

We find that in 95 per cent. of cases of gout, the disease originated in the metatarsophalangeal joint; that fermented liquors with a full stomach have been the shibboleth of the sufferer, and that a good proportion of cases have to thank their sires for vitiated diathesis of gout. Dr. Darwin, an English physician of great note, affirms that he never saw a case of gout where the

age, the estimation and comparison of the urea, uric and phosphoric acids output, as suggested by Fitcher, and the test as recommended by Garrod for uric acid in the blood, may be of great value. The higher temperature curve, with the drenching acid sweats, is in marked contrast to the rather low or afebrile temperature, with a greater and more frequent tendency to

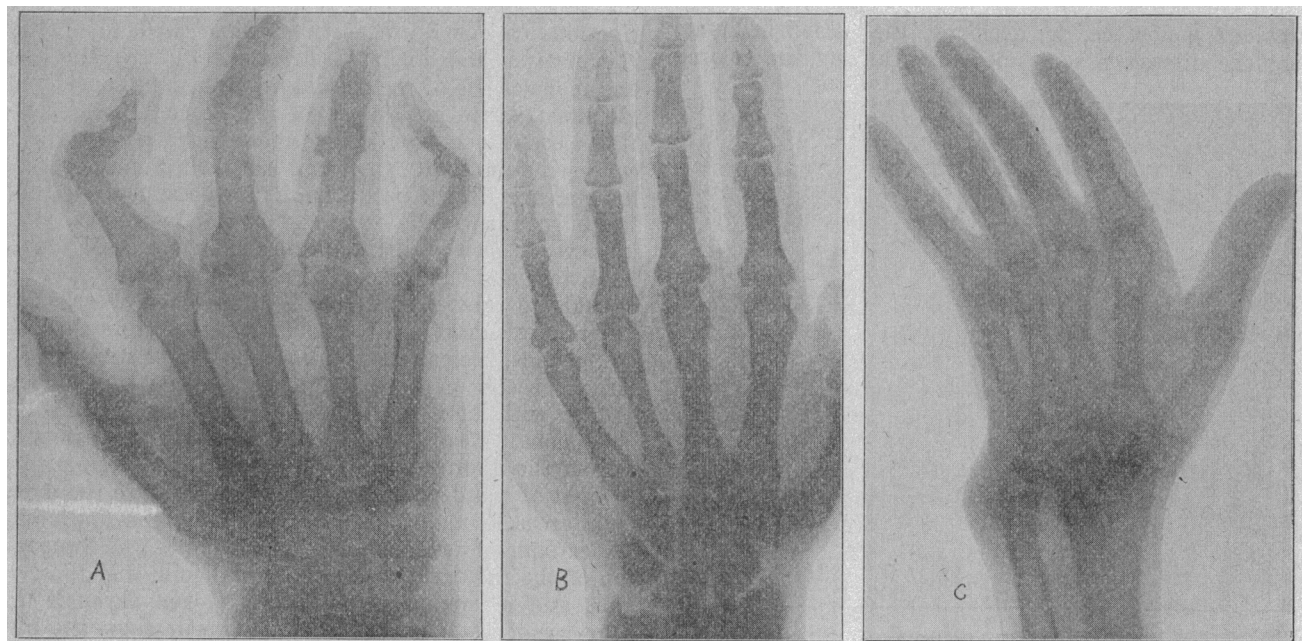


Fig. 3.—Radiograph of (A) gouty, (B) normal and (C) arthritis deformans hands.

person did not drink freely of fermented liquors, such as beer and wine.

