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"The Clinical Significance of an excess of Indican in the Urine"

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"The Clinical Significance of an excess of
"Indican in the Urine"

During the past six years in general practice I have had occasion to examine carefully some seven or eight thousand urines, and in many of these I have discovered a marked excess of the substance called Indican, and as most of the specimens in which such an excess was found were from patients suffering from diseases of the alimentary canal I concluded that there must be some connection between the two, and on searching various authorities I found that their views generally agree with my researches. The authorities I mention are, Lauder Brunton, Klein, Watson Cheyne, Clifford Allbutt, Martin McKenna, Hoppe Seyler, Van Jaksch, Jaffé, Bristowe Osler, Drosfeld, Fenwick and Pearce Gould. Hilton Fagge passes the subject of Indicanuria by with the remark that "the detection of Indican "is never become of much clinical importance" but with this statement I cannot quite agree, as since I have had my attention drawn to it, I have on several occasions, as I hope to show in the cases I shall

necessitation later on, been able, excepting in some cases of Typhoid fever to prove or disprove the presence of an intestinal obstruction or ulceration, and in all probability when a larger number of facts have been obtained with reference to the excess of Indican in the urine, its value as a symptom will be more generally utilised.

The presence of Indican was first pointed out by Schunck of Manchester, who discovered it as a normal constituent, and supposed that this product was identical with the Indican found in the vegetable kingdom, but this has since been disproved, although they differ in only a slight degree. Baumann being the first to prove that urinary Indican is not a glucoside as is the Indican of plants, but an ethereal compound of sulphuric acid with Indoxyl.

The substance and its production in the urine.

Indol is formed in the intestine by the decomposition of albumen under the influence of bacteria. When absorbed this is oxydised in the tissues to Indoxyl which combines with potassium sulphate, forming indoxylsulphate of potassium. ℈ Normal urine

Dr. C. A. Hoskr of New York in a valuable paper in the British Medical Journal, Dec. 25 1897 seems to separate Indican from the ethereal sulphates, for in the deduction from facts observed by himself he states 1. "The introduction of large numbers of
" the common colon Bacillus into the intestine
" markedly increases the Indican of the urine, and
" with it the ethereal Sulphates. 3. The introduction
" of large numbers of the Lactic acid bacillus
" into the intestine may markedly lessen the
" Indican of the urine Together with the ethereal
" Sulphates"; but in the nomenclature of Sheridan Lea & Foster's Physiology & and other English authors Indican is an ethereal sulphate, produced, may possibly by a microbe or ferment distinct from those which produce other ethereal sulphates. Thus Lea states; "a part of this Indol found
" in the alimentary canal leaves the the body
" as a potassium salt of indoxylsulphuric
" acid". The presence of Indol does not appear to be due to the tryptic ferment of the pancreas, as was at first supposed, but attributed to a simultaneous putrefactive change taking place under the influence of bacteria, for if laboratory digestion be conducted with strict antiseptic

precautions, with the presence of salicylic acid, no putrefaction occurs, no Indol appears, & no Skatol, and the products of digestion have no characteristic smell of faeces. This, of course might be due, though very unlikely, to the destructive action on the ferment which produced the bodies Indol and Skatol. It is well known that bacteria are present in the alimentary canal from end to end in great quantities in the small intestine but increasing in numbers towards the rectum. These would easily account for the presence of the Indol & Skatol in the small intestine of a man where pancreatic digestion is proceeding rapidly; and when from any cause there is a considerable retardation in the amount of absorption from, or the onward movement of the intestinal contents or changes in the mucous lining of the canal, the excess of the substance Indican, which in certain cases is found in the urine has a ready explanation. Jaffé has proved & Hoppe Seyler's Handbook that by feeding dogs on Indol, obtained by the pancreatic digestion of proteids, or by injecting the same substance under their skin a large excess of Indican can be made to appear in the urine.

Again it has been proved that by feeding dogs on an excess of proteid food, in which it is supposed that much Indol must be found during the pancreatic digestion in the alimentary canal, a large quantity of Indican can be discovered coming away in their urine. Indol being the final & reduction product of Indigo it can be easily imagined, that after its absorption from the intestine, and during its conjunction the blood, and its passing out by the urine, it can become oxydised into the product Indican. No Indol, so far as I can learn, has ever been found in the blood, but it has been easily detected in the renal epithelium, from which it has been concluded that the final ~~oxy~~ transformation takes place, during the very act of excretion, as is well known occurs with other excretion products which are got rid of by the kidneys. Indol also occurs in and may be separated from some collections of pus.

