composing the tumor is columnar and in places is apparently ciliated. In portions of the nodule the epithelium has a tubular arrangement, while in other portions the growth is very irregular. Extending about a portion of the nodule there is a flattened cavity, making it appear probable that the growth has originated from the epithelium lining cyst. Near the surface of the nodule is a mass of eosin-staining material consisting chiefly of dead epithelial cells. There are several long-pointed crystals in this material.

The kidney proper presents marked changes. Many of the tubules are dilated with dense, refractive, homogeneous material, in some instances staining with the basic stain, in others appearing yellowish and unstained. There are also interstitial changes in the cortex with increase in connective tissue and occasional groups of lymphoid cells. The cortex is much thinner than normal and scattered throughout its substance are cysts of various sizes lined with swollen epithelium.

FEATURES OF INTEREST.

The tumors in this case present several features of interest. The fact that no cells were found in mitosis in the tumor of the lung seems rather remarkable and may account for the negative results of the inoculations. The appearance of a small cyst at the site of inoculation in one mouse is of little significance on account of its failure to continue growth. There is also a possibility that this cyst resulted from the displacement of epithelium in the trauma of the inoculation, but this result has never occurred in a large series of similar inoculations employing the same technic. In view of the opaque appearance of the tumor and the lobe in which it grew and the absence of blood microscopically, it seems very probable that the blood supply to this lobe was cut off at a time just prior to the animal's death, perhaps being the direct cause.

The nuclear inclusions are not without interest. If they present the result of retrograde changes they are important in the analogy which they bear to cancer inclusions in general. Their non-specificity is clear in that they occur in other tissues and in other mice without tumors. The tumor found in the kidney is of another type and bears no relation to the tumor of the lung.

SUMMARY.

1. Two non-related primary tumors, an adenocarcinoma of the lung and an adenoma of the kidney, were found in an old uninoculated mouse which had been kept apart for breeding purposes.
2. Inoculation of other mice with the tumor of the lung resulted negatively.
3. Nuclear inclusions numerous in the tumor of the lung are not regarded as specific, since they are found occasionally in the tissues of other mice.

Pollakiuria in Liver Affections.—Wasserthal observed pollakiuria in a case of cirrhosis of the liver. The patient had to urinate every twenty minutes, especially at night. This caused insomnia. Hot baths gave him three or four hours of rest. The amount of urine in twenty-four hours was 2,000-3,000 c.c. without any pathologic properties. Artificial distension of the bladder with 5vi of a solution of boracic acid was well borne, and the solution was well retained. The pollakiuria in this case was evidently due, not to the so-called "irritable bladder," but to some peculiarities of the more or less concentrated urine, as well as to an abnormal amount of ammonium and sarcolactic acid.—*Vratch. Gaz.*, No. 16, 1906.

THE USE OF SODIUM CITRATE AS A MODIFIER OF COW'S MILK.

FROM A CHEMICAL AND PHYSICAL POINT OF VIEW.*

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The use of sodium citrate with cow's milk, first recommended by Wright (1893) and later by Poynton (1904), Variot (1904), Vanderslice (1905) and Shaw (1906), has attracted considerable attention, the claim being made that it furnishes an exceedingly valuable method for the treatment of proteid-indigestion and the vomiting of chronic gastric catarrh.

It is entirely apart from the purpose of this paper to discuss the therapeutic aspects of the subject, the purpose being only to consider the chemical and physical facts in relation thereto.

The chemical ground has been taken by the earlier investigators that the addition of sodium citrate to milk resulted, on contact with the gastric juice, in the decomposition of the calcium-casein of the milk, with the precipitation of insoluble calcium citrate, and the separation of the casein in a more flocculent form than ordinarily obtains. But Shaw's experiments have clearly demonstrated that such is not the case. He treated milk with sodium citrate solution, filtered the mixture through asbestos filter paper, by means of a suction pump, and dried and ignited the filter; then weighed the residual ash. In no instance did he obtain an appreciable amount of ash, and, hence, no precipitation in a chemical sense occurred. He believes that some unknown and undetected action or combination takes place between the sodium citrate and the calcium-casein, but advances no theory.

What is the nature of this action or combination? Is it a chemical or physical one, or both? Shaw has shown clearly that the calcium-casein combination is not changed in the reaction. What other chemical reaction could take place? When sodium citrate solution is brought in contact with hydrochloric acid, it would seem very possible that the stronger inorganic acid would displace the weaker organic acid, from the salt used, and form sodium chlorid and free citric acid. Such a reaction would be a most logical one, chemically; and, if such is the case, it would follow that the value of sodium citrate, as a milk modifier, is not dependent on the sodium citrate, but on the sodium chlorid and free citric acid formed when the sodium-citrated-milk comes in contact with the gastric juice.

