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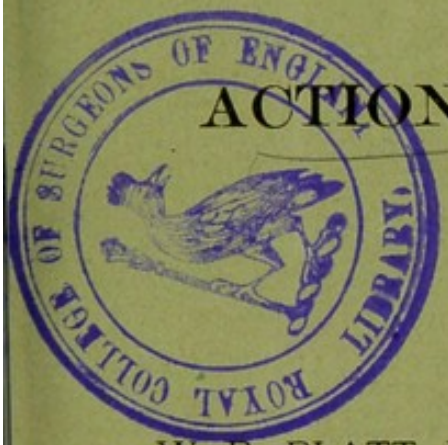

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SOME OBSERVATIONS ON THE ANTISEPTIC AND PHYSIOLOGICAL ACTION OF RESORCIN.

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Resorcin was discovered by Hlasiwitch and Barth, in Vienna, in 1864. They obtained it from galbanum and ammoniac, two well-known gum resins. It has also been obtained from Brazil-wood, but is now usually made by melting phenol-sulphonic acid with caustic potassa. In America it costs about $2.50 per ounce; in Germany, half that sum. Any increased consumption would doubtless largely reduce the market price, as it is at present made only on a small scale.

Chemically.—Resorcin belongs to the phenol group, phenol (carbolic acid) being $C_6H_5(OH)$, while resorcin is $C_6H_4(OH)_2$. It is isomeric with two other members of the same group, hydrochinon (which is already known to possess antiseptic qualities) and pyrocatechin. The latter has been little studied as yet.

Hydrochinon, quite similar in its general action to resorcin, is reported to have been investigated by Brieger, who finds it possesses a stronger antipyretic action than resorcin. Two decigrammes internally (0.2) depress the temperature of the body half a degree Cent. (nearly $1\frac{1}{2}°$ F.). The effect in depressing temperature is very brief. Larger doses, up to 1 gramme, cause symptoms of excitement, etc., similar to resorcin. It has no more local irritant action than water.

Resorcin.—Within the last few years attention has been called to the *antiseptic* action of resorcin, especially with reference to the question of its substitution for carbolic acid. Dr. J. Andeer, of Würzburg, as reported in the *Lancet*, Nov. 13, 1881, thinks a "1 per cent. solution of resorcin retards fermentation, a stronger solution arrests it, destroys movement of infusoria and low organisms. He finds a 1 per cent. solution pre-

vents putrefaction in blood, urine," etc. I shall endeavour to show that the antiseptic power of resorcin is much less than that of carbolic acid or alcohol, as far as its effect upon bacteria or the prevention of putrefaction may denote.

Therapeutically.—Resorcin has been employed internally and locally for the most diverse affections. Dr. J. Andeer[1] has used it extensively in acute and chronic cystitis, in which he claims for it an almost specific curative power. He reports "156 cases where, either by him or to his personal knowledge, it was injected into the human bladder, with the best results, in vesical catarrh. Acute cases have been entirely cured by the injection of a 5 per cent. solution of resorcin. In 1871 he injected 5 grammes into his own bladder." It has also been used as a local application in various diseases of the skin, caused or accompanied by low organisms, with alleged curative effect, and as an injection in gonorrhœa.

Andeer recommends a 1–2 per cent. solution as a spray for surgical purposes, and a 1–5 per cent. aq. solution for use internally. In Prof. B. von Langenbeck's clinic in Berlin, it has been used more or less since 1878 as an antiseptic to replace carbolic acid, with the best results, and with freedom from toxic effects when applied to wounds, etc. Resorcin catgut has also been employed by various surgeons recently as a ligature for arteries.

Lichtheim, as quoted in the *Lancet*, Nov. 13, 1881, finds that resorcin, in doses of 2–3 grammes in solution, causes giddiness, tinnitus, flushing of face, acceleration of pulse, and respiration. In ten or fifteen minutes patients begin to perspire freely; with the sweating, the primary stimulating effect passes off, and the pyrexia (in fever patients) subsides. An hour after the resorcin had been administered, the pulse and respiration were normal, and the diaphoresis had ceased. The depression of temperature in some cases amounted to 3° C. (=5.4° F.), and the fall in the pulse-rate to $\frac{1}{3}$. Pneumonia and erysipelas were influenced less as to lowering of temperature than typhoid fever, and severe cases of the latter less than mild ones. The antipyretic effect was of briefer duration than that of salicylic acid or quinine. In three hours the temperature usually rose again, often with a rigor. The dose may be repeated without injury to the patient. As a rule little excitement is produced, but occasionally delirium and tremor. The urine, after its administration, becomes brownish-black on exposure to air, and with hydrochloric acid and heat a dark-brown precipitate may result. Resorcin has apparently no specific effect in pneumonia, erysipelas, or typhoid fever. In acute rheumatism it has no influence on the joint affection. In intermittent fever it has a specific action comparable to that of quinine.

Soltmann is reported to have employed it in 91 cases of "cholera infan-

[1] Centralblatt für die Med. Wissenschaft., Sept. 3, 1881.

tum," of which 74 recovered. He thinks it reduces the mortality of that disease from 34 per cent. to 15 per cent., arresting vomiting and restraining the diarrhœa. He gives it to children under one year old in doses of 0.1–0.3 (1½ grains to 5 grains) in 60 c. c. chamomile tea.

Dujardin Beaumetz reports resorcin poisonous in doses of more than 6 grammes (93 grains).

J. Andeer (*Lancet*, Nov. 13, 1881) believes that sublimed resorcin is much less poisonous. He says it has a slightly caustic action on the mucous membrane, not causing a slough, and that the epithelium is regenerated in two to three days. He advises its use in chronic gastric catarrh, to wash out the stomach when dilatation is present. He also believes it to possess hæmostatic properties.

