was made in July, 1934. His course was fairly satisfactory until October, 1934, when tarry stools, hematemesis and violent epigastric pain re-appeared. Again he was admitted to the Hospital and this time silica therapy was instituted. An excellent symptomatic response was obtained and he was discharged after a stay of 9 days. His hemoglobin was 85% and his Kahn reaction was negative. Ten days later he was re-admitted because of the renewed onset of tarry stools, epigastric distress and hematemesis. The medical staff felt that a strict Sippy regime was indicated and this was followed for three weeks with a satisfactory result. He has been attending the Out-Patient Clinic regularly and a strict adherence to a bland diet with alkalies has given him only partial relief. Unfortunately no gastric analysis is recorded in his charts. He weighed 190 pounds in 1933 and 125 pounds in April, 1935. No recent roentgenologic examinations have been done.

C O M M E N T

It is recognized that the foregoing group of cases is entirely inadequate to justify any final conclusion as to the efficacy of diatomaceous earth in the treatment of peptic and marginal ulcers. However, the evidence is quite suggestive that this medication was of decided influence in the favorable results which were obtained. It would be most unlikely that the improvement was a matter of chance as the patients were for the most part highly refractory to the Sippy regime. Yet, caution in attesting the beneficial effects of silica is made necessary when one considers the immumerable drugs which have been recommended in the treatment of peptic ulcers and which later have been discarded.

It is interesting to compare the results in this series with the experience of the mountaineers. They, too, have found it necessary to continue indefinitely the ingestion of "fine river sand" in smaller amounts in order to avoid a recurrence of their symptoms. This agrees with the concept of Emery and Monroe who believe that once the diseased process is well established it tends to persist throughout life. No statistics were found which gave the evidence of peptic ulcer among workers exposed to silica dust. Inquiry among physicians who see many cases of silicosis gives the impression that peptic ulcers are not uncommonly found in association with silicosis of the lungs.

C O N C L U S I O N S

1. A rather definite favorable influence was exerted by finely powdered diatomaceous earth following its oral administration to patients with peptic and marginal ulcers who had been refractory to the usual medical treatment.

2. The beneficial effect of diatomaceous earth may be ascribed to one or more of the following mechanisms: (a) Mechanical cleansing of the ulcer; (b) Adsorption of toxic products; (c) Local stimulation of the amoeboid activity of the phagocytes in the base of the ulcer and, (d) Stimulation of the proliferation of granulation tissue in the base of the ulcer as a result of the liberation of colloidal silicic acid from the particles of silica which have been phagocytized.

3. Diatomaceous earth apparently does not cure or remove the underlying cause of peptic ulcer once the diseased process has become well established, as is witnessed by the necessity for the continued ingestion of small amounts of silica in order to maintain symptomatic relief.

4. A study which revealed a slight adsorption of diatomaceous earth from the gastro-intestinal tract makes it likely that the beneficial effect is purely local on the ulcer.

5. Ingestion of diatomaceous earth is devoid of danger to the kidneys and other internal organs.

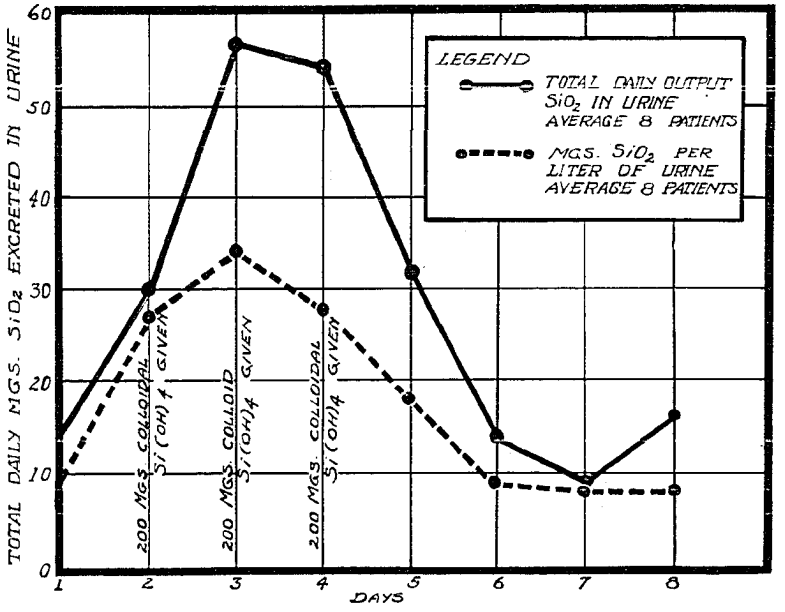

Fig. II. The urinary excretion of Silica following the oral administration of colloidal silicic acid.

