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POISONOUS CHEESE.*

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It is well known that cases of severe illness follow the eating of some cheese. Indeed, such instances have been observed in various parts of the world for the past three hundred years. They are of frequent occurrence in the north German countries and in the United States. In England, they are less frequently observed, while in France, where much cheese is used, we find no record of any such cases.

The number of instances of cheese-poisoning in this country per year must be several hundred, if it does not extend above one thousand. In many reports of the different State Boards of Health we find notices of the effects of poisonous cheese. During the years 1884 and 1885, there were reports made to the Michigan State Board of Health of nearly three hundred persons who became suddenly and violently ill after eating of cheese.

It will be seen from the above statements that this subject is of sufficient importance to demand the attention of those interested in public health. The writer has, therefore, spent a large part of the past two years in the study of this subject, and the object of this paper is to present the results obtained.

The symptoms produced by "sick" cheese, as reported by German and American physicians, agree quite closely and are as follows: Dryness of the throat, nausea, vomiting, diarrhœa, nervous prostration, headache, and sometimes double vision. In short the symptoms resemble very closely those of a gastro-intestinal irritant, with marked effects upon the nervous system. In individual cases, some of the above mentioned symptoms may not appear at all, or, on account of the greater prominence of some of the others, may not be observed. Notwithstanding these alarming symptoms, recovery generally follows.

I stated in my preliminary report of this investigation to the American Public Health Association in St. Louis, October, 1884, that I had failed to find any record of a case terminating fatally; although I then inferred from the language of Hiller, whom I quoted, that a fatal termination was not unknown. Since that time I have found that Husemann, in his work on toxicology, refers to some fatal cases. Dr. Henry B. Baker states that a

* For history of outbreaks of cheese-poisoning in Michigan, and of the beginning of the investigations in regard to the cause, see pages 122-128 of the Annual Report of this Board for 1884.

fatal case occurred in Lansing a few years ago. Death results from prostration, and in the observed cases did not appear until from eight to ten days after the eating of the cheese. There were no deaths reported from the cases in this State in 1884 and 1885. From one of the reports made by a physician to the secretary of the Board, I take the following quotation concerning the symptoms: "Every person who ate of the cheese was taken violently sick. They were attacked with vomiting of thin, watery substance at first; later the vomited matter became thicker and reddish. At the same time there was diarrhœa, the evacuations being thin and watery. There was not much pain, except in the stomach. The tongue at first had a white coat, but later became red and dry. The pulse was very weak and irregular, the face pale and cyanotic. One little boy who ate freely of the cheese came very near dying. His body was covered with blue spots."

The symptoms of cheese-poisoning and those of sausage and fish-poisoning are very similar, though death from eating poisonous sausage and fish frequently occurs in Germany and Russia. Böhm reports the mortality from sausage-poisoning in Germany as from 23.2 to 54.2 per cent.; while Müller reports only six deaths in 343 cases occurring in Holland in 1874; a mortality of less than 2 per cent. It is altogether probable that many of the earlier cases reported were in reality produced by trichinæ. The mortality from fish-poisoning among the inhabitants along the Volga is reported as high, although exact figures are wanting.

From the studies of Sengbusch, Owsjannikoff, and Berkowsky, it is evident that the toxic agent in the fish arises from partial decomposition. The fish consist of three species of the genus *Acipenser, A. sturio, A. huso,* and *A. ruthemes.* For the purpose of preservation, they are cut into pieces, salted and buried in wooden casks in the earth. As needed they are taken up and eaten raw. Likewise, Kerner, Paulus, Schlosser, Niedner, and Müller, from special studies on sausage-poisoning, conclude that the toxic agent is due to partial decomposition. I mention these facts in regard to poisonous sausage and fish for the reason that they may throw some light upon our study of poisonous cheese.

Böhm and several others state that cheese which has proved harmful to man may be eaten by the lower animals with impunity. In order to test this, I kept a cat in confinement for seven days, and furnished it only water and cheese from a cake which had poisoned some 30 or more persons. The cat fed upon the cheese freely, and at the expiration of the time appeared in excellent health. The animal was then killed, and a careful post mortem examination failed to reveal any lesion. There was not even the slightest evidence of irritation of the stomach. However, from what I now know of the toxic substance, I am satisfied that the reason why the lower animals were not affected by the cheese was that they did not get the poison in sufficient quantity.

All the cases occurring in this State in 1884 and 1885 were due to twelve cheeses. Of these, nine were made at one factory, and one each at three other factories. I was furnished with a smaller or larger amount of each cheese. Of ten of them I secured only small amounts. Of each of the other two I received about 38 pounds.