In the *Physician and Surgeon* (U. S.), April 1, 1882, a case of poisoning is reported where a woman of nineteen, who had been taking resorcin in doses of one to one and a half drachms, experienced from a dose of two drachms vertigo, formication, loss of consciousness, and depression of temperature to 35° C., but by use of the stomach-pump was out of danger in two hours. The resorcin had been employed in this case for the relief of spasmodic asthma. Resorcin causes an increased elimination of sulphur, probably by the breaking up of sulphur compounds in the body. Resorcin is eliminated by the kidneys (J. Andeer, *Centralblatt für die Med. Wissenschaft.*, Dec. 17, 1881) largely as such, but also as etheral resorcin sulphate of potassium. The so-called "resorcin-blue" is obtained by heating portions of the viscera from animals poisoned by hypodermic injections of resorcin, and collecting the sublimate. It is said to be identical with the colouring-matter obtained from the urine of typhus and cholera patients.

According to Fittig (*Organische Chemie*, p. 340) resorcin crystallizes in tables or columns, melts at 104° C., boils at 271° C., but evaporates at a lower temperature. It is very soluble in water, alcohol, and ether.

The resorcin used in the following experiments was obtained from Alfred Reichardt (N. Y.) as "pure resorcin;" melted at 104–106° C., and contained 1 per cent. of water, as kindly determined by Mr. C. J. Bell in the Chemical Laboratory of the Johns Hopkins University. It may therefore be assumed to be practically pure.

Unless otherwise especially stated, the baccilli urinæ, the ordinary bacteria seen in the urine of alkaline fermentation, are meant by the word "bacteria."

The vessels, glass rods, etc., were kept scrupulously clean during the examination. The latter, as well as the glass slides and cover glasses for microscopical examinations, were first cleaned and wiped; then passed through a gas-flame immediately before use to destroy any adherent bacteria. In experiments 1 and 2 a power of 220 diameters, in the succeeding ones of 550 diameters, was employed.

SERIES A.—*Experiment concerning Action of Resorcin upon Serum of Ox-Blood.*

Expt. 1.—*March* 6, at 4.40 P. M. The serum from ox-blood obtained from the animal this morning was filtered through animal charcoal, after which it appears pale red, almost transparent, showing under the microscope no bacteria, only a few red blood-corpuscles. Of this, 20 c. c. (5.3 fluidrachms) were placed in a clean wineglass just washed with boiling distilled water. 1 c. c. of a 5 per cent. sol. (aqueous) of resorcin (= 0.050 gram. = ¾ grain) was added. The glass with its contents was next placed in an incubating closet, covered, and kept at a temperature of 33°–35° Centigrade. This was labelled "1."

Expt. 1ª.—11 c. c. (about 3 drachms) of serum in a wineglass without addition of resorcin was subjected to the same conditions otherwise, placed in the incubator along with the resorcin-serum, and labelled "1ª."

Expt. 1. Serum *with* resorcin.—*March* 7, 3.45 P. M. After 23 hours. Temp. 35° C. Clear, pale red. A few white flakes adherent to sides of glass. A very slight sediment. Reaction faintly alkaline; odour fragrant. Rarely bacteria are seen. These are *not* in motion.

8th, 12.40 P. M. After 44 hours. Temp. 35° C. Fluid dark red or smoky; otherwise same as last. A few motionless bacteria present.

9th, 3.45 P. M. After 71 hours. Temp. 35° C. Upper layer of serum dark olive-green; fluid opaque. Reaction alkaline. *Moving organisms present.*

Expt. 1ª. Serum *without* resorcin.—*March* 7, 3.45 P. M. After 23 hours. Temp. 35° C. Turbid; redder than No. 1; otherwise the same, excepting that numerous rod-shaped, moving bacteria are *present.*

Conclusion.—¾ (.0.50) grain of resorcin retards the active development of bacteria in 5 drachms (20 c. c.) of ox-blood serum at least 21 hours.

SERIES B.—*Concerning Antiseptic Action of Resorcin and Carbolic Acid upon Normal Urine originally free from Bacteria.*

Expt. 2.—*March* 6, 1882, 5.15 P. M. Recently passed normal urine, faintly acid, transparent, and having as a sediment only an occasional epithelial scale or minute foreign body, is employed. Entire absence of bacteria large enough to be seen with a power of 220 diam. (Zeiss obj. D, ocular No. 2). In each of three wineglasses, labelled 2^1, 2^2, 2^3, is placed 20 c. c. of urine. To each glass 1 c. c. of the resorcin 5 per cent. sol. is added. They are placed in the hot closet and maintained at 30°–35° C., mostly 34° C. (each glass covered with a ground-glass plate). Two glasses labelled 2^a and 2^b containing each 20 c. c. of urine, without addition of resorcin, subjected to the same conditions, and likewise placed in hot closet.

7th, 11.20 A. M. After 18 hours, two of the glasses containing urine with resorcin, viz., 2^2 and 2^3, contain a few bacteria in motion. Urine appears otherwise normal. Urine alone, 2^a and 2^b, without resorcin, is strongly alkaline, pale, has an iridescent pellicle, contains crystals of triple phosphate, and many moving bacteria.

11th. After 6 days, 2^3 has become opaque, very black (almost like ink), strongly alkaline.

Conclusion.—0.050 (= ¾ grain) of resorcin has a very slight influence in retarding development of bacteria in 20 c. c. of urine, for a time, within 18 hours.

Expt. 3.—*March* 7, 1882, 4.30 P. M. Clear, yellow, freshly passed, slightly acid urine, free from bacteria, was employed. 20 c. c. of this is placed in each of three wineglasses which contain 2 c. c. each of a 5 per cent. aqueous solution of resorcin. These are labelled respectively 3^1, 3^2, and 3^3. 20 c. c. of same urine without resorcin placed in a marked glass, and about 40 c. c. of urine placed in a flask stopped with cotton. All the above 5 glasses placed in hot-air closet where the temperature is kept by a self-regulating gas-jet at 33°–35° C.

8th, 10.30 A. M. Temp. of closet 35.°1 C. The marked glass and the flask containing *urine alone* examined, eighteen hours after beginning of experiment.

Urine in *marked glass.*—Turbid. A white precipitate in apex of wineglass.

Reaction strongly alkaline. Strong urinous odour. An iridescent pellicle on surface of urine. Rod-shaped, beaded bacteria, in motion, *present*.

Urine in *flask*.—Turbid; white precipitate in bottom. Reaction strongly alkaline. Strong urinous odour. Iridescent pellicle upon surface of fluid. Rod-shaped, beaded bacteria, in motion, *present*.