Jaffé has found Indican in excess in the urine clinically in cases of intestinal obstruction. I have also done the same, ~~see~~ Case No 6. He has done the same experimentally by obstructing the intestine of dogs especially the small intestine,

he obtained Indican in excess in their urines, thus proving that any obstruction to the onward flow of the contents of the bowel leads to an increase of the Indican forming substances in the blood; but it appears from both clinical facts, and experimental observations that obstruction in the large bowel does not produce the same excess of indican in the urine. This might be either due to further changes having taken place in the contents of the bowels in their onward progress along the canal, so that no longer any Indol is formed, or else, from the peculiar construction of the large bowel, absorption of Indol is rendered difficult; for if the changes be simply a putrefactive action there is no reason why plenty of Indol should not be formed, as the large intestine contains many more organisms of putrefaction than any other part of the canal. But it has been shown above that the Indol is formed during the digestion of proteid food, and as this is mostly completed, and the products absorbed, before arriving at the great intestine, which only absorbs the water constituents of the contents, rendering the faeces drier, a ready explanation is obtained.
Obstruction of the bowel does not appear to be the only cause

of Indican in excess in the urine, as Senator {Jaggs Medicine Vol 2} refers it to states of incanition, as cancer of the stomach, gastric ulcer, and phthisis with diarrhoea. Hennige, also quoted by the same authority, insists upon its appearance in wasting affections of the canal as well as its presence in cases of diarrhoea and constipation, though Vogel denies its presence in the latter cases, in this I differ with him as shewn in cases Nos 13. 19. I should mention that Dr Bristowe of St Thomas's Hospital has worked at the same subject and come to the same conclusions as the above mentioned observers.

Tests for Indican in the Urine.

When concentrated acids or strong oxydising agents are added to the urine the Indican is decomposed and the Indigo set free. 1. The presence of Indican can be demonstrated by adding Hydrochloric Acid to a large quantity of urine placed in a long glass vessel, and then allowing the mixture to stand for twenty four hours, when a darkish blue scum of Indican appears on the surface. The objections to this method from a practitioners point of view are obvious. 2. A second method of determining its presence is by adding Hydrochloric Acid and Chloride of Lime to the urine, and then shaking the mixture with Chloroform,

which becomes bluish from the presence of Indican, and on being examined with the spectroscope shows the characteristic bands. There are many objections to this method. 3. A third method simply requires the urine to be warmed and then Nitric Acid, yellow with Nitrous to be added, when if the Indican be present in any quantity above the normal a dark brown colouration appears, which goes quite black on further addition of the acid. 4. The method that I have adopted as being the most convenient is as follows:- Add to ℥j of urine an equal quantity of strong Hydrochloric Acid and afterwards a few drops of Liq: Calcis Chlorinata, or Liq: Sodæ Chlorinatæ. Indigo blue colour shows the presence of Indican. Brown red shows Skatol compounds and Purple a mixture of the two. In this test it is possible to roughly estimate the quantity of Indican by the depth of the colour and the quantity of fresh solution of chlorinated lime required to decolorize it. In some cases and in some instances when the Hydrochloric Acid is very strong I have found the blue colour without the addition of the chlorinated lime and especially if I have previously heated the urine. 5. Dr Thurston of Leeds recommends the following test; "drop into a ℥j of Hydrochloric Acid in a test tube a minute granule of Chlorate of Potash then add ℥j of urine and mix gently

by shaking the tube. The blue colour is quickly developed. This he tells me is now his usual method though previously he had used the test I have given above {No 4}.

— Cases —

1. Elizabeth T. æt 28. History of loss of flesh, slight diarrhœa, pain and tenderness in left lumbar region and also in the left iliac region, with a slight sensation of fluctuation here. no evident tumour. Temperature rose each night to 103°-104° 7, morning fall. Patient got worse. At first I was inclined to think there was an abscess connected with spleen or kidney. Urine gave Indican reaction with Hydrochloric Acid and Chloride of Iron, the reaction was most marked, washing out the bowel and treatment with grain doses of calomel did not materially lessen the reaction. The patient became more and more emaciated and diarrhœa increased. Patient died after twenty seven days attendance. I was fortunate enough to persuade the husband to allow me to make a post mortem, he giving me permission to open the abdomen only, {this being one of the very few cases in which I could get a post mortem examination} I found ulcerations along the intestines, probably tubercular, not any sign of mischief in any other organ.

