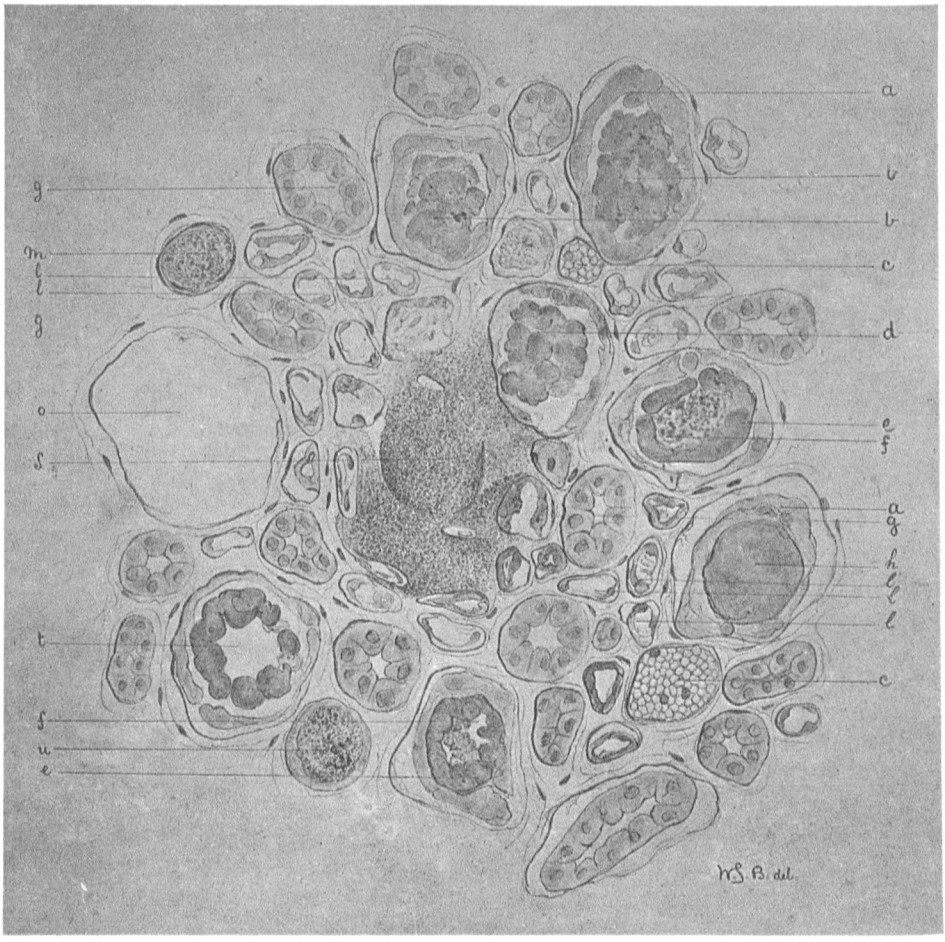

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AN UNUSUAL RESULT OF SEPTIC POISONING: DISCOLORED SKIN; DIPHTHERIA; HÆMATURIA; SPORES.

A GRADUATION THESIS, JULY, 1874.

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BETWEEN the months of September and December, 1873, ten of the newly-born children at the Boston Lying-in Hospital were attacked by well-marked symptoms of an unusual character. Eight died and two recovered. The microscopical examination of a kidney and larnyx from one of these subjects having shown certain exceptional appearances, the records of the hospital were examined for a history of the cases. The symptoms and the autopsies there recorded, although less complete than might be desired, distinctly traced the existence of a curious endemic affection. As the symptoms of this disease and the gross appearance of the affected organs were similar in all the cases, it is not unfair to infer that a microscopical examination of the diseased tissues would have revealed a corresponding general resemblance in their minute changes. The following account of the cases is taken from the hospital records.

FATAL CASES.

1. Male, six and a half pounds. Born September 8th. September 17th. Skin dark, discharges green and fœtid. 18th. No better; one

EXPLANATION OF PLATE.

TRANSVERSE SECTION NEAR THE BASE OF A MALPIGHIAN PYRAMID.

a. Epithelium in tubes of Bellini. Outline of cells obliterated.
b. Lobulated masses of globulin.
c. Vein containing blood corpuscles.
d. See *b.*
e. Tubular cast of globulin.
f. Granular globulin in centre of cast.
g. Tubes of Henle. Epithelium intact.
h. Solid mass of globulin in tube of Bellini.
l. Henle's loops.
m. Artery containing granular débris of blood corpuscles, similar to *f.*
o. Tube of Bellini, empty.
s. Spore colony extending through walls of tube into parenchyma.
t. Annular cast of globulin.
u. Granular globulin in tube of Henle.

diaper covered with blood and the dark green discharge from the bowels. 20th. Much weaker. 24th. Died.