Heberden's nodes, which are described by most authors—some considering them rheumatic, others gouty—are small rounded growths arising principally from the phalanges of the fingers, and produce considerable deformity of the joints, without, as a rule, exciting much pain. They contain no mineral constituents, but are made up principally of fibrous tissue, and are found mostly, as Lyman says, in elderly women. Heberden believes that they have no connection with gout, being found in persons who never had it; whereas, the gouty, crab-eyed indurations are rough and uneven and are composed of urates. Levison of Copenhagen draws a marked difference between gout and arthritis deformans. Gout has a strong hereditary predisposition (77 per cent.); it occurs more in the males, and in those who have used beer or strong wine. Workers in lead have a decided tendency (33 per cent.), and dyspeptic and renal colic often precede the acute attacks of gout. The urine is often found deficient in urea, and uric acid and hyaline and granular casts are not unusual. Tophi are found on the ears, eyelids and joints. The Roentgen photographs of the foot or hand show the clear lines between the bones, and even the large deposits of urate of soda are quite invisible. In arthritis deformans the articulation affected by the disease, even if it be not developed far enough to cause stiffness or enlargement of the joint, has lost its clear, transparent appearance and is almost black in color.

To draw a line sharply between acute gout and rheumatism is often very difficult, especially if the gouty pains occur simultaneously in many joints and are associated with considerable pyrexia. A consideration of the habits and occupation of the individual, the sex and

fluctuation between great agony and absolute well-being. Aretæus has known the Olympian race to be won by those who were in the throes of gout the night before.  
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#### A STUDY OF A CASE OF GREEN URINE, RESULTING FROM THE ADMINISTRATION OF METHYLENE BLUE IN A PROPRIETARY REMEDY.

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While cases of green urine are by no means unknown, the circumstances surrounding a recent case are so much out of the ordinary that they will interest the general practitioner. On the other hand, the report will not be without scientific interest and value, since one of the foremost American text-books on diagnosis, in speaking of this condition, dismisses the subject with the statement that, "while green urines have been described, the cause of the color has not been definitely ascertained."

#### THE CASE REPORTED.

On Dec. 1, 1903, there was submitted to me for examination about 120 c.c. of urine of a bright grass-green color, and possessing a peculiar aromatic odor, not unlike that of oil of juniper or wintergreen. The patient was a woman, 76 years of age, who had been for a long time troubled with sciatic rheumatism, for which she had tried numerous remedies, but with little permanent beneficial effect. She first noticed the passage of colored urine on the morning of November 27, the day after she had begun taking some pink-colored pills known as "Magic Regulators," which had been sent to her as a sample by a patent medicine concern located at Jackson, Mich. With the pills were directions to take one before each meal, followed by a glass of hot water; and there was also enclosed a circular reading as follows:

"A simple test: To prove the action of our 'Magic Regulators' on the kidneys, the organs which in rheumatism are always diseased and fail to do their work, allowing the poisonous acids to accumulate and lay the foundation for a long and painful run of rheumatism, watch the color of the urine voided. If it assumes a light-blue or greenish color, you may rest assured that the 'Magic Regulators' are doing their work."

In all, 14 of the pills were taken, as directed, and during this time the patient continued to pass urine of practically the same color as the sample submitted for examination. During this time the patient's diet consisted largely of bread, butter, milk, tea, meat, and potatoes. The vessel into which the urine was voided was clean, as was also the bottle in which the urine was sent for examination.

#### THE LITERATURE OF GREEN URINE.

Instances in which green urines have been passed have been known from very early times. A comparatively large number of cases are to be found reported, particularly in French literature. Within the last few years several papers on this subject have appeared in Scottish and English journals, but American literature seems to be singularly lacking in this regard.

Braconnot<sup>1</sup> describes two cases of blue urine, from which the color could be removed by filtration. Hassall<sup>2</sup> states that the above blue color was due to the presence of particles of indigo deposited in decomposing urine. Hughes<sup>3</sup> reports a case in which blue urine was passed from the bladder. Garrod<sup>4</sup> records a case of a child passing green urine after sucking a cloth dyed with indigo. Fletcher<sup>5</sup> reports a case of blue urine being passed after methylene blue had been taken unintentionally. Good<sup>6</sup> reports a case in which the blue color was diagnosed as indigo, although the patient was shown to have taken methylene blue.