March 7, 4.30 P. M., 3^1. 20 c. c. of clear, yellow, acid, fresh urine free from bacteria, to which is added 2 c. c. (0.100 resorcin) of a 5 per cent. aqueous solution of resorcin.

8*th*, 4.45 P. M. After $24\frac{1}{4}$ hours. Temp. 34° C. 3^1. Perfectly clear; reaction neutral or faintly alkaline; no sediment. *No bacteria*.

9*th*, 3.45 P. M. After $47\frac{1}{4}$ hours. 3^1. A very slight commencing turbidity. Reaction neutral. *Bacteria* (beaded) *present and in motion* (bacteria have Pasteur's aureole well marked). Bacteria having been found after $47\frac{1}{4}$ hours, the specimen was examined as to the reaction March 10th and 11th, the latter at 3.45 P. M., thus after about 96 hours, when it is *still acid*. At 12 noon, March 12th, after 120 hours, the reaction *found alkaline*.

March 7, 4.30 P. M. 3^2. 20 c. c. of clear, yellow, fresh, faintly acid urine, free from bacteria, was employed. To this is added 2 c. c. of a 5 per cent. sol. of resorcin (= 0.100 resorcin). Same as 3^1.

8*th*, 4.45 P. M. After $24\frac{1}{4}$ hours. Temp. 34° C. 3^2. Clear. Reaction neutral or slightly alkaline. A very few motionless bacteria present.

9*th*, 3.45 P. M. After $47\frac{1}{4}$ hours. Temp. 34° C. Slight commencing turbidity. Reaction faintly *alkaline*. Odour as of stale urine. *Bacteria present in motion*.

10*th*. Reaction acid. 11*th*. Acid. 12*th*. Neutral. 13*th*. Neutral. Up to 27*th*. Clear.

March 7, 4.30 P. M. 3^3. 20 c. c. of clear, yellow, freshly passed, faintly acid urine, free from bacteria, was employed. To this is added 2 c. c. of a 5 per cent. sol. of resorcin = 0.100 resorcin. Same as 3^1 and 3^2.

8*th*, 4.45 P. M. After $24\frac{1}{4}$ hours. Temp. 34° C. 3^3. Clear. Normal. *No bacteria*.

9*th*, 3.45 P. M. After $47\frac{1}{4}$ hours. Temp. 34° C. 3^3. Contains *bacteria in motion*.

10*th*, 11.05 A. M. After $31\frac{1}{2}$ hours. Temp. 34° C. 3^3. Clear. Acid. A very slight deposit in glass (phosphates).

11*th*. Reaction acid.

12*th*, 11.05 A. M. After 4 days 19 hours. Reaction alkaline.

Expt. 4.—*March* 9, 4.30 P. M. Freshly passed urine is filtered and boiled, 4 drops of hydrochloric acid added to dissolve the phosphates separating.

5.30 P. M. Divided into 8 portions of 20 c. c. each, placed in wineglasses as follows:—

No. 4. Urine alone. No addition.

No. 4^1. " "

5, 5^1, 5^2. 3 c. c. of a 5 per cent. solution of resorcin added to each.

6, 6^1, 6^2. 1 c. c. of a 5 per cent. solution of crystallized carbolic acid added to each. (Calvert's No. 1.)

All the above are put in the hot-air closet and kept at temperature of 32°–34° C.

March 10, 1882, 11.05 A. M. Thermometer at 34° C. $17\frac{1}{2}$ hours after experiment began. No. 4. Urine clear, yellow, acid, no precipitate. No bacteria.

11*th*, 3.45 P. M. After 46 hours from commencement of experiment. Thermometer 35° C. Clear, transparent, acid, no ppt. No bacteria.

12*th*, 11.05 A. M. After $65\frac{1}{2}$ hours. Commencing dimness of urine. Reaction slightly acid. Odour about normal. *Plenty of bacteria*, beaded, *moving* (2-, 4-, 6-celled).

13*th*, 10.50 A. M. Thermometer 34° C. After $89\frac{1}{4}$ hours. Paler. Slightly turbid. A slight white ppt. in apex of glass; flaky ppt. on sides of glass. Odour stale urinous. Reaction faintly acid.

14*th*, 3.20 P. M. Thermometer at 35° C. Same as last, excepting a slight film has formed on surface. ($117\frac{3}{4}$ hours.)

15*th*, 4.10 P. M. After about 6 days. Turbid. Reaction acid, pale yellow.

Urine No. 4[1].—*March* 10, 11.05 A. M. Thermometer at 34° C. After 17½ hours. Apparently perfectly normal. No bacteria.

11*th*, 3.45 P. M. Thermometer 35° C. After 46 hours. Commencing dimness of fluid; slight ppt.; reaction acid; very rarely a moving organism seen.

12*th*, 11.05 A. M. After 65½ hours. Same as before, except reaction neutral, and moving, beaded *bacteria are present.*

13*th*, 10.50 A. M. Thermometer 34° C. After 89¼ hours. Paler, slightly turbid; white ppt., stale odour; reaction faintly acid. Bacteria as before.

14*th*, 3.20 P. M. Thermometer 95° C. After 117¾ hours. Somewhat more turbid; a film forming on surface, as in No. 4.

15*th*, 4.10 P. M. After about 6 days. Clearer; reaction acid; a precipitate on bottom and sides of the glass.

Expt. No. 5.—20 c. c. urine containing 0.150 gramme of resorcin (3 c. c. of sol.).

March 10, 11.05 A. M. Thermometer 34° C. After 17½ hours. Fluid clear; reaction acid. *No bacteria.*

11*th*, 5 P. M. Thermometer 35° C. After 47½ hours. Clear flakiness on sides of glass; faintly acid. *No bacteria.*

12*th*, 12 noon. After 66½ hours. Clear; a very slight ppt.; reaction neutral. *No bacteria.*

13*th*, 12.55 P. M. Thermometer 34° C. After 92 hours. Reaction acid; colour yellow, clear. *No bacteria.* Crystals of oxalate of lime seen.

14*th*, 3.20 P. M. Thermometer 35° C. After 117¾ hours. Same as last note.

15*th*, 4.10 P. M. After about 6 days. Same as last note.

6*th*, 8.35 P. M. After about 7 days. Same as last note. Still no bacteria.

