CXXX. THE BIOCHEMISTRY OF SILICIC ACID.

II. THE PRESENCE OF SILICA IN TISSUES.

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(Received May 30th, 1933.)

THE presence of silica in animal and vegetable tissues has attracted interest for a considerable time. As early as 1857 Witting recorded 0.5 % of SiO_2 in the ash of a sample of human blood. Schulz [1901] made the first thorough investigation of the presence of silica in biological materials, and Gonnerman [1917; 1918] extended the analyses and collected the results of much previous work. Vegetable matter was shown to contain silica in amounts varying from 1.2 % of the ash for yeast up to 68 % for wheat straw and 80 % for horse-tail (*Equisetum arvense*). Feathers of grain-feeding birds had a higher silica content than did those of flesh- and fish-eaters. The hair of men and of animals invariably showed the presence of silica, even in the case of the new-born, but there appeared to be no definite relation between the silica content and either the species of animal or colour of the hair. Of the many samples of animal and human tissue, organs and fluids examined, all contained silica, though in very different and variable amounts. This earlier work has recently been summarised by Kühn [1926], in whose monograph are collected the results of a large number of investigators.

In the present investigation analyses of several tissues for their content of silica have been made following the colorimetric method previously described [King and Stantial, 1933]. The results have been checked repeatedly by gravimetric controls, and are believed substantially to represent the actual silica contents of the different samples. In most cases the figures are in accord with those of previous workers, but some discrepancies have been noted and are discussed in connection with the individual tissues.

Urine. In general it may be said that the carnivorous and omnivorous animals have a much lower urinary excretion of silicic acid than do the herbivora. This point is well illustrated in Table I.

Herbivora, and particularly those feeding on whole grains (including the hulls), straw and hay, ingest large amounts of silicon. While it is improbable that a very large percentage of this silicon is absorbed, a considerable amount must pass into the blood-stream to give the high concentration which is found in the urine. The values for herbivorous urine show very marked variations, but this is to be expected because of the very marked differences in the silica contents of different vegetable foods.

That the silica content of the urine may be influenced by the diet is also well shown in Table II. A group of four rabbits, which had been kept on whole oats and carrots and which showed high urinary silica values, was placed for

Table I. *Silica content of urine.*

	mg. SiO ₂ per 100 cc.		No.	mg. SiO ₂ per 100 cc.
Normal human:				
Average of 10 morning samples	1.2	Cat	1	0.5
	(high 2.1)	"	2	0.3
	(low 0.8)	"	3	0.5
Average of 17 afternoon samples	1.0	"	4	0.8
	(high 2.2)	"	5	0.7
	(low 0.7)	"	6	0.4
Silicotic human:				
		Rabbit	1	11.1
W. L. C. (gold miner 6 years)	1.4	"	2	27.2
J. L. (gold miner 7 years)	6.6	"	3	22.7
J. L. (gold miner 7 years)	1.9	"	4	21.3
	(1 week later)	"	5	7.2
J. D. (gold miner 14 years)	1.0	"	6	14.0
J. M. (gold miner 9 years)	0.6	"	7	15.6
		Guinea-pig	1	14.0
Dog	No. 1 0.9	"	2	22.4
"	2 1.3	"	3	28.6
"	3 1.8	"	4	16.6
"	4 0.7	"	5	14.6
"	5 1.3	"	6	8.2
"	6 2.7	Sheep	1	17.2
Rat (lab. diet)	1 3.0	"	2	12.8
"	2 5.7	"	3	11.9

Table II. *Effect of diet on silica content of rabbit urine.*

Rabbit No.	...	...	...	232	233	*234	235
Diet	Days on diet			mg. SiO ₂ per 100 cc. urine			
Oats + carrots	20			8.5	12.8	10.3	34.3
White bread	7			3.6	2.5	2.1	4.0
	10			4.4	3.9	5.6	4.6
	15			0.9	2.8	1.4	2.2
	17			0.7	2.5	2.9	2.9
	22			4.1	2.6	—	3.1
	26			—	2.7	0.9	3.6
	32			5.5	2.2	1.5	0.7
Oats + wheat straw	1			15.1	27.2	25.7	19.3
	4			27.0	24.5	12.0	24.7

a month on a diet of white bread supplemented with a little canned tomato. The amount of silica excreted dropped almost immediately and remained at a lower level during the course of the white bread feeding. On placing the rabbits again on a diet of whole oats, carrots and wheat straw, the amounts of silica in the urines returned to much higher levels. This agrees with the observation of Riessner and Kindt [1928] in human beings.

