33 (642)

The toxic character of the colostrum in parturient paresis.

By **JOSEPH H. KASTLE** and **DANIEL J. HEALY.**

[*From the Laboratory of the Kentucky Agricultural Experiment Station.*]

Parturient paresis is preëminently a disease of plethoric heavy milking breeds of cows, and of those individuals which give the greatest yield of milk. Among the prime and immediate causes of the disease are parturition, a permanent or transient plethoric condition of the blood vessels, with corresponding increase of pressure on the nerve centers of the brain. The phenomenal trophic and secreting activity of the udder of the heavy milker and intense physiological activity of the mammary glands resulting in the sudden rise and absorption into the circulation of leucomaines or toxic alkaloids of the cells of the mammæ. These according to Law[1] are the principal causes operating to bring on an attack of this disease. In the present state of our knowledge it is of little moment whether we call the substances, other than milk, resulting from the sudden disintegrative changes in the udder at or about the time of parturition, leucomaines, alkaloids, toxins, or what not. It seems reasonably certain, however, that there is no gland of the size and physiological activity of the udder of a heavy milking cow, but what must contribute very largely and sometimes malignantly to the internal secretions of the animal.

The question, therefore, immediately before us in the study of parturient paresis and of eclampsia in the woman is to determine experimentally whether the udder and the breast, respectively, do under these acutely toxic conditions actually secrete poisonous substances, which if not quickly eliminated or prevented from entering the circulation might be held responsible for these diseases.

It therefore occurred to one of us, Kastle,[2] to test the conduct

[1] "Text-book of Veterinary Medicine," 2d ed. (1905), Vol. 3, pp. 301–317 Ithaca, N. Y.

[2] On the day after our three papers on parturient paresis and eclampsia were mailed to the editor of the *Journal of Infectious Diseases*, Chicago, viz., on February 13, 1912, Dr. Surface called our attention to an abstract by Helfer of a paper by Hoyois in the *Berliner Tierarztliche Wochenschrift*, October 5, 1911, No. 40, pp. 727–

of the first fresh colostrum of the cow obtained during an attack of parturient paresis, upon the lower animals. We have not yet been able to obtain a case of eclampsia. Accordingly eighteen experiments have been carried out on guinea pigs. These experiments have included a few other substances besides the first colostrum of a cow suffering from parturient paresis, by way of comparison, and these of course serve as controls on our other results. Up to the present, therefore, the following substances have been tested on the guinea pig, and in all instances were given intraperitoneally, by hypodermic injection, using 10 c.c. or in some cases less, viz., the first, fresh colostrum of the normal cow, fresh milk from a high-class dairy herd, the first urine of a cow suffering from parturient paresis, the urine of a healthy cow, normal salt solution, and aqueous solutions of the residue from colostrum and milk left after precipitating the same with dilute acetic acid and finally the first, fresh colostrum of a cow, obtained during an attack of parturient paresis. Briefly the following results have been obtained.

The normal salt solution, the urine of the healthy cow, and the fresh milk from the healthy herd produce no bad effects when injected intraperitoneally into guinea pigs. The first fresh colostrum of the normal cow produced diarrhea in the guinea pigs from which they speedily recovered and these pigs are now alive and well. The dried residue obtained by evaporating the filtrates from normal colostrum after precipitating with dilute acetic acid and neutralizing produced no effect.

Three female guinea pigs received 10 c.c. each, of the first, fresh colostrum of a cow in an attack of parturient paresis. (1) The whole colostrum, (2) skimmed colostrum, (3) colostrum cream. Pig 1 had no diarrhea, but died on the sixth day. On post-mortem this pig showed acute parenchymatous nephritis with interstitial hemorrhages, acute parenchymatous hepatitis with interstitial hemorrhages, acute degeneration of the cells of the adrenal cortex with complete destruction of the medullary

728, the original of which appeared in the *Annales de Med. Vet. de Bruxelles*, July, Aug., Sept., 1910, in which according to Hoyois the colostrum in cases of parturient paresis, on intraperitoneal injection in doses of 10 to 20 grams, caused paralyzing symptoms in rabbits and guinea pigs, with subsequent death at the end of seven to twelve days.

cells, and interstitial hemorrhages. No evidence of tuberculosis. Cultures from the liver, kidney and spleen showed no micro-organisms. No peritonitis. The pig was not pregnant.