17*th*, 11.30 P. M. Thermometer 33°. After about 8 days. Same as last. Reaction still acid. In addition a very few distinct rod-shaped, *motionless bacteria* are seen.

18*th*, 10.30 A. M. After 9 days and 17 hours. Clear, darker in colour than yesterday; reaction acid. *No bacteria*, but a few large motionless double cells are seen. Oxalate of lime crystals as before.

20*th*, 10.35 A. M. Temperature 26°. After 10 days and 17 hours. Same as last note, only a *few* minute oval moving organisms are seen.

21*st*, 3.30 P. M. Temperature 35°. After about 11 days. Same as last note. No beaded bacteria now seen; other organisms rarely seen.

27*th*, 3.45 P. M. Temperature 34° C. After 18 days. Clear, red, yellow, acid. Same as last, except no further examination for bacteria. A slight flaky film on surface.

5[1] (20 c. c. of urine containing 3 c. c. of a 5 per cent. resorcin solution = 0.150 gramme).

March 10, 11.05 A. M. Thermometer 34° C. After 17½ hours. Same as No. 5. No bacteria.

12*th*, 12 noon. After 66½ hours. Same as No. 5, except reaction slightly acid. *No bacteria.*

13*th*, 4 P. M. Thermometer 34° C. After 3 days 22½ hours (94½). Clear, acid, crystals of oxalate of lime seen. *No bacteria.*

14*th*, 3.20 P. M. After 117¾ hours. Thermometer 35° C. Same as before, only a few motionless bacteria seen.

15*th*, 4.10 P. M. About 6 days since experiment began. Urine still clear, yellow, acid. No moving bacteria seen.

16*th*, 3.35 P. M. Thermometer 36°. After about 7 days. Same as last note.

17*th*, 11.30 A. M. Thermometer 33°. After 7 days 18 hours. Same as last note.

18*th*, 10.30 A. M. After 8 days 17 hours. Clear yellow, but darker than before. Reaction acid; a large gelatinous mass has formed in the urine. *Many bacteria in motion* seen.

20*th*, 10.35 A. M. Thermometer 26°. After about 11 days. Clear; colour, orange-red; slight cloud in bottom of glass. Not examined further for bacteria.

27*th*, 3.45 P. M. Thermometer 34°. After about 18 days. Reaction acid; colour of Port wine, otherwise as last note.

5^2. 20 c. c. of urine to which was added (Mar. 9th) 3 c. c. 5 per cent. resorcin sol. = 0.150 gramme resorcin.

March 10, 11.05 A. M. Thermometer 34°. After 17½ hours. Same as 5^1. No bacteria.

12*th*, 12 noon. After 66½ hours. Clear, slightly acid, normal.

13*th*, 4 P. M. About 4 days after beginning of experiment. Clear, acid, crystals of oxalate of lime. A very few *motionless* bacteria seen.

14*th*, 3.20 P. M. Temperature 35° C. After 117¾ hours. Clear, yellow, acid. No bacteria seen. Oxalate of lime crystals.

15*th*, 4.10 P. M. About 6 days after experiment began. Clear, yellow; a cloud-like growth in bottom of glass; a tree-like fungus (species not identified) floating in fluid; reaction slightly acid. No bacteria seen. A few large, spherical, granular, nucleated cells seen.

16*th*, 3.35 P. M. Thermometer 36° C. About 7 days after beginning of observations. Clear, dark, reddish-brown, acid. The mould on surface is now brownish-black, with white fringe. No bacteria seen.

17*th*, 11.30 A. M. Temperature 33°. After 7 days 19 hours. Same as yesterday, only mould increasing rapidly in diameter. A few motionless beaded bacteria seen.

18*th*. Acid.

20*th*. Acid; numerous moving organisms, not the typical bacteria of urine; oxalate of lime crystals; uric acid crystals.

23*d*, 10.30 A. M. After 14 days. Reaction alkaline; bacteria seen March 13th (*after* 4 *days*), *motionless*; other moving organisms seen March 18th, *after* 9 *days*.

Expt. 6 (20 c. c. of urine + 1 c. c. of a 5 per cent. sol. of crystallized carbolic acid = 0.050 carbolic acid).—*March* 10, 1882, 11.05 A. M. Thermometer 34° C. After 17½ hours. Clear, acid, no ppt. No bacteria.

11*th*, 3.45 P. M. Temp. 35° After 46 hours. Clear, acid, slightly flaky ppt. on sides of glass. No bacteria.

12*th*, 11.05 A. M. After 65½ hours. Clear, slightly acid, a slight deposit, crystals of calcic oxalate present. No bacteria.

13*th*, 10.50 A. M. Temp. 34° C. After 89¼ hours. Clear, yellow. Same as last note.

14*th*, 3.20 P. M. Temp. 35°. After 117¼ hours. Same as last note. Perhaps crystals of oxalate of lime increased.

15*th*, 4.10 P. M. After about 6 days. Same as last note. No bacteria.

16*th*, 3.35 P. M. Temp. 36°. After about 7 days. Same as at last note. No bacteria.

17*th*, 11.30 A. M. Temp. 33°. After *about* 8 days. Still same as last note.

18*th*, 11.10 A. M. After about 9 days. Same as last, except fine flakes floating in fluid

20*th*, 10 35 A. M. Temp 26°. After 10 days, 17 hours. Same as last note.

21*st*, 23*d*, 27*th*. Same as last note. *No bacteria.*

28*th*. Gross appearances still the same.

29*th*, 4.15 P. M. After 20 days. Clear; reaction acid; light brown, flaky deposit on sides of glass resembling ppt. of urates. *Bacteria present* in motion.

No. 6^1 (20 c. c. of boiled, filtered, acidulated urine plus 1 c. c. of a 5 per cent. solution of crystallized carbolic acid).—*March* 9, 5.30 P. M. Same as No. 6.

10*th*. Same as No. 6. No bacteria. An occasional iridescent flake seen on surface of the solution.

12*th*. Clear, acid

13*th*, 4 P. M. Temp. 34° C. After 3 days 22½ hours. Clear, slightly acid. No bacteria. Many crystals of calcic oxalate.

14*th*. Same as last note

15*th*. Same as last. No bacteria.