The maker of the greater number of the poisonous cheeses has been engaged in the manufacture of cheese for a great many years, and has quite a reputation, justly earned. He owns three large factories. I visited one of these and was furnished every facility for studying the methods of manu-

facture, the agents used and the vats. The milk is brought in every morning by the farmers of the neighborhood, is poured into a large tin receiver, and thence is emptied into the vats. The milk brought by different persons is mixed, and then used for filling each of the vats, three in number. Many of the rennets are also prepared by the farmers. This is done by emptying the stomachs, scraping off the fleshy parts, filling with salt and drying. The rennets thus prepared and found on hand at the time of my visit were examined and found to be free from any sign of decomposition. The same rennet was used in each of the three vats. If it be true, as the manufacturer thinks, that all the poisonous cheese came from one vat, the rennet cannot be the carrier of the toxic substance. The cheese is colored with annotto, which was examined and found to be free from harmful adulteration. Moreover, the same stock of this coloring agent was used in making the cheese which had proved poisonous and that which remained good. From these facts it is evident that we cannot charge the deleterious effects of certain cakes of the cheese to this ingredient. Coloring cheese with annotto has been so long practiced, and the public demand for this color in cheese is so well established, that it may be regarded, I suppose, as a justifiable adulteration. The vats were lined with tin and seemed to be kept scrupulously clean. They were heated by steam pipes placed underneath. Each vat furnished curd for seven or eight cheeses. The curd is cut, placed in cheesecloth, and subjected to pressure in iron hoops, the expressed fluid finding free exit beneath. The curing room was found to be large and well ventilated. In this the cheeses are placed on shelves and left for fourteen days or longer, when they are placed on the market. The manufacturer states that all the cakes which proved poisonous were made between April 26 and May 6, 1884.

Nearly every cheese manufacturer has his theory as to the cause of poisonous cheese. The majority of them think that it is due to some poisonous plant which the cow eats. I have received a large number of letters from cheese makers on this subject. While many of them think that it is some plant, no two of those writing to me agree as to the special plant. One says that it must be some plant which appears early in the spring, because all the poisonous cheese made in his factory has been the product of early spring work. For a similar reason, another thinks that the plant must appear in midsummer, while a third is equally certain that the plant is eaten by the cows only late in the fall. One, Mr. C. B. Lambert, argues that the poison arises from the whey, and that poisonous cheese will be made in factories from which the milkmen carry home whey in their cans. But poisonous cheese has been made in factories where this practice is altogether unknown.

All the samples of poisonous cheese examined by me were found to be similar in many respects. From the freshly-cut surface, there exuded drops of a watery, slightly opalescent fluid, which was found to redden blue litmus paper instantly and intensely. If a small piece was dried thoroughly by prolonged exposure to the air, and then moistened with distilled water, the water would give the same intense and immediate acid reaction. I have tested with litmus many samples of good cheese, and have found that while all new or green cheeses feebly and slowly redden blue litmus paper, only the poisonous cakes give the intense and instantaneous reaction. I think that it can be stated that any cheese which will instantly and intensely redden blue litmus paper should be regarded with suspicion. Whether or not all poisonous cheeses have this reaction, remains to be determined by the exam-

ination of a larger number than it has fallen to my lot to study. However, this test is easy of application, and every grocer should make it on cutting a fresh cheese. If the sample is dry, a bit of it should be moistened with water, and the paper then applied. The old, foul-smelling cheeses, such as Limburger and Schweitzer, are alkaline in reaction, and poisoning does not result from their use.

Microscopical examination of the opalescent drops appearing on the freshly-cut surface of the cheese revealed constantly small spherical bodies, which have been determined by Dr. Sternberg to be micrococci.

My first step in searching for the poisonous principle of the cheese consisted in treating some of it cut into fine bits, with 90 per cent alcohol, filtering and evaporating the alcoholic extract to dryness at a low temperature. This residue consisted of a fatty mass. Of this I ate a small bit. It had a bitter, acrid taste, and produced within a few minutes marked dryness of the mouth and fauces and constriction of the throat, much the same as that produced by a large dose of belladonna, or its active principle, atropia. Later, there was considerable nausea, and I could readily imagine that a larger amount would have produced vomiting. This experiment was repeated a number of times with the same result, and from it I concluded that the poison, whatever it might be, was contained in the alcoholic extract. This would indicate a chemical poison and not a bacteric one. However, this chemical poison might be generated by the growth of bacteria. For some months I tried to isolate the poison from this alcoholic extract, but was unable to do so; for whatever I tried to dissolve the poison in would either dissolve the fat as well, or would fail to take out the poisonous principle. Besides, the compact, fatty mass extracted with the alcohol was not suitable for further extractions. After many attempts in this direction, I gave it up and made a water extract of the cheese. This I also found, by an experiment upon myself, contained the poison. The watery extract containing only traces of fat was much more suitable for study than the alcoholic one. I then evaporated the watery solution to dryness, at a temperature not exceeding 110°C., but was disappointed to find that the residue was not poisonous. The active principle had been volatilized or decomposed by the heat employed. Next, I tried distilling the aqueous solution. By doing this, I found that the first few drops collected in the receiver had the odor of old cheese, and when taken into the mouth produced the characteristic dryness and constriction. But the amount of the poison obtained in this way was small; and, besides, I thought it altogether probable that partial decomposition of the substance might be produced in making the distillation. Then, I took the aqueous extract of the cheese, shook it with ether, removed the ether with a pipette, placed it in a porcelain dish and allowed it to evaporate spontaneously. The residue contained traces of the poison. Another attempt was made by rendering the aqueous extract of the cheese alkaline with potassium hydrate, then extracting with ether. This process gave the poison in greatest amount, and was followed in all the subsequent work. By re-dissolving the etherial residue in water and again extracting the residue, the poison was obtained in a state of sufficient purity, so that after allowing a concentrated, aqueous solution to stand in vacuo over sulphuric acid, the poison formed in needle-shaped crystals. A small bit of one of these crystals, which, as obtained from one cheese, were large enough to be plainly seen with the unaided eye, placed on the end of the tongue, caused a very sharp, burning sensation, which was soon followed by dryness and constric-