2. Male, nine pounds. Born September 5th. On the 12th the child seemed unwell and would not nurse; discharges watery; skin very blue. 13th. Died. The color of the skin resembled that resulting from continued doses of nitrate of silver; discharges dark green and fœtid; mouth almost black, and very sore. Death in sixteen hours.

3. Female, nine and a half pounds. Born September 7th. September 14th. Taken sick at three this morning; discharge from bowels dark green and very offensive; skin of the color produced by repeated doses of nitrate of silver; respiration normal and rather slow; heart regular; will not nurse. 15th, evening. Rather better. 16th, evening. Better. Skin more yellow. 17th. Better. 20th. Mouth bleeding; mucous membrane sloughed off. 21st. Worse; hæmorrhage from kidneys. 25th, 10 A. M. Died.

Autopsy. Dark color somewhat faded out. Peritonitis. Adhesions about spleen. Upper part of larynx, pharynx, and œsophagus covered with a diphtheritic membrane, which could be stripped off œsophagus. Larynx ulcerated. Intestine apparently healthy throughout. A clot of the size of a finger's end existed in the bladder, being a cast of the interior of the organ. The pelves of the kidneys and the ureters were filled with coagulated blood, as were also the Malpighian pyramids. At this time an opinion was expressed that diphtheria was the primary cause of the child's death.

4. Female, ten pounds. Born October 16th. 23d. Became ill. Vulva inflamed. 24th. Metastatic abscess on back of hand. 25th. Patient worse; circumscribed abscess on scalp; other new abscesses forming. 26th. Odor offensive; left leg purple; hand swollen; right arm paralyzed. 9 P. M. Died.

5. Female, six and a half pounds. Born November 3d. November 10th. Child became blue last night; the mouth is very sore; diapers black and offensive; some blood on diaper from urine. 11th, 8 A. M. Died.

Autopsy. This child was almost black after death, the skin resembling that of a negro. There was no disease of the umbilical vessels, and no diphtheritic inflammation of the larynx or pharynx. Some change existed in the structure of the liver, simulating acute yellow atrophy. A large coagulum was found in the bladder. The other organs were healthy, including the brain.

6. Female, six pounds. Born November 1st. 10th. Child became sick; mouth very sore. 11th. Much worse; turned very dark; dejections black and offensive. Evening. Child worse; refuses to nurse, and moans continually. Died at midnight.

Autopsy. Dark color but little faded after death. Umbilical vein in

a state of thrombo-phlebitis; contents in a condition of puriform softening. Spleen large and dark. Kidneys dark, with clots in pelves. Other organs, including larynx and pharynx, healthy. No coagulum in bladder.

8. Male, seven pounds. Born December 8th. December 18th. A little dark; diaper dark and offensive; mouth very sore. 19th. Two operations last night, with the latter of which the urine was bloody; two during the day. 20th. One operation last night, and one during the day; worse in the evening. 21st. One operation during the night, and another in the course of the day; will not nurse. Evening. Mouth worse; cannot swallow. 22d. One operation last night; worse to-day. 8 P. M. Died.

Autopsy. Emaciation. Color had been deep but is now faded. Umbilical vessels healthy. Liver normal; ductus venosus closed. Spleen large and dark. Pelves of the kidneys full of blood; Malpighian bodies injected; whole organ engorged and dark. Larynx diseased, a diphtheritic membrane covering part of vocal cords and glottis. Other organs healthy. No clot in bladder. Small purple points of extravasation over whole body.

CASES OF RECOVERY.

9. Male, nine pounds. Born November 2d. Was attacked November 12th, and turned dark.

℞ Tincturæ ferri chloridi, gtt. iij., every two hours.
Wine and water every two hours, alternating with the iron.

November 13th. Child was much better and continued improving up to November 17th, when the mother and child were discharged.

10. Female, nine and a half pounds. Born November 16th. November 24th. Child turned dark last night; mouth very sore; hæmorrhage from kidney.

℞ Tincturæ ferri chloridi, gtt. iij., every three hours.

Evening. Four operations; urine bloody; discharge from eye. 25th. Child a little better, and nurses a little; three operations last night. Evening. About the same; eye still discharging; during the day three dark and very offensive operations. 26th. Much better; one operation last night; three during the day; better color. The eye being about the same, was washed with

℞ Zinci sulphatis, gr. j.
Aquæ destillatæ, ʒj.