16*th*. Still unchanged since last note.

21*st*. Same as last.

23*d*. Same as last.

25*th*. Removed from hot air-closet, exposed to ordinary temperature of laboratory (about 70° F.).

27*th*. After 18 days. *Moving organisms seen*, but not the usual bacillus. Reaction acid.

28*th*. Same as last.

29*th*. After 20 days. Numerous large rod-shaped moving bacteria seen (not the ordinary beaded bacteria of stale urine). Reaction still acid.

6^2. 20 c. c. of freshly passed filtered or boiled urine, to which four drops of hydrochloric acid has been added to dissolve the precipitated phosphates. *March* 9, 4.30 P. M. To this is added (as in 6 and 6^1) 1 c. c. of a 5 per cent. sol. of crystallized carbolic acid (= 0.050 carbolic acid).

10*th*, 10.05 A. M. Temp. 34° C. No bacteria. Unchanged. Reaction acid.

12*th*, 12 noon. Clear, faintly acid.

13*th*, 4 P. M. Temp. 34° C. No bacteria. Crystals of calcic oxalate. Reaction faintly acid.

14*th*, 3.20 P. M. Temp. 35° C. No bacteria. Same as last note.

15*th*, 4.10 P. M. Clear, acid. No bacteria.

16*th*, 3.35 P. M. Temp. 36° C. Same as last note (after 7 days).

21*st*, 3.30 P. M. Temp. 35° C. Clear, yellow, *acid*; a few specks in fluid; very rarely a *moving organism* is seen (after 12 days).

23*d*, 10.30 A. M. Clear, yellow, acid. No beaded bacteria seen (ordinary variety). Numerous circular, colourless, motionless cells, half size of red blood-corpuscle. After careful search one or two circular or molecular organisms found with apparent motion (after 14 days). Temp. 33° C.

27*th*, 3.45 P. M. Temp. 34° C. Large bacteria, in motion, seen. Not the B. urinæ. Evidences of organic life seen after 7–12 days.

SERIES C.—*Concerning action of various Antiseptics upon Bacteria in Urine.*

March 14, 3.20 P. M. Urine is taken which has stood in a flask one week, found to contain moving bacteria, and to be alkaline after 19 hours. It contains now plenty of moving bacteria of the ordinary variety. Reaction neutral. A 5 per cent. sol. of resorcin is dropped in from a burette, and frequent examinations made to determine the quantity necessary to cause the motion of the bacteria to cease. 5.15 P. M. To 20 c. c. of the urine 0.6 + 0.4 + 0.6 c. c. of the 5 per cent. resorcin sol. added. At the third examination many bacteria are motionless, but still moving bacteria remain. Then 0.4 and 1 c. c. added; motion still persists in some bacteria. 3 c. c. in all were added (= 0.150) of resorcin to 20 c. c. urine.

Expt. 7.—*March* 15, 1882, 6.00 P. M. To 20 c. c. of boiled and filtered freshly passed urine is added 1.1 c. c. of a 0.1 per cent. solution of *thymol*, and placed in hot-air closet. Amount of thymol = to about one milligramme (0.001). About 60 c. c. of the urine without any addition, placed in a flask, marked O, and also put in hot-air closet.

16*th*, 3.35 P. M. Temp. 36° C. After 21½ hours. Urine in *flask O, acid*, clear. Many moving, rod-shaped, large, 5-6 celled bacteria present.

16*th*, 3.35 P. M. Temp. 36° C. After 21½ hours. Slightly dim, reaction neutral, plenty of moving rod-shaped beaded bacteria present. Evidently no appreciable effect from this proportion of thymol.

31*st*, 12.05 A. M. 1 c. c. thymol solution (1:1000) added to 1 c. c. urine containing many actively moving typical bacteria. Motion of bacteria almost entirely ceases, difficult to say whether the motion here is inherent or is caused by currents in the fluid. After 4 hours. Bacteria seen plainly to move. 1 c. c. more added (2 in all) of thymol sol. Bacteria still more. 1 move, 3 in all; bacteria still move. That is three milligrammes of thymol in 1 c. c. urine does not destroy motion of bacteria. To 1 c. c. of bacteria urine, is added 1 c. c. of 95 per cent. *alcohol*. Bacteria disappear almost entirely. The few seen were motionless. To 1 c. c. bacteria urine is added 2 c. c. 95 per cent. alcohol. No moving bacteria seen. These last two especially difficult to examine since the alcohol evaporates with great rapidity, leaving the solid constituents of the urine on the slide.

Expt. 8.—*March* 21, 1882, 3.30 P. M. Temp. 35° C. Urine 6 days old from flask O employed. It is alkaline, contains many 2-celled rod-shaped, typical, moving bacteria. 20 c. c. placed in wineglass, 3 c. c. of 5 per cent. sol. resorcin

added. Bacteria still move. 1 more (9 in all), motion persists. More added up to 6 c. c. Motion ceases (6 c. c. = 0.30 resorcin).

23*d*, 3.15 P. M. Temp. 40°. Urine from flask O, filtered (8 days old). Reaction alkaline, contains many 2-celled rod-shaped, typical, actively moving bacteria, 20 c. c. of the urine employed. To this 4 c. c. of the resorcin solution added: motion persists: 5 c. c. added. Bacteria nearly all float, vertically and motionless in fluid. The resorcin solution now added in small quantities up to 8 c. c. (= 0.40 resorcin): motion persists in a few bacteria.

24*th*, 11.45 A. M.—After 20½ hours. The solution last mentioned (20 c. c. urine and 8 c. c. sol. resorcin) is swarming with bacteria in motion. Urine labelled No. 8 containing 6 c. c of 5 per cent. sol. resorcin in 20 c. c. (alkaline bacteria containing urine), shows now, after 68¼ hours, a very *dark-red olive* colour. Appears much like the "carbolic urine after carbolic poisoning."

27*th*, 3.45 P. M.—The urine after 6 days (c. resorcin), is almost inky-black: perfectly opaque in wineglass.

31*st*. After ten days. Still almost inky-black. Reaction alkaline: no offensive odour; occasionally a few moving bacteria seen; no sediment.

May 3*d*.—After six weeks, unchanged: odour fragrant: no sediment: colour same as before.