tion of the throat, and nausea. The taste was especially sickening. A drop of the fluid in which the crystals formed, placed on the tongue, produced, in addition to the symptoms mentioned above, griping pains in the bowels, followed by one or more diarrhœal discharges. This was tried several times, not only upon myself, but upon some of my students, who kindly offered themselves for experimentation.

For this substance, I have proposed the name tyrotoxicon,—cheese poison. With potassium ferricyanide and ferric chloride, tyrotoxicon produces Prussian blue. It also reduces iodic acid readily. With the general alkaloidal precipitants, it fails to react. It is freely soluble in water, alcohol, ether, and chloroform. Chloroform was also used in a few trial experiments to separate the poison from the aqueous extract of the cheese, but the amount obtained with this agent was not so great as that secured with ether. Besides the more rapid spontaneous evaporation of the ether rendered it the more suitable. The amount obtained from the cheese was exceedingly small. From one cake, which was nearly entire, not more than two pounds having been removed by the grocer, I secured an amount which I estimated at not more than eight grains; but, from the same quantity of another cheese, I did not obtain more than two grains. I do not suppose, however, that all of the poison was extracted from the cheese. In future experiments I shall endeavor to discover some better method of separation.

The crystals have a pungent odor resembling that of old cheese, and it may be stated here that this odor has been observed in poisonous sausage, according to Husemann and Böhm. It is probable that tyrotoxicon or a similar substance will be found in poisonous sausage. If the crystals be left exposed to the air at the ordinary temperature of a room they decompose, some organic acid, whose composition was not determined, being formed.

I regret very much that I did not obtain the poison in quantity sufficient to enable me to make an ultimate analysis. The question as to the origin of this poison is one of great practical interest, and one which I am not yet able to solve with satisfaction. Tyrotoxicon belongs to a class of poisons known to the chemist under the name of ptomaines. They originate in organic substances which are undergoing putrefactive changes. Only a very small number of ptomaines have been separated. The majority of them have been recognized simply by their poisonous effects. They are, undoubtedly, quite widely distributed, and vary much among themselves in their toxic and other properties. In one sample of ether I found a ptomaine, a small bit of which, injected under the skin of a frog, caused death in a few minutes. Therefore, in using ether to extract tyrotoxicon from cheese, it became necessary to test the ether first. This was done by allowing one pound of ether to evaporate spontaneously in a porcelain dish, and examining the residue, if there was any. At first I was inclined to the theory that the tyrotoxicon originated in imperfectly cured rennets, but I have found it in milk to which no rennet had been added. A student brought me a four ounce bottle which was about half full of milk. The bottle and its contents had stood in the laboratory for more than six months. I removed the glass stopper with which the bottle had been closed, and observed the same odor as that given off from the crystals of tyrotoxicon. The decomposed milk was strongly acid in reaction. It was filtered, the filtrate rendered alkaline, and then extracted with ether; the etheral solution, on evaporation, deposited a small but distinct amount of tyrotoxicon. I then placed one gallon of good milk in a bottle, stopping

it tightly, and another gallon in a jar which was covered only with a thin cloth to keep out the dust. After two months these were examined and tyrotoxicon found in the milk from the stoppered bottle, but none in that from the jar. However, the milk in the jar contained other ptomaines, only one of which, trimethylamine, have I succeeded in separating up to this writing.

Evidently, then, tyrotoxicon may originate in milk on long standing in closed vessels. As the putrefactive changes in the milk are due to the growth of minute organisms, the introduction of these organisms into the milk may hasten its putrefaction, and, consequently, the formation of the ptomaine. The germs may be present in portions of milk which adhere to the sides of vessels which are not cleansed as often or as thoroughly as they should be. I would suggest that cheese manufacturers frequently inspect the cans in which milk is brought to them. When cows are kept in filthy stalls, the milk is likely to undergo speedy putrefaction.

I shall continue these investigations, and hope to ascertain with more exactness the conditions under which this poison is formed.