Evening. Condition improved. 27th. One operation last night; none during the day; child much better. 28th. One operation during the night; still improving; eye much better; mouth nearly well; no operation during the day. 29th. Two operations during the night. Evening. Much better; eye about the same. 30th. Much improved. Discharged.

The house physician [1] states that in these cases four symptoms were prominent although not always recorded, namely, —

1. Deep discoloration of the skin.
2. Hæmaturia.
3. Diphtheritic inflammation of some of the mucous surfaces, in every case but one, where a thrombo-phlebitis of the umbilical vein existed.
4. Dark green offensive dejections.

The order of appearance of these symptoms may be approximately determined from the record. In eight cases the discoloration appeared on the first day; in one on the second. The diphtheritic symptoms appeared in six cases in the first day, but in one on the sixth. The hæmaturia appeared three times on the first day, in three cases on the second, once on the seventh. The dark dejections, seven times on the first day and once on the second. The duration of the shortest case was sixteen hours; that of the longest fatal case was eleven days; the average length being about five days, and the average age of the infants when attacked about eight days.

Autopsies. — Post-mortem examinations were made in every instance. Four only are recorded, but Dr. Fitz, by whom they were made, states that these may be considered as fairly representing the rest. The following results were arrived at: —

The brain, intestinal tract, and lungs were normal.

The spleen was always enlarged and dark, peripheral inflammation being sometimes indicated by the existence of adhesions.

The liver was as a rule relatively unaltered; but in one case presented alterations simulating acute yellow atrophy.

The kidneys showed evidence of engorgement. The pelvis of the organ was generally filled with coagulum, as were the ureters and bladder.

The mucous membrane of the mouth, and in one instance that of the vulva, showed evidence of active diphtheritic inflammation. In some instances the larynx and pharynx were involved, and in one case the œsophagus.

Thrombo-phlebitis of the umbilical vessels was found in one or two cases.

A *microscopical examination*, by the writer, of between two and three hundred sections of a kidney gave the following results.[2] (See Fig.)

The small arteries were generally dilated, either with blood corpuscles or with an unevenly granular mass (m), of a color varying from

[1] Dr. Samuel Howe.

[2] The specimens were prepared for examination by hardening them while fresh in a two per cent. solution of chromic acid in water for several days. They were then preserved in alcohol. The sections were washed, stained with hæmatoxylin, again washed, the water displaced by absolute alcohol, and this by oil of cloves.

nearly gray to brown, the color being in proportion to the fineness of the granules. In the latter substance there was no trace of blood disks. The small veins (c) were filled with corpuscles, but in no case so far as observed with granular matter. The tubes of Bellini were distended with matter resembling that found in the arterioles, but varying in consistency from the granular condition above mentioned (f) to that of large, brown, semi-transparent, lobulated masses, inclosing deep red amorphous granules of hæmatin (b). These sometimes filled the tube entirely, and sometimes lined it in the form of a hollow cylinder (e).[1] In the latter case the central cavity of the cylinder was seldom empty (b), but filled with similar material in a granular condition (f). More rarely, two or three cylinders occupied the same tube, as if they had been formed in one of the smaller tubules and floated to their present position. The looped tubules of Henle (l) were for the most part empty, but occasionally contained masses of the same substance. The convoluted tubes were generally filled with the same material, but only in one or two cases was there any trace of extravasation into the Malpighian capsules. The Malpighian corpuscles were generally injected. The renal epithelium was usually displaced and shrunken, but sometimes absent; changes in part, perhaps, due to the action of preservatives. In the large straight tubes it was generally contracted away from the walls into close contact with the inclosed cast (a), the outline of the cells being lost, and only an occasional nucleus remaining visible. In Henle's loops it was generally represented by one or two detached shreds (l), while in the straight tubes lying between the convoluted tubes and those of Bellini it was best preserved (g).

Distinct from the brownish material of these casts, the tubes contained at various points accumulations of a gray, homogeneous, and finely granular material, in the form of a long, broken cylinder of which the outline was interrupted at intervals by continuations of the substance through the walls of the tube into the interstitial tissue. A cross section of such an accumulation is indicated in the centre of the figure (s), where the outline of the tube originally containing the granular matter is nearly obliterated by the extent of the extravasation. In their gross appearance these granules resembled spores, the "cocco-bacteria" of Billroth, and on the addition of potash hydrate they were found to be insoluble. The optical and chemical properties thus gave strong evidence of the identity of the granules observed in this case with those usually regarded as spores.