March 24, 11.45 A. M.—20 c. c. of *urine* from flask O. 9 days standing, alkaline, and containing many typical rod-shaped bacteria in motion. 8 c. c. resorcin sol. added (= 0.40 resorcin). The bacteria float for the most part vertically motionless in the fluid. Some still vibrate horizontally: 1 more c. c. added, 1 more c. c. added up to 15 c. c. of resorcin sol. (= 0.75 resorcin). Motion persists in a few bacteria. Urine now stands 4 hours, when all bacteria seen in active motion again; 5 c. c. more resorcin sol. added gradually (20 in all) to 20 c. c. s. urine. Bacteria motionless for most part. A number still vibrate. To one small drop of the bacteria urine from flask O, are added two drops 5 per cent. sol. (crystallized) *carbolic* acid. Some bacteria still retain active motion. To 2 c. c. s. of the bacteria alkaline urine from O, are added 6 c c. s. resorcin sol. (Three times as much resorcin solution as urine.) Bacteria mostly float vertically motionless. Some still move.

25*th*. 3.45 P. M. To 2 c. c. bacteria urine from O, ten days old, are added with frequent examinations 12 c. c. s. resorcin 5 per cent. sol. Motion of bacteria persists. Thus 0.60 resorcin does not destroy motion in 2 c. c. s. of bacteria urine ten days old.

28*th*. A 10 per cent. sol resorcin made (1 gramme to aq. 10). An alkaline filtered urine containing many bacteria used. 2 c. c. s. urine, to this are added by degrees 4 c. c. s (= 0.40) resorcin of the resorcin sol. Motion of bacteria much slower; the remainder of the 10 c. c. s. added—1 *gramme* resorcin in all to 2 c. c. s. urine—motion persists in the bacteria. 1 gramme resorcin dissolved in 5 c. c. water; this was added to 1 c. c. bacteria urine; motion of bacteria very slow, but persists. 1 gramme resorcin dissolved in 1 c. c. water; this added to 1 c. c. bacteria urine. By most careful observation a slight vibratile motion detected. Mostly they float motionless vertically. 1 gramme solid resorcin dissolved in 1 c. c. urine (bacteria containing), *faint motion* persists, although fluid crystallizes on sides of glass.

31*st*. 12.05 A. M. 1 c. c. 5 per cent. carbolic acid solution added to 1 c. c. of urine containing bacteria. The 2–4-celled rod-shaped bacteria continue in motion, although much less after ten minutes than at first. Still very active. 1 more (2 in all) c. c. of carbolic solution added, mixture smells strongly of carbolic acid. Motion of bacteria almost nil, still it is distinct although slight. 1 more added (3 in all) of carbolic solution to 1 c. c. urine. Slight motion persists in bacteria. (Brownian.)

Summary.—From the above experiments, taking the *minimum* time in each series that bacteria developed in 20 c. c. of urine, exposed to favourable conditions, it appears that 0.050 of resorcin has no appreciable influence, bacteria developing within eighteen hours.

Twice that quantity (0.103) kept urine free from bacteria twenty-four hours, six hours longer.

While 0.150 deterred their development to four days.

Urine without any addition showing bacteria within eighteen hours.

If urine be *boiled*, organisms are found usually considerably later, forty-six to sixty-five hours.

0.050 gramme of carbolic acid hinders development of other *living organisms* (large enough to be detected by a power of 550 diameters) in boiled urine at least twelve days, bacteria eighteen days, the usual bacillus not developing at all. While 0.150 of *resorcin* (about $2\frac{1}{2}$ grains) hinders development of bacteria four days; one-third that amount of carbolic acid preserves a similar amount of urine free from organic life, under similar conditions, three times as long.

The cause of the olive-black coloration of No. 8 (urine with resorcin) was not determined. The same appearance was observed in several other specimens where the amount of resorcin was not noted.

Since resorcin is one of the phenol series and the above-mentioned coloration is so strikingly similar to that observed in urine of carbolic poisoning, may it not be possible that the urine in carbolic poisoning receives its distinctive olive-black colour after secretion by the kidneys, or while in bladder. In none of the *animals* poisoned by resorcin was the urine seen to be coloured as above.

The same bacilli (apparently) seem to have greatly differing power of resistance to action of antiseptics at different ages, and while a few milligrammes of resorcin or carbolic acid deter their development, yet when *once formed* three times the quantity of 5 per cent. carbolic acid solution, as compared with the *bacteria* urine, does not entirely destroy their motion; and 1 gramme of *solid resorcin* added to 1 c. c. of urine does not entirely destroy motion of the baccillus urine.

While all antiseptics do not destroy motion of bacteria already in existence, they may prevent their increase, and so greatly diminish the bad effects of their presence in the discharge from wounds, etc.

The experiments with thymol in arresting motion of bacteria show it to have proportionally considerable power. Its feeble solubility in water prevents its being used in strong solution.

Alcohol arrests motion of bacteria at once (agrees with exp. of Dr. Sternberg, *vide* Studies from Biological Laboratory of the Johns Hopkins Univ., April, 1882).

It must not be forgotten that experiments with antiseptics upon bacteria show antiseptic power only in a general way—different species of bacteria and micrococci require widely different fluids and temperatures for their development—temperatures and fluids in which one species thrive may be fatal to another. The same may be true of antiseptics not actually caustic in their nature. The power of resistance to the action of

antiseptics, of the *same species* of bacteria, appears to vary with the age of the bacteria if kept in the same fluid. The introduction of one species of bacteria or micrococcus into a fluid seems often to be fatal to the existence of another variety already present. The same fluid at different times showing a regular series of bacteria, each in its turn breaking up some complex organic substance into simpler ones. This done, and their nutriment being thus exhausted, they perish, only to allow of the development of a variety capable of attacking and breaking up remaining organic compounds.

The following experiments were undertaken to determine the amount of resorcin, and the time necessary to produce death in dogs and rabbits of different weights, the cause of death in such cases, and the duration of symptoms in cases where the animals recovered. Also, the physiological action, as far as that could be determined by hypodermic injections, of an aqueous solution of resorcin.

Series D.

