cases without diarrhœa or tenderness, it seems indicated. Electricity may be used for the same purpose. Means must be employed to empty the bowels either by purgatives or enemata. Objections exist to the use of either, since eventually they tend to weaken still further the muscular power. In the case of Hughes the child seemed to be made distinctly worse by enemata. Yet it is often a case of "needs must," and that remedy has to be selected which best unloads the bowels and gives relief. The use of the rectal tube to remove gas has sometimes been a great comfort to the patient. In three instances—Martin's, Hobbs' and de Richemond's, and one of Hirschsprung's—puncture of the intestine with a fine trocar has been performed, in order to allow gas to escape.

In any severe case tending to grow worse reasonably early operation of some sort is to be advised. In spite of the gravity of the procedure, not to employ it seems still more grave. Exploratory laparotomy was performed on the patients of Fütterer and Martin, but nothing more radical was attempted. An artificial anus was made by Halsted in Osler's case, and the child recovered. The same operation was performed in my own case. Had it been done earlier, before the rapid failure of health set in, the chance of recovery would have been greater. The operation done by Treves (*loc cit.*) on a child with dilatation consecutive to congenital stenosis might well be employed in idiopathic cases—viz., the entire removal of the functionally useless dilated colon and the joining of the small intestine with the anus. As this is a serious operation the attempt to relieve by the formation of an artificial anus may well be made first.

ON THE TOXICITY OF THE URINE.[1]

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The question of the toxicity or non-toxicity of urine has been engaging the attention of scientists for a long time, and the number of authors who have contributed to this subject is very great. From a practical point of view the subject has received its greatest impetus by

[1] Read at the meeting of the Association of American Physicians, May, 1899.

the appearance of Bouchard'a charming book,[1] Paris, 1885; translated, with a preface, by Thomas Oliver. Philadelphia and London, 1894.

Without going into a chemical discussion of the agents producing toxicity of urine, this work has offered to us a simple, practical test, which consists in injecting a quantity of urine proportionate to the weight of the animal; if the animal dies the urine is toxic; if not, there is no toxicity. Now, to those of us who believe in auto-infection as an important etiological factor in disease, this test was very welcome; first, because it appealed to us on account of its simplicity; and, secondly, because it seemed to give us an index as to the prime cause of the diseased condition of our patient. It could not he final or complete, because of the fact that the substances which produce toxicity in urine had not been isolated, and, therefore, their origin in the body not disclosed. But, under all circumstances, this test seemed a valuable one for clinical purposes, and, probably, more exact than many others upon which diagnoses are based. As this paper has not been prepared as a literary digest of the subject, but simply to determine a method by which the toxicity of urine can he determined, and to discuss conclusions arising from the comparatively large number of experiments made, we will be justified in beginning with Bouchard. Bouchard's method consists in injecting, in the rabbit, from 30 to 60 c.c. (average 45 c.c.) per kilo of animal into "the posterior marginal vein on the dorsal part of the face as it spreads over the ear." (Bouchard, *loc. cit.*) "We can, even in the rabbit, penetrate directly into the median artery of the ear." He discards subcutaneous injections, because, as he has proven by experiment, absorption does not take place with sufficient rapidity. One of us' first began using a modification of Bouchard's methods by injecting the urine into the peritoneal cavity of rabbits under certain aseptic precautions, a method which was, afterward, fully justified hy the investigations of Vollhard,[2] by whom is disclosed the fact that in intravenous injections the results are changed by the rapidity of the injection, by the pressure which is used, and, finally, that in two cases extensive thromboses were produced by urine injected intravenously. But that which finally induced us to discard the method of Bouchard and the subsequent observers was the fact that there were so many differences of opinion expressed, especially in connection with the toxicity of urine in pregnancy, and that, with one of us, experiments made with the urine of one patient gave absolutely varying results. The tentative conclusion was arrived at that it was not the observers that were at fault hut the method. To prove or disprove this view,

[1] Leçons sur les Auto-intoxications dans les Maladies, etc.