BIBLIOGRAPHY

Alexander, J.: Colloid Chemistry, Vol. 3:249.

Bechold, H.: Colloids in Biology and Medicine. Translated by J. G. M. Bullowa, p. 344, 1919.

Brednow, W.: Zur Alkalitherapie des Ulcus. Med. Klin. 22:921, 1926.

Bruhns:: Cited by Kuhn.

Chitwood, W. T.: Personal Communication.

Collis, E. L.: The Statistical Characteristics of Dust Phthisis. Jour. Ind. Hyg. 8:457, 1926.

Crämer: Zur Behandlung des Magen-und Zwolffingerdarmgeschwürs. Munch. Med. Wchnschr. 59:615, 1922.

Dammann: Eine Massenerkrankung von Ochsen durch Kieselsaüre-Harnsteine und deren Vorbeuge. Deut. tierztl. Wchnschr. 4:435, 1897.

Emery, E. S. Jr., and Monroe, R. T.: Peptic Ulcer: Nature and Treatment Based on a Study of One Thousand Four Hundred and Thirty-Five Cases. Arch.Int. Med. 55:271, 1935.

Fridrich, L.: Ueber die Behandlung der Hyperazidität des Magens mit Neutralon. Munch. Med. Wchnschr. 68: 1621, 1921.

Gardner, L. A.: Studies on Experimental Pneumonoconiosis: VIII. Inhalation of Quartz Dust. Jour. Ind. Hyg. 14:18, 1932.

Gye, W. E., and Purdy, W. J.: The Poisonous Properties of Colloidal Silica. I. The Effects of the Parenteral Administration of Large Doses.
II. The Effects of Repeated Intravenous Injections on Rabbits - Fibrosis of the Liver.
Ibid. 3:86, 1922.
III. The Poisonous Properties of Colloidal Silica. Ibid. 5, 238, 1924.

Kadletz, F.: Bismoterran in der Ulcus Therapie. Med. Klin. 25:395, 1929.

Kent, J. T.: Materia Medica, 3d edition, p. 890, 1925.

King, E. J., and Stantial, H.: The Biochemistry of Silicic Acid. I. Micro-Determination of Silica. The Biochem. Jour. 27:990, 1933.

Kramer, S. P.: Personal Communication.

Kuhn, A.: Die Kieselsäure. Ferdinand Enke, Stuttgart, 1925.

Rosenheim, T., and Ehrmann, R.: Experimentelles und Klinisches über die Behandlung von Magenkrankheiten mit Aluminium silikaten. Deut. Med. Wchnschr. 36:111, 1910.

Schlesinger, J.: Ueber die Behandlung der Hyperaziditats zustände des Magens mit Neutralon. Münch. Med. Wchnschr. 58: 2163, 1911.

Unna, P. G. Cited by Kuhn.

Vas, S.: Ueber der The apeutischen Wert des Kieselsauren Witmuts (Bismoterran). Wien. Klin. Wchnschr. 42:50, 1929.

Willvonseder, R.: Zur Therapie des Magensgeschwurs. Qien. Klin. Wchnschr. 40:1416, 1927.

IX.

THE ROLE OF SILICON IN OTHER DISEASED CONDITIONS

SILICON AND CARCINOMA

The treatment of carcinoma with compounds containing silicon has been recommended by many authors. The evidence of its beneficial effect is not convincing, yet is worthy of a brief notation.

Leriche summarized the reports in the literature which are suggestive that the silicon content of the soil is of influence on the regional frequence of malignant lesions. He mentioned the work of Nason, in England; Kolb, in Germany; Printzing, in Italy; Barth, in Switzerland and Tchok, in France which revealed an increase in the death rate from carcinoma in those regions containing less silicon. Kuhn has reviewed the use of silicon in the treatment of carcinoma. Schuh (1854) reported favorable results after the oral administration of powdered silica in two patients. Battye (1874) believed he could retard the growth of malignant tumors by the oral administration of finely powdered silica. Zeller (1912) noted encouraging results in skin carcinoma after the oral administration of calcium and sodium silicate. The supplementary aid of an arsenic and mercury paste to the local lesion was said to hasten healing! Kuhn could not corroborate Zeller's findings. Neither was Lotz impressed with the clinical results following Zeller's mode of treatment. Pollock observed a complete disappearance of all clinical signs of an adeno-carcinoma of the stomach with metastases to the liver, confirmed by biopsy, after the oral administration of a silicate preparation. The patient was

followed for two years. Netrolitzki recommended silica after operation to prevent recurrence of carcinoma. The homeopaths advise sodium silicate per os for "adenoma of the breasts" (Zimmer). Kent gave silica in the treatment of "warty growths and blood tumors".