That such a decomposition takes place, is indicated by the following chemical reactions. When a slightly warmed solution of sodium citrate is acidulated with hydrochloric acid and shaken and then has some freshly precipitated strontium carbonate added to it, a milky white precipitate of strontium citrate immediately forms at the surface of the liquid, and falls to the bottom of the container. The reactions are in two stages, as follows:

This precipitation of insoluble strontium citrate, formed by the neutralization of insoluble strontium carbonate, shows that there is free citric acid in the solu-

* Read in the Section on Diseases of Children of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906.

tion, and not free hydrochloric acid, because if free hydrochloric acid be treated with insoluble strontium carbonate, a clear, transparent solution of soluble strontium chlorid is formed, according to the following reaction:

That the milky precipitate formed is not an excess of insoluble strontium carbonate was proved by adding a quantity of strontium carbonate insufficient to neutralize all the free acid, so that the solution remained slightly acid.

It may be claimed that there is free hydrochloric acid in the mixture, and that this is first neutralized by the strontium carbonate to form soluble strontium chlorid, and that this latter is then precipitated by the sodium citrate. That such is not the case can be very clearly proved by physiologic experimentation, that is, a solution of sodium citrate in water has the cooling taste of the salt which is absolutely not "salty," while the same solution acidulated with hydrochloric acid and warmed to body-temperature for five minutes is unmistakably "salty" in taste.

At the meeting of the Section this morning, Dr. A. C. Cotton reported the theory suggested to him by Prof. Jerome Salisbury that, possibly, sodium citrate modified milk by decalcifying the calcium-casein, forming sodium-casein and insoluble calcium citrate, and that the latter was dissolved by the sodium-casein. This is essentially the view of Poynton except that, in addition, it is held that the calcium citrate is made soluble by sodium-casein, and thus kept in solution.

It is a well-known fact in chemical analysis, and one that is used to differentiate citrates from tartrates, that the calcium salts, in the presence of soluble citrates, precipitate calcium citrate only when the solution is *boiled*. While calcium citrate is practically insoluble in water, it is slightly soluble, though far less soluble in boiling water. In addition, if the milk is thus changed, a part or all of its casein should be dissolved, as sodium-casein is water-soluble; and this, apparently, is not the case. But, if so, what chemical change takes place when the sodium-casein comes in contact with the hydrochloric acid of the gastric juice? Clearly, the formation of sodium chlorid and insoluble casein.

In further demonstration I have made a series of experiments with milk and various reagents, and present a score or more of specimens of different combinations. The first four specimens were prepared with milk and varying percentages of hydrochloric acid (0.1, 0.2, 0.3 and 0.4 per cent.). In the first specimen, only a part of the casein has been precipitated by the acid; in the second and third specimens the curds were tough and cheesy, as they were also, in the fourth specimen. But in this last, and to a slight degree in the third, the curds are more or less broken up by reason of the excess of acid over and above the amount required to precipitate the casein.

In the next two specimens the milk was treated with a gastric solution (made by glycerin extraction from the fresh healthy hog's stomach, by Fairchild Brothers and Foster, New York), which was slightly acid, and not with a rennet solution, as used by Shaw. The gastric solution contains both the proteolytic and clotting enzymes, while the rennet solution contains the clotting

enzyme only, or chiefly. Hence, the former is a better representative of the actual gastric conditions that obtain on feeding milk.

Pepsin occurs in the gastric juice of both adults and new born infants. This condition is peculiar. "While in a few herbivora, such as the rabbit, pepsin occurs in the mucous coat before birth, this enzyme is entirely absent at the birth of those carnivora which have thus far been examined, such as the dog and cat."¹

The fifth specimen was treated with neutral gastric solution; there was a thickening, but little or no curdling; in the sixth specimen, the gastric solution used was slightly acid, and abundant curds were produced which, later, shrunk in size and left clear whey. When the milk was treated with a neutral or faintly acid rennet solution, it curdled, more rapidly in the acid condition than in the neutral.

