

medium, have a direct bearing upon the present problem. The synthesis of these forms was preceded by the creation within the reaction medium of a whole series of diffusion regions with conditions alternating between those favoring and those adverse to peptization. This led to a corresponding periodic succession of transitions (to the inert acidic polymer) and decompositions (to silica and water) of the reactive basic silicic acid gel. The aggregation and orientation of the highly dispersed particles of silica were greatly influenced by experimental conditions resulting in semi-permeable, porous, or impervious membrane bands. Again, under specific conditions the finely divided silica was carried in the upward movement of the acidic gel (a case of thixotropy), giving rise to the opalescence or opacity effect by the orientated deposition of laminar or fibrillar silica within the micellar structure of the medium. Apart from anomalies due to disturbing factors, it would seem that the network pattern of the silica orientation throughout the Liesegang phenomenon is primarily and fundamentally determined by the prototype structure of the colloidal medium.

This link between the various forms of the secondary polymer of silicic acid extends to the genetically and structurally related dehydration product, i.e. the tertiary polymer. Van Bemmelen (8) found that the gel of silica hydrate under the microscope appeared to have a cellular structure composed of a kind of network—Wabenstruktur—formed by the two solutions, the more concentrated forming the walls of a mass of cells, which enclose the other more dilute solution. This was confirmed by Bütschli (3), who also observed the accentuation of the network structure on drying the gel, as well as the fact that the natural opals exhibit a very fine cellular structure requiring the very greatest magnification to be rendered visible. Hydrophane, for example, with a magnification of 2,090 diameters, shows the cellular structure and is very little different from gelatinous silica. We thus perceive that all available evidence supports the observations and theory of Behrens. However, the results of the rhythmic separation of silica and its hydrates, outlined earlier, agree to the number but not to the character of opal constituents. Thus, Behrens' opal, a composite of two forms of opalite varying in density and refractive index, should be viewed as silica lamellae orientated within the network structure of a clear hyalite medium, which itself may be regarded as the pure tertiary polymer of silicic acid.

The formation of opal by the combination of external and internal (syneresis) pressure makes L'Abbé Haüy's theory hardly admissible. Any such fissures would be adventitious and a source of weakness.

As to Brewster's cavity theory, it seems to be untenable because of the fact that the appearance and general properties of the opalescent and opaque acidic silicic acid gel, the precursor of opal, were not affected by previous boiling and cooling *in vacuo* of the water-glass and the redistillation of the hydrochloric acid. These features of acidic silicic acid gels therefore were governed by osmosis and temperature conditions rather than by the presence of dissolved air in the reagents. In this respect a close analogy may be found in the rhythmic forms, especially the opacity bands, of calcium carbonate (5).

The formation of milky opal, opal agates, and chalcedony obviously fall within the scope of the present conception. It may be added also, that while the reactions outlined here no doubt find their prototype in nature, natural processes are not without variants, as may be seen in the function of organic life, superheated steam, carbon dioxide, and diffusion in connection with the formation of diatomite, flint, geyserite, chert, and gelatinous silicic acid (in the Alps) (?).

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The Metabolism of a Very Small Mammal

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It is well known that small mammals have a higher metabolism per unit weight than large ones. Thus, basal metabolic rates in Cal./kg. day ranging from 12 for the steer to 170 for the white mouse have been observed (1). The latter, with an average weight of 20 grams, is the smallest adult mammal on which metabolic studies have previously been made.¹ We have now made measurements on a shrew whose weight averages less than one-fifth that of the white mouse and thus is at the lowest limit of mammalian size.