[2] R. W. Stewart: Toxicity of Urine of Last Month of Pregnancy. The American Journal of Obstetrics and Diseases of Women and Children. xxxv. 3, 1897.

[3] Monatsschrift für Geburtshülfe u. Gynäkologie, Studien zur Pathogenese d. Eklampsie, 1897.

both of us began a series of experiments: the one taking the urine of pregnant women during the last month of pregnancy, and the other that of healthy subjects and of patients who could be considered from clinical manifestations, and are so considered by Bouchard, as being affected with gastro-intestinal auto-infection. Bouchard speaks of these cases as being primarily connected with dilatation of the stomach. We have failed to find the stomach dilated. These patients were:

CASE I. Female, aged thirty years, suffering with chronic constipation, headaches and hysterical (neurosal type, Bouchard).
CASE II. Female, aged forty-five years, constipation, Rigg's disease, headache, dyspepsia and recurrent urticaria.
CASE III. Male, aged fifty years, constipation, dyspepsia, asthma (asthmatic form, Bouchard).
CASE IV. Female, aged thirty years, constipation, migraine (neurosal form, Bouchard).
CASE V. Boy, aged nine years, constipation, asthma, repeated attacks of coryza, furuncles (mixed form, Bouchard).
CASE VI. Male, aged forty years, constipation, chronic urticaria (cutaneous form, Bouchard).
CASE VII. Female, aged thirty-nine years, neurasthenia, anæmia (neurosal form, Bouchard).
CASE VIII. Male, aged twenty-two years, constipation, acne vulgaris (cutaneous form, Bouchard).
CASE IX. Boy, aged eleven years, constipation, extreme nervousness, migraine (neurosal form, Bouchard).
CASE X. Female, aged twenty-four years, constipation, chlorosis.

In all we took urine from twenty-four patients, thirteen of the former class and eleven of the latter; also urine from healthy persons, and with this urine one hundred and fifty-four animals were injected. All the experiments were conducted on the strictest principles of surgical asepsis. Details are unnecessary, except to state that all the instruments, vessels, and cotton plugs were carefully sterilized by heat before being used, and the fluid used for injection was always warmed. As it was impossible to obtain as many rabbits as were required, and, as Bouchard neatly puts it, "there are economical necessities before which it is necessary to bow," white mice were used in a large number of cases. That urine under proper conditions may become toxic to white mice was abundantly proven; but, in order to be positive in regard to this, in most of the experiments the ratio of 45 to 1 kilo of animal was increased to 100 to 1 kilo, or even more; but even with this enormous increase we arrived at the distinct conclusion that urine is less toxic to white mice than to rabbits. This was due more to the fact that more mice recovered after having been made ill than rabbits. The experiment, made to show the comparative toxicity of urine upon a mouse and a rabbit, does not, however, prove this.

EXPERIMENT XLVI. November 26, 1898, urine taken from a patient during lahor, 33 c.cm., injected ioto a rahhit.

5.03 P.M.

5.13 P.M. Peculiar noddiog motion of head; throwing head to one side, rouses himself as though startled.

5.16 P.M. Head drawo hackward, pupils dilated, but reactiog to light; falls oo one side, jerking of all extremities; theo jerking confined to muscles of neck; head thrown backward with convulsive motioo; some clooic movements of head, ears, and forefeet.

5.17 P.M. Breathing stopped; heart still heatiog.

5.19 P.M. Lies on side, apparently dead; heart still heating.

5.19½ P.M. Heart stopped.

EXPERIMENT XLII. Same urioe, 2 cc. iojected ioto mouse at 9.10 P.M.

9.16 P.M. Drowsy, teodiog to fall to one side; hreathiog very rapid.

9.21 P.M. Violeot tremhliog, lastiog ahout ooe-half minute, then quiet, followed hy tremhling at regular iotervals.

9.35 P.M. Wabhling gait; throws himself from side to side; tremhling cootinues; rolling over, violent clonic convulsions, then tonic spasms with opisthotonos; seems to he struggliog for hreatb; respiration very rapid; these cease and recur.