Dr F. Parkes Weber,<sup>7</sup> in an article entitled "The Occurrence of Green or Blue Urine and Its Most Frequent Cause," describes several cases in which green or blue urines were passed, and gives a detailed account of the various tests by which methylene blue can be recognized in the urine, noting especially the differences in the reaction of an ordinary solution of methylene blue and a solution of methylene blue in urine.

Stockman<sup>8</sup> reports two cases in which blue or green urine was passed, and which on examination was found to be due to methylene blue, which in one case had been given to the patient as a practical joke, in the form of pilules densely coated with pink-colored sugar. For purposes of comparison, the urine of a third person was examined after two grains of methylene blue had been administered intentionally. Stockman states that the reactions given by the urine varied even in the cases in which methylene blue was known to have been administered. In the first case, when the fresh green urine was shaken with chloroform or amyl alcohol a blue color was extracted, leaving the urine a deep yellow, and he explains the green color of the urine as being due to the mixture of these two colors. At times the urine passed by this patient was dark blue, and at other times bright green. Stockman concludes that when methylene blue is taken internally a blue and a green pigment, probably a yellow

low pigment, and probably also a colorless chromogen appear in the urine, and that these yield reactions and spectra which are slightly different. In Stockman's second case, the patient, who was suffering from a cystitis, passed one specimen of greenish urine. The coloring matter was insoluble in chloroform, amyl alcohol, ether and benzol, and was decolorized by liquor potassii. He is unable to state either the source or the nature of the pigment.

Dun and Douglas<sup>9</sup> report what they state to be probably the first recorded case in which methylene blue was made use of to delude the patient into a belief in the efficacy of the remedy administered. In this case the remedy was taken for chronic rheumatoid arthritis by a lady 65 years of age, being administered in the form of capsules, sent to her as samples by an American concern. The patient was instructed to observe the urine for evidence of the fact that the remedy was taking effect, it being stated that the urine would come to be of a decided bluish tint. A sample of the urine was examined by Dr. Douglas, who decided that the coloration was due to methylene blue, which had been added to the patient's medicine in small amounts. None of the capsules could be obtained for examination. The urine was of a fine, deep, transparent green, with a slight bluish tinge, and possessed the odor of anise. It decomposed more slowly than usual, remaining free from disagreeable odor, at room temperature, for over a week. The results of a number of tests are given, which make it practically certain that the pigment was methylene blue.

#### EXAMINATION OF THE URINE.

The sample examined in this case consisted of about 120 c.c. of a particularly brilliant grass-green color, with the peculiar aromatic odor above described. It was slightly acid and had a specific gravity of 1020. Portions exposed to the air for some days did not change color, and underwent decomposition very slowly. One ounce was poured into a sterile bottle, and has been kept at room temperature for three weeks and is still slightly acid, and without any marked odor of decomposition. Portions to which were added mixed cultures of colon and typhoid bacilli and various other germs obtained from water, were decolorized after being kept for several days at room temperature, but the green color could be restored on shaking the tube. The pigment was found to be insoluble in ether; and on treating the urine with both dilute and strong hydrochloric acid, no change in color was observed, even on boiling. A few drops of a 10 per cent. solution of sodium hydroxid decolorized the urine, the green color being restored on neutralization with hydrochloric acid. Ether failed to take up the pigment, however, at all stages of this reaction. The urine was unchanged in color on boiling, but filtering slightly decreased its intensity, owing to some of the pigment being taken up by the paper. Both chloroform and amyl alcohol, when shaken with the urine, removed the green color completely, leaving a bright golden yellow. On evaporating the chloroform and amyl alcohol solutions of the pigment to dryness over the water bath, a greenish substance was obtained, which, on treatment with strong sulphuric acid, became brown and brownish yellow, and on dilution, at first greenish and finally was decolorized.