The specimen used was a rather large, anestrus, female long-tailed shrew, *Sorex cinereus cinereus* Kerr, captured on Cape Cod and weighing 3.5 grams. It was extremely active, ate large quantities of worms and insects, and in all ways seemed entirely normal

¹This excludes the "dwarf" mouse (8 grams), an endocrinologically defective strain of white mouse. Crude measurements on "a dormouse" of 6-7 grams (5) and measurements at low temperatures on a bat, *Pipistrellus* sp. of 4-8 grams (4), both hibernators, have been reported.

when compared with other captives of the same species. Its oxygen consumption was measured in an automatic, volumetric apparatus to be described in detail elsewhere. The conditions of measurement were adjusted to simulate natural conditions, with ample food and water, a commodious chamber (1 liter) free from noises or drafts, and a moderate temperature. Carbon dioxide and water vapor were absorbed on soda lime and saturated calcium chloride, and the

TABLE 1
OXYGEN CONSUMPTION IN *Sorex*

Food	Hours	°C.	Oxygen* consumption (cc./gram hr.)		
			Min.	Av.	Max.
Yes	12	24	10.9		19.3
Yes	24	27	11.2	16.8	21.5
Yes	24	26	10.6	14.4	18.9
No	11	29	13.7		18.9

* As dry gas at S. T. P.

time required to empty a small (10 cc.), automatically refilled spirometer of oxygen was recorded kymographically. The sensitivity of the method was ± 1 per cent. Oxygen and carbon dioxide concentrations above 17 and below 2 per cent, respectively, were maintained.

One 12-hour and two 24-hour runs were made at 24–27° C., during which the animal appeared to be as comfortable as when in its terrarium. These runs were composed of 245 individual periods of 9–25 minutes duration. They revealed a continuous series of short activity cycles averaging 1.4 hours in length. A digestive cycle of less than 2 hours has been observed in *Cryptotis*, another tiny shrew (3). During the night these cycles tended to fuse into continuous activity, with an average oxygen consumption 20 per cent higher than during the day.

In an attempt to obtain postabsorptive measurements a fourth run without food was made at 29° C. The animal died, presumably of starvation, after 11 hours, but at no time until the period immediately before death did it consume oxygen more slowly than in the other runs. During this 11-hour fast the shrew used 620 cc. of oxygen. Assuming a body composition similar to that of the white mouse (2) with 1.5 Cal./gram, this represents an energy consumption of 54 per cent of the shrew's metabolizable body substance. The loss in total body weight during this period was 12 per cent.

Values for the minimum, average, and maximum rates of oxygen consumption are shown in Table 1. Assuming a value of 4.60 Cal./liter for the caloric equivalence of the oxygen consumed by this carnivorous animal (fat, 4.69; protein, 4.49), the average daily rate of 15.6 cc./gram hour represents 1.72 Cal./gram

day. With such a high metabolic rate this tiny shrew must literally eat its own weight every day in order to live. At the maximum intensity observed, 21.5 cc./gram hour or 2.37 Cal./gram day, the shrew consumed 1 per cent of its metabolizable body substance in 10 minutes. Under conditions of "severe" work, oxygen consumption in man is about 2 cc./gram hour (6), or one-tenth of the above value.

Because of this animal's extreme nervousness and

TABLE 2
THE BASAL METABOLISM OF VARIOUS MAMMALS COMPARED TO *Sorex*

Animal	Weight kg.	Basal metabolism in Cal. per		
		kg. day	sq. m. day	kg. ^{0.73} day
Steer*	500.	12†	1,090†	65†
Man*	65.	25	920	78.
Macaque*	4.2	49	670	73
Guinea pig*	0.41	86	710	68
White mouse*	0.021	170	530	61
<i>Blarina</i> ‡	0.020	370	1,020	130
<i>Sorex</i>	0.0035	830§	1,570§	183§

* See (1).

† Corrected for standing and activity.

‡ Unpublished observations

§ Corrected for "digestive activity."

constant need for food, measurements of basal metabolism comparable to those on other mammals will not be readily obtained. Even the white mouse, which is slothful and lethargic compared to *Sorex*, has been considered difficult (2), but we feel that our conditions have been particularly conducive toward repose. Nevertheless, we might expect to obtain lower minimum values in runs with food under conditions of smaller volume, shorter measuring periods, and perhaps a higher temperature, although observations indicate that even moderately high temperatures may be disturbing to *Sorex*.