9.45 P.M. Death in clonic spasm.

The mice die in the same manner that the rabhits do, either quickly, in the manoer just described, inside of an hour (thirty-five minutes the longest time in our experimeots), or in from twelve to twenty-four hours, the symptoms tben being usbered in by drowsiness, lying down in the bottom of the jar, slowness of breatbiog, convulsions, and then death. The post-mortems have revealed nothing microscopically that could account for death; as far as bad results from the injectioo are concerned, we found lesions only in two instaoces: in the one—a mouse—a blood clot in the omentum; in the other, a seropurulent, offensive fluid in the peritoneal cavity; except in cases in which the urine had heeo staoding a comparatively great length of time, as will be referred to later.

The experiments hegan hy investigating the urine passed hy the patients mentioned ahove, in whom toxicity could he expected with reasonahle certaioty after reading the results of other investigators. It was shown here that in forty mice in only three the urine was toxic. Fresh urine injected immediately, boiled immediately aod injected immediately, filtered urine never; hut fresh urine wheo kept sealed to the utter exclusioo of air, however, proved toxic in a numher of mice when not injected immediately. There seemed to be somethiog in the urine, then, which had the power of renderiog it toxic after sufficient time had heen giveo to cause it to develop its activity. With this in view a large series of investigations was hegun with the results presented in the following tahle:

VARIOUS METHODS IN TESTS FOR UTERINE TOXICITY.

	Number of experiments.	*Result: deaths.*
Fresh urine injected immediately	Mice, 14	1
Filtered urine injected immediately, or after 24 hours	Mice, 21	None
Urine boiled immediately and used immediately	Mice, 22	Mice, 2
" " " "	Rabbits, 5	Rabbits, 2
	—27	14 per ct.
Urine boiled immediately and used after 24 hours	Mice, 26	Mice, 10
" " " " "	Rabbits, 5	Rabbits, 2
	—31	39 per ct.+
Urine boiled with boric acid, allowed to stand 24 hours	Mice, 11	Mice, 2
" " " "	Rabbits, 3	Rabbits, 3
	—14	35 per ct.+
Urine mixed with boric acid, allowed to stand longer than 24 hours	Mice, 18	Mice, 5
" " " " "	Rabbits, 5	Rabbits, 5
	—23	43 per ct.
Fresh urine allowed to stand for a variable length of time longer than 24 hours	Mice, 30	Mice, 20 $66\frac{2}{3}$ per ct.

There are, then, one hundred and fifty-four experiments to draw conclusions from, arranged in seven series:

1. In the experiments made with the fresh urine the urine was passed into sterile vessels and injected into mice within a few minutes after it was passed. It will be seen that one mouse died. This is the mouse which had the lesion in the omentum, but died as all the mice died when the urine is toxic. It is difficult to say, precisely, how much the element of shock had to do with its death, especially in view of the fact that the same urine, after it had been boiled and kept for twenty-four hours, did not kill. The only other explanation that might be offered is the one that the operation was not done under strict asepsis.

2. For the purpose of filtration, urine was passed and then immediately placed in the filtering apparatus, either Kitasato or Chamberlin. All the urine used by this method had first been tested as to its toxicity and found non-toxic. It did not matter whether it was injected immediately or kept in sealed vessels for four days, it never produced death.

3. The urine that was boiled immediately and injected immediately—twenty-seven cases in all—had been tested in twelve cases for toxicity and been found non-toxic. In fifteen cases it had not been tested, so that no conclusion could be drawn as to the comparative effect of boiling. In the twelve cases it was not changed by boiling in one way or another. In the fifteen cases it was impossible to make the experiment by injecting urine immediately drawn. The four deaths show that urine may be toxic when passed. In remains to be shown to what extent boiling reduces toxicity, if at all, on account of a possible effect upon it by ferments or other bodies, as well as by bacteria. The latter must be taken into especial consideration, because all of these specimens were taken from women immediately before, during or immediately after labor.