Expt. 1.—*April* 3, at 4 P. M. A small, white, female poodle-dog, weighing 4310 grammes, injected with 2 grammes of resorcin dissolved in 5 grammes of boiled distilled water. Injections made in five places beneath skin of abdomen. 4.07. Dog, until now quiet, begins to tremble, pants, stands uneasily, constantly raising his paws off the floor. Respiration becomes extremely rapid, 105 to the minute. 4.12. Leans against side of glass cage, growls, whines, and howls. Rapid respiration continues. Urinates. 4.15. Staggers; takes water. 4.18. Falls to floor; tries to rise; cannot walk; remains lying against side of cage. No longer whines, etc. Rapid respiration continues. Tail in constant motion. Twitching of legs. 4.22. Rises, arches back, extends legs, tail erect, eyes protrude. 4.23. Crouches, saliva drips from mouth, tries to walk. Respiration as before. 4.24. Crouches constantly, arches back, saliva flows profusely. 4.26. Cannot rise, paws the air constantly, lying on side. 4.28. Respirations 61 to half minute (61 inspirations). Clonic contractions of legs which remain mostly in extension. 4.31. Respiration same. Eyelids unduly retracted. Motion of hind-legs much slower; tetanic extensions of same; motion of fore-legs extremely rapid. 4.34. Animal lies upon side. Very rapid motion of legs as if running. 4.36. Rolls and tumbles about. 4.38. Much slower movement. 4.40. Head thrown far back, mouth wide open. Incessant motion of legs as before. Respiration as before. 4.48. Exact imitation of running movements well executed. Dog still on side as before. 4.51. Running movements less complete. More complete extension than flexion. Legs are thrust further back; fore-paws sometimes move together, again alternately. The animal, lying on right side, moves slowly in a circle. Respiration as before. 5.09. No flow of saliva for some time. Motion of hind-legs incomplete; much extension. 5.18. Respiration becomes irregular, 73 to ½ minute. Biting motion. 5.20. Respiration stops a full minute. Struggles increase. Apparent spasm of respiratory muscles. Head now not drawn back. 5.23. Respiration now regular, rapid. 5.25. Hoarse sound on respiratory acts. Pawing motion again constant. More flexion than extension; most complete with fore-paws. 5.31. Respirations 70 to minute, slower; nasal râles. 5.34. Dog still on right side. Left fore-paw 48 flexions per minute. 5.36. Motion of legs much less; now only a constant twitching of all legs. 5.37. Winks constantly. Respirations 64 to half minute. 5.39. Animal quieter. 5.42. Yelps a few times. Rapid opening and closing of jaws. 5.44. Attempts to roll over. Muscular contractions intermittent; depressors of lower jaw spasmodically contract; sometimes all four legs contracted at once. 5.46. Raises head. A tetanic contraction of the extended legs. 5.48. Lies

quietly, slowly relaxing. 5.49. Death after one hour and forty-nine minutes. 5.51. Tail, which has been up from beginning, slowly falls.

Autopsy.—April 4, 10.20 A. M. 17 hours after death. Rigor mortis marked. Weight 4170 grammes—a loss of 140 grammes since beginning of experiment. At two places on skin of abdomen where injections made are white, slightly elevated spots surrounded by red areola, resembling a recent burn. On right side, near a nipple, where injection made, is a hard lump, 1½ inches long, adherent to skin. In cornea of left eye a large rectangular opaque area. Just above this, on ocular conjunctiva, a considerable subconjunctival hemorrhage. *Heart.* Right ventricle distended with blood; left ventricle firmly contracted. *Spleen* apparently normal. *Stomach.* 4.10 P. M. On lower aspect, near pylorus, an area of punctiform hemorrhages into submucous coat. On posterior aspect of greater curvature are two subperitoneal hemorrhages, oval in shape, about ½ inch in long diameter. Lungs float in water. Lower lobes much congested; upper portions pink; crepitate on pressure. Color in general dark. Numerous light areas on surface, elevated, containing air. Liver spotted on surface with oval and round spots (white), ¼–$\frac{1}{16}$ inch in diameter. Gall-bladder distended with green bile. Kidneys apparently normal. Bladder firmly contracted, containing no urine. Brain. Moderate injection of cerebral vessels in substance of brain. Much injection of vessels of pia mater. Spinal cord. Membranes of cord much injected. Substance of cord not at all. Sections made every half inch.

Expt. 2.—*April* 8, at 4.39 P. M. Female black and tan dog. Weight 4517 grammes. Injected with *one* gramme of resorcin dissolved in 3 c. c. distilled water. 4.40. Commences gaping and licking jaws; this repeated numerous times. 4.41. Restless, moves about, trembles, lies down and rises almost immediately. 4.42. Sits up and lies down. Continues to lick jaws. Left legs tremble, gait uncertain; leans against cage, with closed eyes. Hind-legs frequently lifted up and put down at once. 4.52. Slightly tremulous, changes position frequently, again lies down with nose between paws. 4.54. Respirations are 22 to the minute. 4 55. Sits quietly. Occasional tremor of head. Tremor of tail marked; also of left hind-leg. Animal sitting. Upper eyelids quiver. Dog leans against the wall, quiet, tends to keep eyes closed. 4.54 P. M. Sits up. 4.55. Holds up right fore-paw high in the air, quivering. Up to 5.07 P. M. Slight twitching and tremor continue. At end of that time twitching almost none. Respirations 14 to the minute. Dog still drowsy. Tail constantly erect. The day following the dog seemed well, and had no further ill effect from the 1 gramme of resorcin.

Expt. 3.—A black and tan male dog, weight 4675 grammes, injected at 5.08 P. M., *April* 10, '82, with 1.5 grammes dissolved in distilled water so that whole amount of solution = 5 grammes. This is injected in 5 places beneath skin of abdomen. The dog urinated copiously while being held. 5.15. Restless. Turns round and round constantly licking jaws; tail curved upwards. Up to 5.24 very restless. 5.24. Picks up feet constantly. 5.29. Same. Seems very unhappy; tremor of hind-legs. 5.30. Back arched as he moves about; holds up left fore-paw high in the air, quivering. 5.34. (Same as preceding dog.) 5.38. Crouches and rises instantly. 5.44. Staggers, tumbles. Steps about constantly. 5.52. Spasms of flexor muscles of tail. 6.14. Tail constantly incurved. Restless; can go about. 6.17. Expt. closed.