Blood. The silica content of the blood of individuals in this country appears to be very different from that reported by several German investigators. Kraut [1931] and Bohme and Kraut [1932] have recently reported an average of about 15 mg. of SiO₂ per 100 cc. of blood for normal men and women. Miners with and without silicosis had considerably more. Reckoned on an ash basis, Kraut's figures agree closely with that originally recorded by Witting [1857]. If these figures, obtained by satisfactory methods, are correct, and if our own results also substantially represent the silica content of the bloods analysed, then it appears that only about one-tenth the amount of silica found by Kraut circulates in the blood of normal human beings in this country.

Only a limited number of blood samples from cases of silicosis have been examined. These were sanatorium patients, former gold mine workers, who showed a history of silicosis, but who had been some time removed from their work. The average figure found was 0.9 mg. SiO_2 per 100 cc. of whole blood, with high and low values of 1.8 and 0.6 respectively.

It is apparent, however, that despite the low level of blood-silica, considerable amounts are passing through the body by way of the blood-stream to the kidneys at all times. Normal human beings on refined diets excrete 15 or 20 mg., and an herbivorous animal of approximately the same size would appear to be putting out 10 to 20 times this amount daily in the urine.

Foetal tissue. All the tissues and biological fluids so far examined have contained at least traces of silicon. The almost universal distribution of silicates, be it in sea-water or in the blood of mammals, makes it probable that if silicon is not an essential ingredient it is at least a likely contaminant of the developing egg. All the marine forms examined have contained silica, and added sodium silicate has been found greatly to enhance the growth of cultures of phytoplankton [King and Davidson, 1933]. Both the white and the yolk of the eggs of birds appear to contain small amounts of silicon, and several embryonic mammals have contained appreciable quantities, both in the whole foetus and in the individual organs. Table III contains the results for several such determinations.

Table III. *Silica content of foetal tissue.*

Tissue	mg. SiO_2 per 100 g. dry tissue
Mouse (whole foetus) (1)	10.7
(2)	10.5
Calf A: lung	4.4, 4.8
Calf B ₁ : kidney	8.2, 9.4
liver	4.4, 6.4
muscle	36.8
Calf B ₂ : lung	3.8, 4.2
kidney	9.6, 7.8
liver	10.0, 8.8
spleen	11.2
muscle	24.2
Calf B ₃ : lung	8.0, 10.4
Human: lung	9.8, 8.4
liver	3.8, 5.6
kidney	13.3
spleen	20.3
heart	20.4
brain	22.0

Adult tissues. The two paths of entry for silica into the body are the lungs and the digestive tract. The greater part of that entering by the latter route is doubtless eliminated in the faeces. A considerable amount probably passes into the blood-stream, however, and it appears that this is excreted in the urine without much retention by any of the organs of the body. The liver, spleen and kidneys of animals, even those ingesting large amounts of silicates in their food, contain only relatively small amounts of silica, and whatever silicate enters the blood by way of the intestine appears to pass quickly into the urine.

In the case of silica entering by the lung—and a considerable amount must enter as finely particulate dust even in the case of most individuals who are seldom exposed to a dusty atmosphere—there is no ready means of exit once

the particles have lodged in the parenchyma. Certainly the majority of particles breathed in are wafted up by the cilia of the bronchial passages and are either swallowed or expectorated, but the smallest particles probably lodge in the lung spaces and are then only capable of being eliminated by phagocytosis or through dissolution by the mildly alkaline body fluid which is constantly bathing them. Some particles which are ingested by cells which have passed into the air space are probably expectorated with their enveloping cell. Other particles may be ingested and drawn into the lung parenchyma, and the migration of the phagocytes may carry them appreciable distances in the lymph channels; some particles may even lodge in the bone-marrow [Chapman, 1933]. How much silica may be carried away by dissolution is entirely a matter of speculation, but it is certain that silica particles in the lung tend to become hydrated and invisible to the polarising microscope, and weak sodium bicarbonate solutions tend to dissolve surprising amounts of silicate from colloidal hydrated silica.