Under these circumstances, the existence of similar spores in the larynx might be anticipated, and such proved to be the case. On examination, its surface was found covered with a diphtheritic infiltration

[1] The possibility of such casts being composed of desquamated epithelium, agglomerated and stained with blood-coloring matter, is not to be denied.

which offered no unusual appearances. The surface was ulcerated at points, presenting shallow, ragged excavations. The individual epithelial cells were generally separated by the accumulation in the interspaces of a translucent, homogeneous material of a high refractive index, the neoplastic nature of which was suggested by the greater readiness, compared with the surrounding tissue, with which it absorbed hæmatoxylin. The submucous areolar tissue was thoroughly infiltrated with wandering cells and granules (bacteria spores), which were at points so crowded as to indicate a tendency to abscess formation. The endothelium of the muciparous glands was slightly more transparent than usual, while around the tubules were occasional extravasations of a translucent, delicately striated, colorless material of doubtful origin. Lastly, imbedded in the epithelial layer, each covering the area of twenty or thirty cells, were numerous groups of spores, exactly resembling, in appearance and reactions, those found in the kidney.

Hæmaturia. — This symptom was in these cases associated with coagula in the bladder, extending up the ureters and filling the calyces of the kidneys, the tubes of which were filled with the highly colored solid materials of the blood which had penetrated to their interior. This was observed, not at isolated points of mechanical rupture or inflammatory softening, but throughout the organ, more especially in the Malpighian pyramids. This material was amorphous, and in no case was a well-defined blood-corpuscle found inside a tube. The supposition which best accounts for the appearances here detailed is either the existence of some alteration of the blood which would allow the passage of the material of the corpuscles through the walls of the tubes, or an alteration of the tubes or vessels themselves, or both. Again, so plentiful a development of spores at remote points would suggest transmission through the circulation.

Discoloration of the Skin. — That this was in some degree due to a capillary hyperæmia was shown by its partial disappearance after death. But to a great extent it did not disappear, either spontaneously or on pressure. Besides, the modifications of color were not such as occur while the blood is contained in the capillaries, but rather resemble those of a subcutaneous ecchymosis from violence. Such a penetration and staining of the subcutaneous areolar tissue by the coloring matter of the blood is fairly attributable, under the circumstances, to the conditions previously mentioned.

Diphtheria. — This symptom affords additional evidence to the same effect, since, in the form in which it commonly occurs, diphtheria is associated both with colonies of spores in the larynx and with a modified condition of the blood.

Dark Dejections. — No alteration of the intestinal tract was found which accounted for this symptom.

Thrombo-phlebitis of the umbilical vein, which occurred in one instance, is of interest as suggesting a possible source of disease in that case, since the puriform contents of a vein might bear the same relation to the disease under consideration that a suppurating wound bears to an ordinary case of pyæmia, a view favored by the absence of well-marked diphtheria in the case referred to. Under these circumstances it is to be regretted that no microscopic examination for spores in the blood was made during life, and that the only fact ascertained with certainty is, that in some of the injected veins of the kidney the white corpuscles were largely increased in number, being in the proportion of about one to twenty-six of the red.

In the *Archives de Physiologie* for September, 1873, M. J. Parrot describes, under the name of "Tubulhématie Rénale," two cases occurring in infants, which, although differing from the above in some points, correspond so closely in their essential features as to leave little doubt of their similarity. The first of these cases is stated as follows: Convulsions, bronze discoloration of the skin, hæmaturia, alteration of the blood, phlegmonous erysipelas of the scalp, softening of the brain, lobular pneumonia, and multiple renal lesions, the latter consisting of a "centre of softening in one kidney" and numerous points of supposed incipient softening of the size of a pin's head, in which the microscope showed everything veiled, so to speak, by extremely fine granulations, into which part of the renal parenchyma appears to have been transformed. Blood casts, in the form of hollow, and more rarely solid, cylinders, were found in the large tubes of Bellini, sometimes to the number of twelve to twenty in a single tube. Here and there was a spot of a lighter color, in no way recalling a blood corpuscle, sometimes isolated in the tubules, sometimes occupying the center of the tubular casts."

The second case was characterized by "bronze discoloration of the skin, mahogany-colored urine, excess of white corpuscles, encephalic disturbance (strabismus), pneumonia, and renal lesions." At the autopsy, the brain, liver and stomach were found normal. A clot of some days' standing was found in the pulmonary artery, and old clots in the renal veins. "Muguet buccal," though without mention of the fungus (*oidium albicans*) characteristic of this disease, is recorded in the account of the symptoms, but omitted in the summary. The occurrence of epileptiform convulsions in the first case is adduced as evidence of uræmic poisoning, a supposition which does not seem to be confirmed.