The mortality statistics of Collis and Yule are of much interest. A higher incidence of carcinoma was found in workers exposed to silica dust than in the general population of the same age.

Battye, R. F.: Upon the Medicinal Properties of Silica in Cancer, Fibroid Tumors, and Diabetes. Edin. Med. Jour. 20:420, 1874.

Collis, E. L., and Yule, G. U.: The Mortality Experience of an Occupational Group Exposed to Silica Dust Compared with that of the General Population and an Occupational Group Exposed to Dust not Containing Silica. Jour. Ind. Hyg. 15:395, 1933.

Kent, J. T.: Materia Medica, 3d edition, 1923.

Kuhn, A.: Die Kieselsaure. Ferdinand Enke, Stuttgart, 1926.

Leriche, J.: Les régions pauvres en silicium et les phénomènes de cancérisation. Progres Med. 149, 1933.

Lotz, A.: Zellersche Krebsbehandlung. Deut. Med. Wchnschr. 39:2438, 1913.

Netrolitzki: Cited by Kuhn.

Pollock, H.: Heilung oder Remission eines bereits inoperablen Magen-Leber-Karzinoms. Munch. Med. Wchnschr. 72:1600, 1925.

Zeller, A. Behandlung und Heilung von Krebskranken durch innerlich und ausserlich angewendete medikamentose Mittel. Munch. Med. Wchnschr. 58:1841, 1912.

Zimmer, G.: Silicum als Reizmittel. Munch. Med. Wchnschr. 70:233, 1923.

SILICON IN DERMATOLOGY

Siebert has given an excellent review of the various preparations containing silicon which have found use in dermatology. He thought silicon was an essential element for cell protoplasm and that the silicates were beneficial in those skin conditions of later life which were associated with a decrease of the silicon content of the body. Freund believed senile pruritus and eczema were particularly benefited by silicon. Luithlen advised sodium silicate in psoriasis, furunculosis and arteriosclerosis. Vessie recommended silica in furunculosis, abscesses and fistulae. Some of the preparations are applied externally and others are taken per os. Zuckmayer injected colloidal silicic acid intra-muscularly in furunculosis. Unna applied diatomaceous earth to chronic leg ulcers and decubitus ulcers with good results. The mechanical cleansing and adsorption of secretions were thought to be responsible for the beneficial effect. The homeopaths are ardent advocates of silica per os in all pyogenic infections of the skin. (Kent; Pierce: Pharmacopeia of the Amer. Inst. of Homeopathy).

BIBLIOGRAPHY

Freund, A.: Zur Kieselsaurebehandlung der Lungentuberkulose. Ther. de Gegenw. 65: 107, 1924.

Kent, J. T.: Materia Medica. 3d edition, 1923.

Kuhn, A.: Die Kieselsaure. Ferdinand Enke. Stuttgart, 1926.

Luithlen, F.: Kieslsaure Therapie. Wien Klin. Wchnschr. 38:762, 1925.

Pharmacopeia of the Amer. Institute of Homeopathy, page 522, 1897.

Pierce, W. T.: Plain Talks on Materia Medica, page 726, 1911.

Siebert, C.: Dermatologische Arzneimittel; Silicum und seine Verbindungen. J. Jadassohn, Handbuck der Haut- und Geschlechtskrankheiten, Vol. V/1, page 351.

Vessie, P. R.: A Biochemical Explanation of the Silica Molecule. Med. Record. 101:106, 1922.

Zuckmayer, F.: Ueber parenteral Kieselsaurezufuhr. Ther. d. Gegenw. 62:376, 1921.

DIATOMACEOUS EARTH IN THE TREATMENT OF PAPILLOMATA AND SEVERE HEMORRHAGIC CYSTITIS OF THE URINARY BLADDER.

A study of the effect of diatomaceous earth on warts was made in view of the praise accorded this material as a homeopathic remedy. However, the evidence was not conclusive that the local application of silica exerted a beneficial influence on warts of the hand, the feet or the genitalia. Three cases of inoperable pepillomata of the bladder were given injections of a watery suspension of diatomaceous earth during the course of the above investigation and rather surprising results were obtained. The hematuria cleared up and the papillary projections became much less noticeable. In two cases it was felt that the apparent decrease in size of the papillomata would have permitted a resection and in one instance this was done with an excellent result. No concretions were formed in the bladder, following the injections and the lining epithelium was little disturbed. In fact, the inflammation of the bladder wall appeared to be favorably influenced. This study was extended to include three cases of severe cystitis accompanied by an intractable hematuria. The results were most gratifying .