4. In urine that was boiled immediately and used after it had been kept the result was n peculiar one. The longer it was kept the more toxic it became. The following experiment was made to show this: 150 c.cm. was passed hy a healthy individual; this was divided into eleven parts, all of which were hoiled except one. This one was injected (1.5 c.cm.) into a mouse nnd found non-toxic; the rest were hoiled and put into Erlemeyer flasks. One of these was immediately injected into a mouse and found non-toxic; the rest were injected twenty-four hours apart until all had heen used. The result was death in all cases, notwithstanding the fact that the quantity of urine was reduced daily. At first the attempt was made to count the hacteria with an eye-piece micrometer, hut this was very soon given up, on account of the enormous increase of hacteria. In these cases, after forty-eight hours, evidences of peritonitis were found in these mice, forming one of the exceptions to the rule stated before. The enormous mortality in this series of experiments, as compared with the general mortality (39 per cent.), is simply explained hy the fact that all the other experiments were made in cold weather, from November to March, while this series was done during the very warm weather of spring (from 70° to 85° F., in the middle of the day). It seems, then, that hoiling once is sufficient to kill hacterin, hut not their spores; and, as in sterilizing milk, as was shown hy Flügge, the spores developed and finally produced the same effects as were primarily produced hy the hacteria.

5. Some authors have recommended the addition of horio acid to prevent development of hacteria; for this reason the series was instituted. Here it was also shown that little influence was exerted, and that the longer the mixture was kept the greater the mortality. In a series puhlished hy one of us (Stewart, *loc. cit.*) the mortality was 100 per cent. In this series no account was taken of time of taking urine and its injection, although the tahle seems to show that urine kept with horic acid does not hecome toxic more rapidly than urine kept and used after heing hoiled; this, again, is on account of the difference in outside temperature, all of the experiments heing made during cold weather.

6. In regard to fresh urine which has heen kept for longer than twenty-four hours, it need only he snid that the largest mortality was arrived at hy this method; and in some of the mice that lived longer than eighteen hours there were also present evidences of peritonitis.

As a result of these investigations we heg leave to present the following conclusions as to the method:

1. Fresh urine injected immediately can he snfely used.

2. Filtered urine, immediately filtered and immediately injected, can he safely used.

3. Urine hoiled and injected immediately should not he used unless

error caused by possible changes within the body of the patient he first eliminated.

4. The addition of boric acid does not give reliable results.

5. Urine should never be used that has stood for twenty-four hours.

6. The method cannot be used for exact determinations of toxicity in that a range of from 25 per cent. to 50 per cent. of error is found for individual cases.

The conclusions as to toxicity of urine can be only tentative as applied to all the cases, but they are positive for the majority. If the table be examined it will be seen that those two methods which exclude bacterial activity absolutely after the urine is passed are followed by comparatively no mortality; in fresh urine immediately used, only one death out of fourteen; in filtered urine, no deaths, even after the urine had been kept as long as four days; in urine with boric acid used before the lapse of twenty-four hours, a mortality of 39 per cent.; after twenty-four hours, a mortality of 43 per cent.; in boiled urine kept for longer than twenty-four hours, a mortality of 39 per cent.; and in fresh urine kept for longer than twenty-fours, a mortality of 66 per cent.

It would seem, then, that most of the toxicity of urine was due to the formation of substances the result of the action of bacteria upon some body or bodies in the urine. As a result of this investigation, we are not justified in stating that there is no other toxicity except that due to bacterial activity; but we are justified in making the statement that all those investigations that have been made in which this activity has been overlooked are to be regarded as inconclusive.

Finally, one of us wishes to make a scientific retraction of a statement made in a paper read before this Society. In connection with some investigations made upon chlorosis, one of us found a toxic body in the urine; this toxic body, in the light of the present investigations, was not the result of chlorosis but of a faulty method. In so far as this body has any effect upon the theory of the origin of chlorosis, this theory is hereby discarded.

THE DISEASE OF CONVULSIVE TIC (GILLES DE LA TOURETTE'S DISEASE),

WITH SPECIAL REFERENCE TO A HYPOTHESIS AS TO ETIOLOGY.

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Some confusion still exists in the classification of conscious spasmodic movements which are not manifestations of well-established clinical entities, such as Sydenham's chorea, Jacksonian epilepsy, etc. Of these