The lowest rate of oxygen consumption observed was 10.6 cc./gram hour, or 1.17 Cal./gram day. Since it is probable that this animal is never resting and postabsorptive at the same time, correction will be made for "digestive activity" when comparing *Sorex* to other mammals. A factor of 0.71 is obtained by comparing the minimum values in runs on mice (*Peromyscus*, *Eutamias*, *Pitimus*) and a larger shrew (*Blarina brevicauda*), with and without food (unpublished observations). In Table 2 this corrected value is compared to those of a representative series of mammals, and it may be seen that in terms of basal metabolism this tiny insectivore with the weight of a dime is equivalent to "half a pound of beef." The surface area of this individual was 18.5 sq.cm., and the basal metabolism is also compared as Cal./sq.m. day. It is further compared as Cal./kg.^{0.73} day, a function which is roughly constant for most mammals. The value of 183 obtained for *Sorex* seems high, but unpublished observations on *Blarina* (Table 2)

indicate that shrews as a group may have a higher basal metabolism than other mammals. Further, since *Sorex* represents an extreme in size, it is entirely possible that it will deviate from the function which relates other mammals.

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The Milk Factor in Blood

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Bittner's (1) discovery that a mammary tumor-inducing agent is present in the milk of high tumor strain mice ushered in a series of researches aimed at the eventual isolation and characterization of this extra-chromosomal factor. As a preliminary to isolation experiments we undertook the investigation of mouse blood with special attention to the serum component.

TABLE 1*

Fraction tested	No. of mice	No. of tumors	
Whole blood	20	1	5% $\pm$ 4.87%. Age, 11.8 mos.
Washed red cells . . .	13	0	
Hemolyzed and dehydrated red cells . .	4	0	
Whole serum	47	0	
Fat-free whole serum . .	16	0	
Serum globulins	83	0	
Serum albumins	21	0	
Neutral fats	14	0	
Total	218	1	Mean age at death of 217 tumor-free mice, 24.4 $\pm$.07 mos. S.D., 1.18 $\pm$.05 mos.

* Only animals surviving six months or more appear in this table.

Woolley (3, 4) had found the agent to be present in the whole blood of his strains, in concentrations suggestively similar to its concentration in milk.

In our experiments whole blood was obtained by heart puncture from 100 mature etherized female Paris mice, whose tumor incidence in our laboratory has been 92.9 ± 1.84 per cent in bred female controls. All blood samples were pooled, and serum and serum fractions were prepared in the appropriate manner from this pool. Single doses of 0.2 cc. of whole blood or serum, or serum fraction equivalent to 0.2 cc. serum,

were injected subcutaneously into young female C57 test mice, a strain in which there have been no spontaneous mammary carcinomata during the past five years in our laboratory. This strain has proved highly susceptible to the milk factor, developing 76.1 ± 4.34 per cent carcinoma of the breast in females by foster nursing (2). The injected mice were subsequently bred and allowed to bring up their young normally under our standard control conditions. The final results appear in Table 1.

The fact that no tumors appeared in the series treated with whole serum is a definite negative answer to any hope of using serum for the isolation of the agent. All serum fractions gave results consistent with those of whole serum. The appearance of one tumor in 20 mice treated with whole blood is probably significant, but the incidence shown is less than that obtained by Woolley with whole blood.

Whole blood and blood fractions do not appear to be a rich source of the milk factor.

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Colistatin: A New Antibiotic Substance With Chemotherapeutic Activity

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Among antibiotic substances inhibiting growth of gram-negative bacteria, streptomycin, produced by *Streptomyces griseus* (6), appears to be particularly interesting at the present time. It was observed by us that some strains of aerobic sporulating bacilli isolated from soil, while growing upon the surface of nutrient agar containing tryptone and glucose, produce a well-diffusible antibiotic substance inhibiting growth of staphylococci as well as of *Bacterium coli*. While growing upon the liquid medium, these bacteria form heavy surface pellicles, and the antibiotic diffuses into the nutrient broth. However, this antibiotic substance is thermolabile and is strongly inactivated by boiling the culture liquid in the water bath for 15 minutes.

After detailed examination of a large number of cultures isolated from chernozem soils, an aerobic sporulating bacillus was found by us which produces a thermostable antibiotic substance, inhibiting the growth of *Staphylococcus aureus* as well as of *B. coli*. The activity of this substance is not decreased by boiling the culture fluid for 15 minutes. Because of its