About 25 c.c. of the urine was then evaporated to dryness over the water bath. As the pigment dried it

1. Ann. de Chimie et de Physique, 1825, xxix, p. 252.

2. Trans. Royal Soc., Lond., 1854, p. 144.

3. Guy's Hosp. Rep., Lond., 1856, vol. ii, 3d series, p. 56.

4. Trans. Clin. Soc., Lond., 1895, xxviii, pp. 307-309.

5. Trans. Clin. Soc., Lond., 1899, xxxii, and Brit. Med. Jour., 1898, ii, 1686.

6. Lancet, Lond., 1901, i, 1535, and ii, 617.

7. Lancet, Lond., 1901, ii, 774.

8. Edinburgh Med. Jour., 1902, liv, 115.

9. Scot. Med. and Surg. Jour., xlii, 142, 1903.

changed in color from green to light brown, but on washing with alcohol the green color was restored, and the pigment passed into solution. The residue was washed several times with alcohol, and the washings carefully evaporated to dryness at about 60 degrees. A portion of the solid pigment obtained on evaporating the alcoholic extract was treated with strong sulphuric acid, which changed it to a brown color and decolorized it on dilution. A dilute water solution of methylene blue when evaporated to dryness and treated in the same way, gave a similar reaction. The remainder of the green pigment obtained from the alcoholic extract was taken up with water, in which it was readily soluble. This water solution was of a deep bluish green color, similar to the original urine, but slightly darker, it being more concentrated.

Portions of the original urine and of the aqueous solution of the pigment obtained as above were then treated with a few drops of Weingärtner's reagent (tannin, 25 g.; sodium acetate, 25 g., and water, 250 c.c.), which precipitates basic anilin dyes. A fine green precipitate was obtained in both instances, the filtrate from the urine being of a bright golden yellow, similar to highly colored urine, and that from the aqueous solution of the pigment being clear. This reagent, therefore, completely removes the pigment from its solution in water and urine, and indicates it to be a basic anilin dye. The precipitate in both instances dissolves readily in alcohol, giving to it a light bluish-green color. The reactions given by the aqueous solution of the dye obtained as above were similar to those given by the urine itself.

Moderately dilute solutions of the pigment extracted from the urine with amyl alcohol, and of methylene blue in amyl alcohol, when examined with the spectroscope, showed in both cases a single, well-defined band in the red at a considerable distance from the sodium line. The urine also, when examined with the spectroscope, showed this same absorption band, but less markedly.

#### EXAMINATION OF THE REMEDY TAKEN.

A sample box of the pills, similar to those taken by the patient, was obtained. They were bright pinkish red, and weighed about 3 grains each. On removing the firm outer coating, all but one were found to be made up of a dark bluish-green substance, which, when pulverized, dissolved readily in water, alcohol and amyl alcohol—completely on boiling—and giving to these solvents a deep blue color. The remaining pill contained a grayish-yellow substance, which burned readily, leaving a small quantity of grayish ash.

The content of one of the first-mentioned pills was dissolved in about 500 c.c. of distilled water. Treated with Weingärtner's reagent, this solution gave a blue-black precipitate and a slightly yellowish filtrate. On treatment with concentrated hydrochloric acid no change was observed. Sodium hydroxid decolorized the solution to a pinkish violet on standing. A solution of chemically pure methylene blue made to the same color as the pill solution, gave exactly the same reactions. The aqueous solution of the dye obtained from the pill, when treated with strong ammonia, became green on heating. The methylene blue solution, when treated in the same manner, was unchanged. Potassium bichromate changed both solutions to a light wine red.

Chloroform removed the color completely from the pill solution, holding it as a light blue. The color was also removed in the same way from the solution of methylene blue, but was almost immediately changed to a

yellow. A solution of methylene blue, to which a small amount of chemically pure methyl green had been added, was then treated in the same way. The color was completely taken up by the chloroform and held as a light blue, of the same shade as that obtained from the pill solution, the methyl green having evidently prevented the methylene blue from being decolorized. Chloroform took up the color from a solution of methyl green, but soon decolorized it, the liquid above being colored a wine red. The same solutions were shaken with ether, but without change in any case.