2. Frank R. æt 49. Came under my care June 2. 1893.

Epigastric pain, slight vomiting sometimes tinged with blood, losing flesh rapidly, much worse after food, and especially at night. Stomach dilated, no tumour felt. The urine showed a marked excess of Indican. Was washed out every other day, Calomel gr ss every other night and Hydrochloric Acid q min before food daily. The patient improved and in 9 days declared himself well. The appetite returning and the vomiting ceased.

3. Robert T. æt 54. Acutely ill, pains in the epigastrium. Had been eating largely of cucumber and onions at supper time, Vomiting but not stercraceous, could pass no feces or flatus, abdomen very distended. Indican in excess in the urine. Washed out and opium administered. Symptoms rapidly became less and then vanished as did the Indican at the same time.

4. Mary H. æt 27. Had suffered from dyspepsia for many years, could not say how long, teeth few and bad. Sometimes the pain was very severe, great flatulence, excess of Indican in the urine but not well marked, ordinary treatment with Hydrochloric Acid, occasional washing out and small doses of calomel, diet regulated, patient improved and ultimately left the district.

5. Henry G. æt 59. A heavy drinker, said to have fallen in a fit

and tore his hand against a hook. Hand dressed but ultimately two fingers had to be amputated. Symptoms of blood poisoning. No previous history of any fit, and as far as I am able to find out no recurrence of any, though I have seen the man almost daily going to and from his work. Urine contained much Indican at the times of his drinking bouts. Washed out and treated with Calomel the Indican disappeared.

6. James D. æt 44. Acute symptoms of intestinal obstruction, no apparent hernia. Patient in two days passed some flatus and a small stool. Patient rapidly got worse, no operation was allowed although recommended by myself and another practitioner. Indican found in large quantities. Patient died on fourth day. No post mortem, but I think from the symptoms there must have been some twisting of the bowel with a perforating ulcer, as there was marked distention of the abdomen, which increased on the first washing out.

4. Hannah H. æt 41. Had suffered many years from rheumatism. Temp: often up to 101½ F. small hard stools and much tormina and tenesmus, occasionally she told me that she had passed blood with her motions, but I never saw any. Indican in excess in the urine + sometimes albumen, Diet regulated, washed out regularly,

calomel administered and hydrocyanic acid mixture given. The abdominal symptoms gradually disappeared and with them the Indican.

8. Herbert L. æt 63. Had been a heavy drinker, but of late years a teetotaller. History of rheumatism, marked oedema of legs, and severe attacks of dyspnœa. Mitral regurgitation, urine showed much albumen and marked Indicanuria. Pulv: Jalapæ Co reduced the oedema. Digitalis and Strophanthus administered. Bowel washed out, but no improvement was made. The man went into hospital at Dewsbury and died.

9. A case communicated to me by Dr Thurston of Leeds Infirmary. A man was admitted in a state of collapse, and died in a few hours, vomited two days before admission. No Indican in the urine. Hernia was strangulated through an aperture in the omentum.

10. Mary R. æt 60. Found unconscious in her bedroom. Urine contained much albumen also Indican. Freely washed out and consciousness was at once restored; partial right hemiplagia and ~~dysphasia~~ aphasia persisted for some weeks and the arm has never completely recovered.

11. Robert Gr. æt 40. I was called to see this man in the absence of his regular medical attendant. Chronic endocarditis, with dyspnœa, I drew off some urine by

means of a catheter, found albumen, but no Indican, so no washing out was ordered. I should have mentioned that the man was comatose at the time of my visit. I heard afterwards that the man recovered for a time but shortly died.

12. William. H. æt 45. Gouty. Urine 1030 large quantity of urea, no Indican, no washing out. nitrogenous or suitable diet.

13. Thomas B æt 35. Very gouty, usually constipated. Large quantity of urates and much Indican, was a great meat eater as so many of the Yorkshire work people are. Washed out regularly. A mixture of Benzoate of Soda and Tr Colchici given with magnesia as an aperient. Indican disappeared and man improved.

14. Elizabeth T. æt 34. Gouty, no Indican in urine, and only a small amount of urates, passes much water of a medium specific gravity, but does not take much liquid nourishment, eats plentifully of meat; occasionally slight diarrhœa. Improved under colchicum and sodium benzoas.

15. William N. æt 51. Had suffered for many years from gout, sometimes diarrhœa, sometimes constipated drank water freely and ate much meat. Though I repeatedly examined this man's urine I never once found any Indican. He always responded to colchicum and magnesia, his symptoms disappearing, but he soon fell into his old habits and was attacked again. I have had many cases of a similar

nature expecting to find Indican in all of them but it was absent.