As is to be expected, lung tissue varies very markedly in its silica content, from what would be a normal value for any other tissue of the body up to values

Table IV. *Silica content of tissues.*

Tissue	mg. SiO ₂ per 100 g. dry tissue	Tissue	No.	mg. SiO ₂ per 100 g. dry tissue
Human:		Rabbit:	No.	
Lung* (normal adult)	140	Lung	430	148, 161
(pneumonia)	93		369	235, 229
(silicotic)	3640	(young)	378	18.4, 14.2
"	1700	(animal exposed to SiO ₂ dust)	651	6755, 7115
"	880	"	693	895, 785
"	1630	"	687	1002
"	810	Liver	687	12.4
Liver* (stone grinder)	196		648	30.6
Spleen*			378	21.4
(normal)	15.1		651	20.8, 14.3
(septicaemia ♂ 30)	16.0		360	20.0
(bronchopneumonia ♀ 75)	43.0	Kidney	373	16.4
(rheumatic heart ♀ 46)	14.2		380	22.2, 17.8
(bronchopneumonia ♀ 36)	23.0		647	14.4
(pulmonary embolism ♀ 67)	30.0	(animal exposed to SiO ₂ dust)	651	50.0, 47.6
(carcinoma ♂ 25)	45	Lymph glands		80
(silicosis, fibrosis of spleen ♂)	345	Spleen	657	16.0
(silicosis, stone grinder)	436	(animals exposed to SiO ₂ dust)	360	22.5
Mesenteric lymph gland*		"	369	76.0
(stone grinder)	1080	Hair (grey)		16.5
Bone-marrow	26.0	(white)		15.6
(lumbar vertebra)	25.2			
Ox:		Guinea-pig:		
Lung	103, 109	Lungs		78.0
	104, 120			48.0
	87.2, 81.2	Hair		19.4
Liver	21.6, 18.0			20.7
	12.0, 15.0	Chicken feathers		15.1
Dog:				12.9
Lung	115			
	270			
Kidneys	28.7			
	31.8			

* These analyses were performed on petrol- and ether-extracted tissues obtained from the wax blocks in which they had been imbedded after fixation for microscopic section and do not represent the silica content of the tissue as a whole. We are indebted to the Department of Pathology for this material.

which show about 50 % of the mineral material present to be SiO_2 . The lungs of gold miners, sand blasters, quarrymen, *etc.*, invariably contain extraordinary, though variable, amounts of silica. The presence of these large amounts in particulate form in the lungs appears to lead to the development of the fibrotic nodules typical of silicosis, which gradually extend, as snowflake-like flecks on the X-ray plate, from the mid-line to the periphery as the disease progresses. It is probable that the amount of effective alveolar tissue in some of these men is very greatly reduced. They become, moreover, very susceptible to tuberculosis, of which many of them die.

A considerable variety of animal material has been analysed with a view to gaining an insight into the possible significance of the presence of silicon in the different tissues. The results, which are illustrated in Table IV, have appeared to indicate a disposal within the body of inhaled and ingested silica along the lines suggested above. No evidence has so far been obtained that silicon is an essential element of animal protoplasm, or that it is a limiting factor in growth, as may be the case in certain microscopic marine plants. Further work will be presented in another paper [King, Stantial and Dolan, 1933], to show that whether or not silicates are an essential in the animal economy, the body possesses a very efficient mechanism for their disposal.

SUMMARY.

Silica occurs in small but significant amounts in foetal tissue.

A considerable excretion of silicate occurs through the kidneys. The silicate level of the urine of herbivora is much higher than that of carnivora. The amount of silica appearing in the urine is markedly influenced by diet.

Circulating blood contains only very small amounts of silica.

A variety of adult tissues shows marked differences in silica content, lung having the largest amount.

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