A brief report is appended of the cases of papillomata and severe hemorrhagic cystitis of the urinary bladder treated by injections of diatomaceous earth.

Case I, #9726. W. P.; white male; age 70, was admitted to the hospital on August 4, 1933, with a fracture of the surgical neck of the left humerus. He had a previcus hospital admission one year prior to this accident and at that time a diagnosis of papillomata of the bladder was made. Operative interference was refused. The hematuria was noted intermittently and a loss of fifty pounds in weight occurred during the year. The hematuria was quite severe the time of the last admission. A retention catheter was inserted and irrigations of one percent acetic acid and one-half percent sodium perborate solutions were given. It was not possible to fulgurate the papillomata due to their extent and his condition became so grave that no further operative procedure was considered advisable due to his precarious condition. Therefore, permission for the injection of a watery suspension of diatomaceous earth into the urinary bladder was given. Approximately one tablespoonful of 200 mesh diatomaceous earth stirred up with 75 c.c. of water was injected into the urinary bladder every two hours and the catheter clamped off for twenty minutes. The bladder was thoroughly irrigated with physiologic salt solution prior to each injection. The injections were less numerous as the hematuria cleared up. The bleeding ceased after three days with the exception of an occasional minimal quantity of blood. A cystoscopic examination after two weeks of treatment with diatomaceous earth revealed a great decrease in the size of the papilloma and the cauliflower appearance was not as impressive. Later examinations revealed a more striking decrease in the size of the papilloma and the patient was urged to have a supra-pubic resection of the tumor,

but he would not give his consent to this procedure. This patient did not return to the Out-Patient Clinic after his discharge from the Hospital on October 10, 1933. On January 12, 1934. he re-entered the hospital almost exsanguinated with his bladder filled with clots of blood and died within three days. The hematuria could not be controlled with irrigations and diatomaceous earth. The autopsy revealed a large papilloma in the region of the left ureteral orifice and a very severe acute necrotizing cystitis.

Case II, #17070. A. S.; white male; age 46, had papillomata of the urinary bladder treated by fulguration four years prior to his admission to the hospital on January 7, 1934. Severe hematuria was his chief complaint and cystoscopic examination of the bladder revealed the right side of this viscus to be covered with a large, fungating tumor which was thought to be inoperable. A retention catheter was inserted and instillations of diatomaceous earth were begun. The hematuria ceased within a few days and another cystoscopic examination on February 7, 1934, gave the impression that the papillomata had decreased markedly in size and two distinct pedunculated papillomata could be distinguished. These were excised with the electric cautery on February 10, 1934, through a supra-pubic cystomy. His convalescence was slow but uneventful and he was discharged on April 14, 1934. He was followed in the Out-Patient Clinic until July, 1934, and had apparently completely recovered at that time. The microscopic diagnosis of squamous cell carcinoma of the urinary bladder was made from the tumor removed at operation.

Case III, #26713. C. B.; white female; age 56, had had recurrent papillomata of the urinary bladder fulgurated repeatedly during the four years prior to her admission to the hospital September 11, 1933. She had been subjected to this procedure four times during the six months preceding her admission to the hospital without controlling the hematuria. Instillations of diatomaceous earth were instituted and the hematuria rapidly cleared up. The cauliflower appearance of the papillomata largely disappeared and the individual papilloma which dotted the wall of the bladder became rounded and more discrete. She was discharged to the Out-Patient Clinic on October 23, 1933, and received three instillations per week of diatomaceous earth. A slight hematuria was occasionally observed. Her symptoms returned in all their former severity six months after leaving the hospital and an examination disclosed an increase in the number and size of the papillomata. She died on September 20, 1934, as a result of a massive hemorrhage into the bladder. No autopsy was obtained.

Case IV, #11068. H. M.; white male; age 37, was admitted to the hospital on the psychiatric service with a diagnosis of tabo-paresis on September 2, 1933. A retention catheter was inserted on the 21st of September because of incontinence and twelve days later a gross hematuria was noted. This became worse despite frequent irrigations and instillations of diatomaceous earth were begun. The hematuria entirely cleared up in a week and no recurrence of this complaint occurred during the remainder of his stay in the hospital. A cystoscopic examination revealed evidence of a severe acute cystitis. He died on November 29, 1933, and no autopsy was obtained.