16. J.S. æt 53. Case communicated. Ill on July 20 1895 a beer drinker, got wet through.

July 21. An hour after dinner cramps, beginning in toes and extending to legs and abdomen, followed by diarrhœa and vomiting.

July 22. Recurrence of cramps in the evening with diarrhœa.

July 23. Went to work but was taken home unconscious at 3.30 pm. Pulse 60, prostration, vomiting, diarrhœa, thirst, pain in abdomen, cramps in legs. Stomach and small intestine rather shrunk, cæcum and colon contained fluid. Urine. No albumen, scanty chlorides, much Indican. Bowels acted 5 times before 9 p.m. Treatment. Calo grs iv-v. milk and soda water, colon to be washed out if diarrhœa continues.

July 24. Ol. Ricini 3ß at 10 a.m. Colon washed out at 1 p.m. Brandy and soda given. On Thursday had 4 motions in addition to the washing out.

July 25. Calo grs x every 4 hours. Peptonized milk 6 motions.

July 26. Three motions.

July 27. Two motions, then some few until Aug 1.

Aug. 5. Up. Very little Indican in urine, neither opium nor astringents were given. The treatment consisted in clearing away the source of the Indican and giving Salol and stimulants. Although there was very marked Indican colourization of the urine when tested in this case, it was certainly not more than is frequently observed without similar prostration. It was however enough to show that the intestinal contents were toxic, {with more than Indol it is otherwise informed} and must be cleared away. The diarrhoea was encouraged or assisted, or replaced by irrigation, not checked by opium etc.

14. Mr. B. æt 43. Diarrhoea had existed for 3 weeks, the dejections were watery and very offensive, sometimes containing blood. Iliocæcal region rather tender. Languid but not prostrate. Pulse quick and occasionally intermittent, tongue dry and rather brown. History of anxiety & and dyspepsia with insomnia, beer taken instead of solid food. Urine. Sp. gravity 1018, no albumen, great excess of Indican. Tengraim of Salol every 4 hours, washing out. Peptonized milk and brandy as required. Rapid recovery followed.

18. Thomas H æt 32. Patient had had Scarlet fever a fortnight previously, was up in a few days when he took some mutton broth, which always disagreed with him, next day some fish. Vomiting and diarrhœa came on, Abdomen distended, succussion splash apparently in colon. Pulse tense. Urine 1020. Very Chlorate lithatic, no albumen, very marked excess of Indican. Patient Calomel, milk diet, colon washed out. Rapid recovery.

19. Fanny P æt 32. A case resembling Typhoid fever. Weakness and frontal headache. Temp. 102°·4 F. Pulse 124. Respirations 24, Face flushed skin dry, tongue furred and dry, brownish in centre, deeply fissured. Some doubtful papular spots on abdomen. Patient lived on a barge plying on a very foul river. Had had dyspepsia and nausea for 4 years. Complained on visiting of pains in limbs and shiverings. Urine showed marked excess of Indican. Had been very constipated and on date of visit had had no motion for 6 days. An enema was given which was repeated next day. The temperature became normal and remained so. On the third day all symptoms and Indican had disappeared. On the fifth day Indican reappeared, another enema was given. On the seventh day she was quite well.

20. Case communicated. M. S. female æt 42, of weak build never very strong, diarrhœa and œdema of legs occasional cramps in hands and twitching of face, has had much anxiety and privations during the past six months. Thirteen Sep. 2. 1895. Treatment Plain diet with fish and chicken. no special drug treatment.

Sep. 12. Flexor spasms of wrists and hands, conduct strange will not answer questions. Urine 1015 no albumen, very large quantity of Indican.

Sep. 19. No improvement. Temp 99° F. Pulse 96 Calomel gr i Salol gr x every 4 hours.

Sep. 20. Much better. Still marked Indican.

Sep. 23. No Indican.

Sep. 25. Slight return of Indican. Sp. gr. 1022.

Sep. 28. Well.

21. Case in British Medical Journal Supplement July 3rd 1897 page 1, mentioned by Gustav Seiger of a man aged 41 suffering from "Tetany with Indicanuria cured by calomel and irrigation.

22. Cases of Hysteria with Indicanuria are mentioned in British Medical Journal by Anderiegen, May 16, 1896, p. 1204. They were cured by naphthalin.