11*th.*—Dog of yesterday seen at 3.20 P. M.; has passed much fecal matter (apparently normal). Has a prolapse of rectum, considerable. Drags hind-legs after him, as if paraplegic; with much difficulty manages to stand. A viscid saliva drips from mouth. Animal passes urine copiously in leaning posture. 3.40. Froths copiously at mouth; lies down as if to sleep; frequent deep inspiration. 5.00. Sits up as if better. Believing dog would recover, I left him. He was seen at 6.12 by Mr. Lee, who kindly observed him until 7.31 P. M. Following said to have occurred, summarized: "6.12. Running movements of legs, dog lying on side. 6.14. Gasps, barks, foams at mouth, eyes glare, jaws snap. 6.14½. Running movements very rapid. 6.17. More violent movements, head thrown back. 6.20. Movements faster or slower, still continue breathing 150 per minute. Expirations take place synchronously with backward

movement of fore-legs. Up to 6.36 nearly same with occasional short intermissions. 6.36. Struggles further, a violent spasm, head drawn back at right angles to body, intermittent jerking of limbs. 6.42. Temperature very high, dog does not notice objects placed close to head Erection of penis. 6.54. Movements almost none. 6.57. Movements almost none, confined almost entirely to fore-legs. 7.02. No movement of limbs. Respiration 144 per minute; gasps. 7.08. Running movements recommence with fore-paws for a few seconds. 7.22. Dog appears almost normal, with slightly rapid respiration. Still does notice noises or objects; greatly exhausted. Animal *now left.*"

12*th* at 6 A. M.—Animal found dead, after at least 26 hours.

Autopsy.—April 12, at 11 A. M. Shows right side of heart greatly distended with blood. Left firmly contracted, endocardium stained red. In right auricle a firm gray-yellow fibrinous adherent clot. In lungs wedge-shaped infarctions. Stomach.—Near pylorus, staining red of mucous membrane, large amount of mucus in stomach. Bladder contained about 5 c. c. of greenish, turbid, faintly alkaline, highly albuminous urine, containing many spermatozoa, a number of epithelial and coarsely granular casts and leucocytes. Many oil globules. Brain and cord show nothing abnormal, macroscopically, except distension of cerebral vessels. Liver, spleen, and kidneys nearly normal.

Expt. 4. *May* 2 —Black and tan male dog, weight 5610 grammes, receives 2 grammes of resorcin in 8 c. c. water hypodermically at 5.15 P. M. 5.17. Uneasy, trembles, vomits frequently. 5.23. Fell over when trying to stand. 5.25. Twitching begins (of limbs). 5.29. Lifts up right front paw often. 5.39. Snaps with jaws frequently. 5.58. Can *stand;* twitching continues; conscious and intelligent. The snapping and twitching continued until at least 8.00 P. M. Dog apparently well next day from two grammes of resorcin.

Expt. No. 5.—*April* 5, '82, 3.55 P. M. A full-grown rabbit, male, weight 1935 grammes, injected hypodermically with 0.500 grammes resorcin at 4.54 P. M. 4.57½. Movements of fore-paw. 5. Movements of fore-paw continued. 5.08. *Very rapid respiration.* 5.21. Can stand up on hind-legs. 5.35. With exception of a few twitchings runs well and now normal. None the worse for ½ gramme of resorcin after 41 minutes.

Expt. No. 6.—*April* 13, 4 17 P. M. A female white albino rabbit, weighing 1915 grammes, injected beneath skin of abdomen with 1 gramme of resorcin dissolved in 2 c. c. distilled water. Injected in 3 places. 4.19. Very rapid respiration. 4.25. Some twitchings of limbs, also of neck muscles. 4.27. Some twitchings of abdominal muscles. 4.29. Ears twitch together; trembles. 4.30. Constant and rapid twitchings of legs. 4.38. All symptoms increase. 4.40. Staggers, nearly falls. 4.48. Constant twitching of tail. 4.53. Fore-legs kept extended as rabbit squats down; constant twitching of hind limbs. 5.04. Right hind-leg twitches 40 to a minute. 5.10. Twitchings almost stopped; respirations lower and shallower. 5.13½. Death after 56½ minutes from 1 gramme resorcin.

Summary.—Of four dogs, apparently healthy, 2 grammes were *fatal* to one female poodle weighing 4310 grammes (in proportion 1 to 2155), after 1 hour and 49 minutes, but *not* fatal to a small terrier, weighing 5610 grammes (proportion of 1 to 2805). Symptoms continuing at least three and not more than 17 hours. 1½ grammes killed a dog, male terrier, weighing 4675 grammes (proportion 1 to 3116.6), after 26 hours and within 37 hours.

One gramme was not fatal to a female terrier weighing 4517 grammes (proportion 1 to 4517), the symptoms passing off mostly in half an hour.

Of two rabbits, 1 gramme caused death in 56½ minutes in a female albino weighing 1915 grammes (proportion 1 to 1915).

One-half gramme did not cause death in a full-grown male, weighing

1935 grammes (proportion 1 to 3870). The symptoms nearly gone in 41 minutes.

The action of resorcin upon these six warm-blooded animals was as follows :—

1. Restlessness and trembling.

2. Rapid respiration very early in both rabbits. Early and very marked after a lethal dose in one dog, later after a lesser, but fatal dose, in another. Not marked after non-lethal doses.

3. Staggering, unsteady gait, loss of co-ordination, especially in hind limbs, present early in all the animals excepting one rabbit where small dose exhibited.

4. Twitching of muscles, especially of hind limbs, constant in all.

5. Clonic contraction of nearly all flexors and extensors of body, more especially of those attached to the pelvis and shoulder.

6. In the animals that died the imitation of the natural running or hopping movements before death, as the animal lay upon its side, was striking.

Experiments upon six frogs, by hypodermic injections of resorcin, produced clonic contractions of muscles of extremities, whether the frog was pithed or not. Curarized frogs were affected scarcely at all by resorcin given hypodermically. Division of the sciatic nerve or sacral plexus caused quiesence of muscles supplied by the nerve trunks after giving resorcin.

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