The susceptibility of enzymes to changes in environment or physical conditions is remarkable. Rennet, as Green² states, in his most interesting and instructive work, is active in neutral or in faintly acid or alkaline solutions, but the presence of only a little more than the optimum quantity of either acid or alkali speedily destroys the enzyme at the ordinary temperature. Hammarsten found that clotting occurred most rapidly when a faintly acid extract was used, and Ringer has confirmed the observation, care being taken that the acid was added in an insufficient quantity to precipitate the casein. The clotting was not due to the action of the acid on the casein, as the addition of the same amount of acid without the rennet produced no effect on the milk. The study of the actions of acids, alkalies and salts on albuminoids is a most interesting subject, but one that can be considered here only most briefly. It may be of interest to quote the following statement:³

Recent researches have shown that the albumins of the blood have no real acid-combining power or alkali-combining power, as has been thought. In other words, there are no acid-albuminates or alkali-albuminates in a true chemical sense, such as one would liken to the union of an acid with an alkali. Albumins may loosely combine with acids or alkalies in weak solutions without change of properties, but such combinations are apparently more physical than chemical, more intermolecular than interatomic. By the action of strong alkali solutions, the albumins are converted (with the elimination of nitrogen as ammonia and sulphur as alkali sulphid) into modifications called alkali albuminates, but these are clearly the products of disrupted molecules, and radically different from the original molecules. In a somewhat similar manner these so-called acid-albuminates may be obtained with albumins and acids (but without the elimination of nitrogen or sulphur), together with albumoses and, sometimes, peptones; the nature of the products varying with the temperature and strength of the acid used.

The albumins possess some very interesting physical features. The white of an egg (the albumins of which are very closely related to the albumins of blood plasma and its globulins to serum globulins) consists of a frame-work of thin membranes enclosing a yellowish albuminous liquid of light density. Its viscosity is due to its membranes. It is always alkaline in reaction. Its albuminous bodies are mixtures of albumins and globulins together with a mucin. The albumins are soluble in water. On diluting white of egg with water, the globulins separate as a glairy mass, and on diluting it with four volumes of water, the mucin is precipitated. I have observed that if to 25 gm. of the white of an egg sufficient sodium chlorid and water be added to make 100 c.c. of a 0.6 per cent. solution of NaCl, the globulins and mucin are brought

1. Hammarsten, Mandel: "Physiological Chemistry, 1900, p. 260.

2. "Soluble Ferments," 1899, p. 238.

3. England, Joseph W.: "The Reactions of Albumin with Acids and Alkalies," Am. Jour. Pharmacy, 1903, p. 510.

immediately into solution, and a transparent solution results. This is a remarkable fact, especially if organized material has been made to yield a transparent solution by a change in the physical condition of the solvent. If the solution be saturated with sodium chlorid, the globulins are precipitated.

The proportion of six parts to the thousand of sodium chlorid in water corresponds in strength with that of physiologic saline solution, and the valuable therapeutic results following the injection of this solution into the body, in certain pathologic conditions, is apparently due to the fact that the saline solution not only dilutes the poisons in the blood by increasing the volume of blood plasma, but makes this increase under normal physical conditions whereby the globulins and mucin are kept in solution, and not under abnormal physical conditions such as obtain with the injection of water alone. In health, the amount of sodium chlorid in blood plasma is remarkably uniform (six parts to the thousand). So closely is the rule observed that with food containing an excess of sodium chlorid, the latter is quickly eliminated by the urine, and with food poor in chlorids, the volume of blood first decreases, but increases after taking chlorid from the tissues. The secretion of chlorids by the urine is correspondingly diminished.

The next four specimens (Figs. 1, 2, 3 and 4) were made with milk, neutral gastric solution and varying proportions of free HCl (0.1, 0.2, 0.3 and 0.4 per cent.). The curds formed were analogous in appearance to the acid curds, but somewhat gelatinous in consistency. Shaw states that the acid curd is chemically different from that produced by rennet. The specimens shown in Figures 5, 6, 7 and 8 were made with milk, sodium citrate and gastric solution with varying amounts of free HCl (0.1, 0.2, 0.3 and 0.4 per cent.). The curds were gelatinous and superior in physical appearance to those formed by acids and gastric solution. The specimen shown in Figure 5 is barely curdled; that in Figure 6 is strongly curdled; the one shown in Figure 7 is less curdled; the one in Figure 8 is still less curdled and is about equal to that in Figure 5 in appearance. Each is distinct and characteristic, both in the amount and kind of curd produced. The next four specimens (Figs. 9, 10, 11 and 12) were prepared with milk, sodium chlorid and gastric solution, with varying amounts of free HCl (0.1, 0.2, 0.3 and 0.4 per cent.); and each is remarkable in its similarity of appearance to the corresponding one made with milk, sodium citrate and gastric solution.