A piece of the solid dye from the pill was treated with concentrated sulphuric acid in a porcelain capsule. The color was changed to a bright grass green, with a yellowish tinge, becoming blue, and finally blue violet on dilution. Solid methylene blue, treated in the same way, gave a bright green, becoming blue and then blue violet on dilution. Solid methyl green gave a dark orange red to carmine, on dilution becoming brown, then olive green, then blue green, and blue.

The solution of the pill and the solution of methylene blue, when treated with picric acid and glycerin, gave a blue-black precipitate and a bluish-green filtrate, of exactly the same shade in both cases. The spectroscopic appearance of the pill solution corresponded exactly to that described above for the solution of methylene blue.

Strips of cotton cloth were then dyed in the solution of the pill, in the solution of methylene blue, and in a solution of methyl violet of approximately the same strength, for the purpose of comparison. After having been allowed to dry in the air over night, the following tests were applied and results obtained as recorded below. The strip dyed in the methylene blue solution was of exactly the same shade as that dyed in the solution of the pill.

TABLE OF COMPARATIVE TESTS.

Treated with.	Pill Solution.	Methylene Blue.	Methyl Violet.
HCl.	Fiber nearly decolorized; liquid blue green.	Fiber nearly decolorized; liquid blue green.	Fiber brownish yellow; liquid amber yellow; violet not restored on dilution.
H <sub>2</sub> SO <sub>4</sub> .	Fiber and liquid green.	Fiber and liquid green.	Fiber and liquid brownish yellow.
NaOH.	Fiber changed to blue violet.	Fiber changed to blue violet.	Fiber changed to pale reddish violet.
NH <sub>4</sub> OH.	Fiber not much changed; somewhat paler.	Fiber not changed.	Fiber changed to red violet; then almost decolorized.
HNO <sub>3</sub> .	Green spot.	Green spot.	Green spot surrounded by a bright yellow ring.
Alcohol.	Greenish blue color extracted.	Greenish blue color extracted.	Violet color extracted.

It will be noticed that, as a whole, the tests of the aqueous solution of the material obtained from the pill correspond closely to those given by the aqueous solution of methylene blue, made to the same color. The solid dye treated with sulphuric acid gave a reaction corresponding almost exactly to that of chemically pure methylene blue. There was at first a slight yellowish tinge, resembling the first reaction of malachite or benzaldehyde green, although the end reaction was the same as that of methylene blue. The solid dye obtained by evaporating the various solutions of the pigment, both from the pill and the urine, when treated with strong sulphuric acid, did not give the characteristic bright green color, changing to blue and violet on dilution, given by solid methylene blue; but it was noted that when solutions of pure methylene blue were evaporated to dryness, the residue also failed to respond to this

test in the characteristic manner, but behaved the same as the residue from the pill and urine.

The reaction of the pill solution with chloroform is exactly similar to the chloroform reaction of a solution of methylene blue, to which a small amount of methyl green had been added. The possibility of the pill containing small amounts of an anilin green was therefore considered. The dye contained in the pill is entirely soluble in amyl alcohol, and is completely removed from its aqueous solution by this reagent. Amyl alcohol also completely removes it from the urine. It does not change to violet in any of its solutions on heating to 100 degrees C., and consequently, neither the pill nor the urine contains methyl green or its allies, these being insoluble in amyl alcohol, and changing to methyl violet on heating to 100 degrees C. The aqueous solution of the pigment obtained from the urine corresponds very closely in its reactions to the aqueous solution of the pill, the small differences noted being probably due to the presence of urinary salts and coloring matters in the first solution. The spectroscopic examination of the various solutions of the pigment and the reactions to various reagents of the fibers dyed in the same, are both positive for methylene blue. There is, therefore, little doubt that the pills which this patient ingested consisted entirely of a somewhat impure preparation of methylene blue, the impurities consisting very probably of small amounts of basic anilin greens, either malachite or helvetia green.