Case V, #27600. T. H.; white female; age 23, was admitted to the hospital on August 18, 1934, on the gynecological service with a diagnosis of a chronic bilateral salpingitis and an adherent retroverted uterus. This was complicated by a cord bladder as a result of a spina bifida. An alarming hematuria developed shortly after her admission to the hospital and this did not yield to the usual irrigations and internal medication. A blood transfusion was required. On September 8, 1934, bladder instillations of diatomaceous earth were begun and the hematuria cleared up within three days. Cystoscopic examination revealed an acute cystitis and the pyelograms were not remarkable. She was discharged to the Out-Patient Clinic on October 4, 1934. and no recurrence of her hematuria has been observed. No operative procedure was thought advisable for her original complaints after the development of the hematuria.

Case VI, #14220. L. B.; colored female; age 56, fell and sustained an intertrochanteric fracture of the right femur on November 7th, 1933. She was placed on a modified Russel's traction with a pin through the tibia. The urinalysis of a catheterized specimen on admission showed many pus cells but no red blood cells. Repeated catheterizations were required as she was unable to void and dribbled continually. A retention catheter was inserted on November 16, 1933, as evidence of a severe cystitis accompanied by hematuria became evident. The hematuria did not decrease with the routine irrigations and instillations of diatomaceous earth together with bladder irrigations with one percent acetic acid were begun on November 20, 1933. The hematuria was completely checked within six days and the urine remained free of blood until her death on December 10, 1933. The autopsy revealed among other lesions an acute and chronic cystitis with a pyelonephritis.

C O M M E N T

It is difficult to explain the apparent beneficial effect exerted by instillations of diatomaceous earth in the three patients with papillomata of the bladder. From their subsequent course it may be inferred that the bases of the papillomata were not affected. However, the villous portions were largely destroyed. The mechanism through which this was accomplished may rest on a purely traumatic effect of the particles of silica which would cause a thrombosis of the blood vessels of the villous processes. It would be unlikely for particles of silica to be phagocytized and transported into the base of the papilloma and there excite a proliferation of connective tissue and incidentally constrict the blood supply.

The same factors may play a role in acute hemorrhagic cystitis as may be operative in the beneficial effect exerted on peptic and marginal ulcers. The adsorptive action of diatomaceous earth on proteins in the urine and in the exudate from the urinary bladder would certainly tend to inhibit bacterial growth. This would permit the reparative processes of the body to function to a better advantage. However the practical value of diatomaceous earth in the treatment of papillomata and acute hemorrhagic cystitis cannot be definitely evaluated on the basis on this restricted clinical study.

M I S C E L L A N E O U S

Zickgraf recommended intravenous proprietary preparations containing silicon in the treatment of asthma. Kuhn also saw some asthmatic sufferers benefited by the use of silicates.

Kramer found evidence of varying concentrations of silica in the cerebro-spinal fluid in different diseased conditions.

Zimmer observed marked focal reactions with much improvement in patients with chronic arthritis following the oral and intravenous administration of silicon preparations.

Kuhn gave sodium silicate intravenously in one hundred patients with arteriosclerosis and a lowering of the blood pressure followed in some instances. Scheffler, Sartory and Pellissier used the same medication for the same diseased condition with encouraging results. Panzer noted improvement after the use of "sklerosol", a proprietary preparation containing silicon, in arteriosclerotic individuals.

Becker reported gratifying results in the treatment of typhoid fever by the intra-muscular injections of "caseosan", a proprietary preparation containing silicon and casein. Thoma used "siliquid" intravenously and obtained excellent results.

BIBLIOGRAPHY

Becker, P.: Proteinkorper bei Typhus als therapeutische und diagnostische Hilfsmittel. Munch. Med. Wchnschr. 69: 1381, 1922.

Kramer, S. P.: The Colloidal Solutions of Silicic Acid. N. Y. Med. Jour. 103:680, 1916.

Kuhn, A.: Die Kieselsaure. Ferdinand Enke. Stuttgart, 1926.

Panzer, O.: Therapie der Arteriosklerose mit Sklerosol. Med. Welt. 6:1174, 1932.

Scheffler, L.; Sartory, A., and Pellissier, O.: Les injections intraveineuses de silicate de soude. Presse Med. 28:806, 1920.

Thoma, E.: Experimentelle und klinische Beobachtungen zur Kieselsauretherapie bei akuten und chronischen Infektionskrankheiten. Munch. Med. Wchnschr. 69:1603, 1922.

Zickgraf, G.: Asthama und Silicum. Munch. Med. Wchnschr. 73: 1477, 1926.

Zimmer, G.: Silicum als Reizmittel. Munch, Med. Wchnschr. 70: 233, 1923.