Both cases exhibit three symptoms characteristic of this disorder, namely, discolored skin, hæmaturia, and inflammation of the mucous membrane of the mouth. The character of the dejections is not mentioned.

The conclusions of M. Parrot from these two cases are as follows: —

"Tubulhématie rénale is characterized, clinically, by encephalopathic

troubles, a bronze discoloration of the skin, an alteration of the blood, and hæmaturia; anatomically, by the presence in the renal tubules of the red blood-globules which there take on a special arrangement."

"Tubulhématie rénale is caused by a primitive dyscrasia of the blood (a diminution, and probably an alteration, of the red globules)."

These conclusions are not altogether corroborated by the Boston cases, which were not characterized by encephalic symptoms, and were accompanied by diphtheria, not muguet. It has been shown also that the alteration of the red corpuscles was something more than an "agencement particulier."

It will be especially observed that M. Parrot, in recognizing a change of the blood as the principal cause, stops short of any further and remote cause of the conditions which have been described.

The Boston cases seem to imply that this alteration of the blood may be secondary, and dependent upon some local process of a septic nature, such as a diphtheritic inflammation or a thrombo-phlebitis, from both of which sources spores might readily be transported to the kidney.

A detailed description of the condition of the blood during life is of interest in connection with the Boston cases. The following points were noted by M. Parrot: —

1. Excess of white corpuscles.
2. Deficiency of red corpuscles.
3. A probable alteration of the red corpuscles, inferred from the existence of numerous bodies of smaller size, each containing from one to three granules.
4. A great number of fine granules floating in the serum.

The last fact deserves attention. It is held by some of the best modern observers that even in health a certain number of organic germs or spores exist in the blood, an increase in the number of which is associated with the development of certain diseases, notably those classed as septic. The numerous small granules observed by M. Parrot in the general circulation suggest a possible origin of the spores which were identified by tests in the Boston cases. But the origin of the granules themselves is not clear. M. Parrot inclines to the belief that they are produced by an alteration in the red corpuscles. It should be remembered that a breaking up of the red corpuscles is by no means unusual in certain febrile and inflammatory disturbances, in which case numerous fragments, although there may be no granules, are found, as in the instances cited.

Since the above was written, a brief notice has appeared in the *Revue des Sciences Médicales*, No. 5, January 15, 1874, of the description of an "epidemic" of the same disorder at the Hôpital de la Maternité, at Lyons, by MM. Laroyenne and Charrin. The cases seem to be generally identical in character with those observed in Boston. The altera-

tion of the blood, consisting of "leuko-cytosis, granulations, and augmentation of the volume of the red corpuscles," is regarded as a primordial phenomenon. "In no case was there any appearance of cerebral symptoms, nor did any lesion of the brain appear at the autopsy." "For want of sufficient materials, M. Charrin has not solved the question of pathogenesis. It remains to be discovered by what cause the alteration in the blood is produced." The hygienic conditions of the Lyons hospital, like those of the Boston hospital, were excellent at the time the endemic occurred. The number of cases was fourteen and all were fatal.

In conclusion, it may be added that in the present imperfect state of knowledge of the relation of germs to disease, involving a probability that any inconclusive theory will be superseded by some other, the following statement appears to be consistent with facts so far as known. Newly born children may be attacked by a disease or diseases generally fatal, with certain conditions in common, but with other conditions, such as diphtheritis and thrombo-phlebitis, of such decidedly local character that it seems advisable to regard these last as the essence of the disease. The characteristic features are, —

1. Discoloration of the skin.

2. Diphtheritic inflammation of some of the mucous surfaces. In one case, thrombo-phlebitis.

3. Hæmaturia.

4. Dark green fœtid dejections.

5. An alteration of the blood, consisting in (*a*) excess of white corpuscles; (*b*) alteration of the red corpuscles; (*c*) the existence of granules.

6. Accumulations of the amorphous material of the red corpuscles in the renal tubules, with clots in some cases in the ureters and bladder.

7. Accumulations of spores: (*a*) in the renal tubes, with extension outside their walls; (*b*) in the larynx, and possibly on the other surfaces affected by the diphtheritic process.

The process is generally endemic. The local accumulation of spores appears to be in close relation to the phenomena of the disease.

The following questions are suggested by the above cases: —

(*a.*) The identity of some of the granules in the blood and the spores.

(*b.*) The origin of the granules in the blood, and their possible connection with atmospheric germs.

(*c.*) The exact nature of the alteration of the red corpuscles.