In regard to the pill which was found to be made up of the yellowish vegetable substance and which can not be told by the external appearance from the pills containing the dye, little can be said, nor is its composition of any great importance in connection with this paper. It is probable that the patient received a larger number of these pills than would be indicated by their proportion in the sample box examined by the writer, that is, that the box examined did not contain a representative sample of the remedy. The pills last described evidently contained the true "remedy," if such it may be called, and were undoubtedly possessed of a mild cathartic action, since the patient states that the remedy had this effect.

A study of the literature shows that blue or green urine is occasionally passed by apparently healthy individuals—especially by children—without there being obtainable any history of the ingestion of an anilin dye. Practitioners unfamiliar with the appearance of methylene blue urine are apt to attribute the urinary pigment to the presence of indigo blue, derived from indican fermentation. Practically all cases, however, of green or blue urine reported in the literature have been due to the ingestion of some anilin dye—in most cases methylene blue. Especially is this the case in those instances in which the patient has complained of no other untoward symptom save the pigmented urine. Cases in children almost invariably result from eating candies highly colored with anilin compounds. Since undertaking this investigation, I have been told of a case in which a child passed a bright red fluorescing urine after having eaten candy colored with eosin.

The question may be raised, why was the urine green in this case, rather than blue? Various workers have shown, however, that the urine is frequently green after a dose of methylene blue, especially the first voided after taking the dye. It was noticed in this case that the urine, after the pigment was removed, was of a bright yellow, and it is not unlikely that this combined

with what would otherwise have been a bluish tinge to give rise to the peculiarly brilliant green of this specimen.

In regard to the cause of the aromatic odor of the urine, and of its marked keeping power, nothing definite was ascertained.

#### COMMENTS ON THE CASE.

The present case is of especial interest from a practical standpoint, inasmuch as it brings to light what seems to be a new method employed by the quack to delude his patient into the belief that the so-called remedy is in reality reaching the kidneys and exerting its remedial effect on them. That this is the sole reason for administering the dye, is evidenced by the fact that the pills containing the substance supposed to be a vegetable purgative are of exactly the same external appearance as those containing the dye.

It is significant that in the case reported by Dun and Douglas, the patient sent to an American firm for a "cure" for chronic rheumatism, and that the urine passed possessed remarkable keeping powers and a peculiar aromatic odor, facts which were both especially noticeable in this case. The directions accompanying the remedy were practically the same as in the present case, and in both instances the medicine was sent as a sample.

It is probable that many cases of blue and green urine will follow the indiscriminate distribution of the above-described "remedy," and will be brought to the notice of physicians, particularly those of southern Michigan and neighboring states. In such cases it will be well to bear in mind the fact that both green and blue urines in nearly every case result from the ingestion of some anilin dye—particularly methylene blue—and to inquire whether the patient has recently taken any proprietary medicine.

#### A REPORT OF TEN CASES OF PNEUMOTHORAX OCCURRING IN PULMONARY TUBERCULOSIS.

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Pneumothorax as an accident in or complication of pulmonary tuberculosis, occurs usually in but a small percentage of cases. According to West this percentage is 5. Eichhorst found 5 per cent in 390 cases, Gutmann, 4.2 per cent in 2,200, while Weil found 10 per cent in 355 cases. It has been the universal experience that pneumothorax is usually total, that is, that the entire lung collapses and contracts up against the spinal column, thus separating the visceral and parietal pleuræ by a considerable air space, and that partial pneumothorax in which but a part of the lung collapses, and the rest remains in place, due to adhesions or other causes, and but a portion of the pleuræ separate to form a cavity, is much less common. Powell and Whitney state that the total form is the rule, and in Weil's series of 36 cases all but four were of this type. Whitney states in the "20th Century Practice of Medicine," that in partial pneumothorax the symptoms are usually mild, very little general disturbance or discomfort being caused.

Out of 41 deaths occurring at the U. S. Public Health and Marine Hospital Service Sanatorium for Tuberculosis at Fort Stanton during the nine months from Sept. 1, 1902, to May 31, 1903, 9, or 22 per cent., revealed