23. Case of great interest communicated by Dr. Chesterton Leeds. Effects of meat broth. John H. R. æt 46. A waiter who

for several years had lived chiefly on alcoholic fluids was admitted Feb 9. 1895 to the Leeds Infirmary, for gouty arthritis. Milk and sodawater agreed well with him, but he believed himself to be starving. He was an intelligent, genial patient, and assented readily to the proposition that want of exercise to his digestive functions had led to their great impairment, nevertheless when he saw other patients eating, he was urgent to join in their meals.

Feb 10th A beginning was made with tea and dry toast

" 14th Wine, milk diet resumed.

" 17th Milk and roast apple.

" 18th Cocoa added.

" 19th Minced fish.

" 21st Minced chicken.

" 25th Wine. Rice and apple only.

" 26th Milk and soda only.

Mar: 1st Tea and milk, oranges.

" 4th Free from pain, not weak or much languid, he begged again, as he had one daily for something stronger. Allowed to chose for himself he selected a basin of broth, and took about 3/4 of a pint. It was thought possible that the broth might restore the gout in the knuckle or toe, but to everybody's dismay on the following morning nearly every examinable joint in his body

was painful and swollen. Indican was found to excess in the urine with lithates & kreatinine. Convinced by this experiment he lived on milk only for 4 days, and took no animal food of any kind during his stay in the hospital. He was cured of his gout and went to the Convalescent House.

24. James K. æt 39. Severe vomiting and prostration after eating largely of sausage and mashed potatoes. Much Indican found. Small doses of Calomel were given and the bowels well washed out. He recovered in a few days.

24.a. Thomas L. æt 58. Slightly gouty, suddenly seized with intense pain in lumbo-sacral joint, so much so that he could not bear the slightest movement or weight. Was in bed for 3 days, on the fourth day the bowels acted freely after a grain of Calomel. Indican had been found in the urine on the third day. Five minutes after the purgation, he got up dressed and resumed his work, though with some occasional pain.

25. Mary H. æt 15 Suffering from acute rheumatism. Temp 103° F. Much Indican in urine, an enema administered before treatment with salicylates was commenced, and this very considerably relieved

the pain. Patient recovered after continued use of salicylates.

26. James P. oct 14. A collier working in a damp pit. Had had many attacks of rheumatism. No indican found in urine on first examination, on the 10th day of his illness and when he was recovering, ate freely of mutton chop. I was sent for in the night and found him in intense pain. Indican in marked excess. I washed out the bowel which relieved him almost immediately of his pain. He recovered under salicylates and properly regulated diet.

27. Amelia H. oct 16. Suffering from acute pericarditis with effusion. Heart's action much hampered, and pulse irregular and intermittent with much pain over the pericardium. Was at first attended by my local nurses who had given her fairly large doses of opium so much so that she had had no motion for 5 or 6 days. I found an excess of indican, and gave a large enema. Large masses of faeces came away, patient was much relieved. The pericardial area was painted with Ty. Iodi perchlor and salicylic acid with cardiac tonics administered. She went on well for two or three days, when in consequence of great

pain I was compelled to administer opium, giving her 3 grains every 4 hours. The pulse became intermittent and irregular, Indican was again found, washing out performed and the patient relieved. By this time the fluid had nearly disappeared and the patient slowly recovered without any bad symptoms.

28. Henry S. æt 22. Suffering from double pneumonia with diarrhœa. Temp: running from 102° to 104° F. Calomel and a large enema given as Indican was present in excess. This was followed by an immediate drop in the temperature. Patient took large quantities of beef tea which invariably caused Indicanuria and diarrhœa, but these were removed on washing him out. At last I persuaded his mother to confine his diet to milk, brandy and egg, which diet caused no disturbance of bowel and he made a good recovery.

29. Walter C. æt 24. Had been ailing 3 days, tongue dried and furred, Temp 102·4 F, Pulse 110. Urine examined, no Indican. This case proved one of Typhoid fever, and the patient ultimately died. Although many examinations of the urine were made, Indican was never found. Patient had much diarrhœa.

30. Four daughters of Henry C. All with typhoid fever, and each patient having many motions Indican was never found.

31. William S. æt 32. Typhoid with double pneumonia much diarrhœa, Indican never found,

32. Anne B. æt 4. Typhoid with constipation, no Indican found.

33. Francis B æt 31. Mother of above, also with Typhoid and constipation, no Indican found.

34. James P. æt 24. Typhoid with diarrhœa, Indican found in small quantity. Bowel carefully washed out, and ½ grain doses of Calomel given. Lowering of temperature followed and relief to patient.