In fact, the similarity is so striking that, apart from the chemical evidence submitted, one can hardly resist the conclusions that the physical action of sodium chlorid as a modifier of milk is exactly the same as that of sodium citrate; and that sodium citrate acts as a physical modifier, not as such, but as sodium chlorid, by being decomposed by the hydrochloric acid of the gastric juice. Whether or not the free citric acid formed has any therapeutic influence is a therapeutic question. The percentage of free HCl in healthy nurslings ranges from about 0.1 to 0.2 per cent. In adults the percentage is usually calculated to be about 0.2 to 0.3 per cent., "but these figures are not based on pure gastric juice, as Pawlow and his pupils have shown that the gastric juice of the dog contains 5 to 6 parts to the thousand, and that of the cat an average of 5.2 to the thousand, of HCl (Riasantzen). According to Verhaegen's researches, "there is no doubt that pure human gastric juice from perfectly healthy persons has a higher acidity than 2 or 3 parts to the thousand."¹ These experiments indicate that the addition of sodium chlorid to milk has, apparently, some physical influence on the proteids of cow's milk whereby they are more rapidly permeated by

the peptic ferments and digested, and the presence of sodium chlorid may stimulate also the gastric glands and the outpouring of gastric juice.

It is well known that the extractive substances of meat (which contain sodium chlorid), are the most powerful of chemical irritants in producing gastric juice,⁴ and that rennin may be entirely absent in gastric atrophy and in certain chronic catarrhs.

Since, as Shaw points out, sodium citrate as a modifier of milk, is of value only when there is proteid-indigestion and vomiting from gastric catarrh, what is more rational to believe, since the sodium citrate is changed into sodium chlorid by the hydrochloric acid of the gastric juice, than that its action is both physical and chemical.

In the use of sodium chlorid as a milk modifier it is essential that only small quantities be employed, as large quantities inhibit the action of rennin (i. e., larger quantities than 1 per cent. of NaCl), and of pepsin i. e., larger quantities than 0.5 per cent. of NaCl).

The remaining four specimens (Figs. 13, 14, 15 and 16) were mixtures of milk, cereal decoctions, with neutral gastric solution and varying amounts of free hydrochloric acid (0.1, 0.2, 0.3 and 0.4 per cent.). Mechanically, the casein in these mixtures is very much better attenuated than with the salines; being uniformly in fine flakes and diffused through the liquid. Doubtless, sodium citrate or sodium chlorid can be added to these mixtures, if desired, and used in the conditions indicated.

In all the specimens made, the milk (25 c.c.), etc., was digested on a water-bath at a temperature of 40 C., 0.4 c.c. or eight drops of the gastric solution being added, and the mixture heated for five minutes.⁵

In conclusion I would express the opinion that sodium citrate, which is a neutral salt, has no decomposing action on calcium-casein in the cold, but that it does exert no important physical influence on the casein of milk; that, when the citrated milk is brought in contact with the gastric juice, the sodium citrate is decomposed into sodium chlorid and that sodium chlorid has important physical, chemical and therapeutic properties in the digestion of the proteids of cow's milk, more important, probably, than has been hitherto believed. Whether the free citric acid formed has any more important therapeutic value than the hydrochloric acid of the gastric juice (stimulated in production by the presence of the sodium chlorid) would seem to be very doubtful.

4. Verhaegen: "La Cellule," 1896 and 1897.

5. The same lot of milk was used for each test, and the most striking result of the test was the similarity, in appearance, of the different specimens of the same acid strength, except those made with the cereal decoction; that is, the curds became progressively finer as were used, respectively, hydrochloric acid, gastric solution and acid, sodium citrate, gastric solution and acid, and sodium chlorid, gastric solution and acid. With the cereal decoction, gastric solution and acid, the results were very different in that the curds were uniformly fine irrespective of the acidity, and they were less bulky, showing the largest degree of peptonization, a result doubtless brought about by the extreme fineness of the curd, which permitted more ready penetration by the ferments and more rapid action.

Field for Art in Medicine.—Beliard of Paris calls attention to the lack of modern, attractive pictures dealing with medical subjects and suitable to hang in a physician's anteroom or elsewhere. Every one is tired of the classic Rembrandt's "Lesson in Anatomy" and the like. He suggests that here is a promising field for aspiring artists to paint subjects that appeal especially to physicians. Rich men would buy the originals, while the poorer medical men would be content with reproductions.