Pig 2 seemed well after the injection; had no diarrhea. Died at the end of five days. On post-mortem showed acute parenchymatous nephritis, with interstitial hemorrhage, acute parenchymatous hepatitis, with interstitial hemorrhage, and marked peripheral necrosis. Acute degeneration of the cells of the adrenal cortex, with complete destruction of the medullary cells and interstitial hemorrhages. No evidence of tuberculosis. The pig was in the very early stages of pregnancy. Cultures from the liver, spleen and kidneys negative. No peritonitis.

Pig 3 seemed well after injection and had no diarrhea. Aborted during first twelve hours after injection, fetus five and five tenths cm. in length. Died in six days. The post-mortem showed acute parenchymatous nephritis, with interstitial hemorrahges; acute parenchymatous hepatitis, with areas of complete necrosis and interstitial hemorrhages. Some degeneration of the cells of the adrenal cortex with complete destruction of the medullary portion, and interstitial hemorrhages. Acute lobar pneumonia of the left lung. No tuberculosis. Pig no longer pregnant. Cultures from the liver, kidney and spleen negative. Cultures from the pneumonic lung contained a diplococcus. No peritonitis except over upper and anterior surfaces of the liver.

A healthy male guinea pig received 10 c.c. of the first, fresh, clear urine of a cow ill with parturient paresis. This pig showed no discomfort and no diarrhea. It developed a very marked diuresis however, passing at least 200 c.c. of urine in 24 hours. This urine contained a small amount of albumin and no sugar. This pig recovered from the diuresis and seemed well, and was chloroformed on the 13th day. On post-mortem this pig showed parenchymatous nephritis with some interstitial hemorrhage, a rather extensive necrosis of the liver cells, but without hemorrhage, and also localized areas of necrosis in the adrenals.

It is evident from these results that normal salt solution, fresh milk, and the urine of a healthy cow cause no disturbances in healthy guinea pigs. The colostrum of the normal cow invariably produced a diarrhea when injected into the peritoneal cavity of

healthy guinea pigs. In this connection it is of interest to note that it has long been known that human colostrum acts as a mild cathartic on the suckling (Williams, " Obstetrics," 1908, 351–352). Otherwise no bad effects followed the administration of the normal colostrum of the cow to healthy guinea pigs. It will be seen from our results that death invariably resulted in guinea pigs from the intraperitoneal injection of the first, fresh colostrum of a cow in an attack of parturient paresis, and that the post-mortem examination of the organs of pigs that had died from this cause showed the same pathologic degenerations and changes that are shown by the organs of women who have died of eclampsia. Unfortunately but little is known regarding the micropathology of the cow in parturient paresis. We have shown, however, that cows recovering from an attack of this disease invariably show a nephritis which may, as the result of repeated attacks, become chronic.

Our results with the colostrum of a cow suffering from parturient paresis certainly go to show the presence therein of some substance or substances toxic to guinea pigs, and certainly point to the udder and the mammary glands as the place of origin of the toxins or internal secretions producing parturient paresis and eclampsia respectively. The fact that the urine of the cow with parturient paresis causes such a profound diuresis in the guinea pig, points to the presence of toxic substances even in the urine of animals so affected. A conclusion which is sustained by the results of the post-mortem examination on this particular case. We hope in the near future to attempt the isolation of the particular substance or substances in the colostrum or the udder, responsible for parturient paresis or at any rate, its more careful study and nearer identification. We would, therefore, reserve the right to continue these investigations along the lines indicated above with the object of throwing further light on the nature of the toxine contained in the colostrum of cows suffering from parturient paresis and also the possible occurrence of such a toxine in the colostrum of women suffering from eclampsia, and with the still further object of arriving, if possible, at the precise conditions under which these toxins are elaborated in the udder and mammary glands.