35. Henry F. æt 41. Typhoid, diarrhœa, no Indican. Patient was recovering when he had a relapse, Indican was then found, although she was on a milk diet. Was washed out and Calomel given, Patient relieved, I cannot say how many times this was done as I left the case in charge of a locum tenens. Patient ultimately recovered,

36. Mary H. æt 34. Had been ailing many months Strong phthisical family history, complained of much diarrhœa, passing blood sometimes, sometimes pus and blood, I found Tubercle

Bacillus in this discharge. Washing out the bowel was performed on many occasions always relieving the patient, but she ultimately sank,

34. Walton S. æt 21. Psoas abscess, much Indican found and patient washed out as usual which always relieved the distended abdomen. he ultimately died.

38. Yarmy G. æt 14. Scarlet fever, Indican found in excess. Washing out performed and Calomel given, marked improvement.

39. James & Frank K. æt. 14. & 12. Scarlet fever bowels normal as in case 38, Calomel given and washing out performed, Indican being found. Marked improvement in both cases, as in many others that I have attended, indeed it is almost always my routine treatment in cases of Scarlet fever, when I have nearly always found Indican in excess.

40. Francis L. æt 38. Confectioner, suffered from Eczema, Had an excess of Indican in the urine, though no marked diarrhœa. He improved under the usual treatment, with calomel and washing out in addition.

41. Norman P. æt 24. Had suffered many years

from Eczema, always improved at Harrogate but got worse as soon as he left. Indican was found in his urine, but not to a great excess. I taught him to wash himself out, put him on a proper diet and arranged his treatment. He made a grand recovery.

42. Case of Bronchopneumonia in a girl æt 4. Temp 104° F very restless, had been taking too much meat juice. I alone do mention that she was the daughter of a fellow practitioner who asked me to take charge of the case, He thought it was Typhoid fever, Indicanuria was very marked, I have rarely seen the reaction more perfect. Under Calomel and repeated washing out of the colon the Indican disappeared, and there was immediate improvement. She made a good recovery under sticky milk diet.

43. Pneumatic stupor Delirium Indicanuria. A case communicated.

William B. first seen Dec 7. 1895. was in a state of stupor. Occasionally he became, it was thought, delirious, insisted on getting out of bed, etc, shouting and struggling but without much vigour when persisted. The original movements

resulted from mental impulse, full bladder etc. the others from efforts made to restrain the patient who was unable to explain. Indican being found abundantly in the urine the colon was at once freely washed out. In a few hours he was quite sensible, and remained so all next day.

Feb. 9th Ate some biscuits.

" 10th Indicanuria and with it the delirium returned and was even worse. Must have Ol Olivæ and a glycerine enema,

" 11th Semi comatose, still an excess of Indican, balance from by the mouth Pil Rhei co grx by the rectum.

" 12th Appetite and stomach relief freely. The delirium disappeared at once, A patch of pneumonia was discovered in the left base, Pt recovered.

44. Pleuritic effusion. Case communicated. Dr Alfred H. aet 30. First seen June 22. 1896. Dull in manner and aspect, suggesting typhoid fever, much Indican found in urine.

June 25th Patient still dull, very silent and apathetic much Indican, washed out, Pulv Ipec x. t.i.d.

July 3rd No Indicanuria in urine, patient became quite cheerful and communicative. The exact condition of the pleurisy was not clear, but miliary pheumatoid or tubercular pleurisy is usually associated with such mental & cerebral sickness as this patient displayed, nor is Indicanuria a constant associate of Pleurisy, but no patient with marked Indicanuria is markedly energetic, hence the lethargic condition of this patient may be fairly attributed to the Indicanuria or the toxine which accompanied it.

45. Case communicated by W. Mayo Robson, Leeds Infirm.y
A boy aged 9 on Oct 1st 1895 ate a piece of uncooked turnip as large as half a cocoa nut, directly after his ordinary dinner.
Oct 2nd Vomited after all food and drink
" 3rd Vomiting continued.
" 4th Admitted to hospital, large hexagonal cells and pago like masses found in vomit. Intense Indicanuria, a quantity of Liq. Sod. Chlorinatæ equal to the volume of urine and acid together not causing complete decolorization.

Operation. A hernia of the small intestine through an aperture in the mesentery was found. The Ileum perfectly empty, Rejunum evidently contained fluid. The hernia was released; a mesenteric cyst containing motile bacteria & B. coli, was also removed, the child died in a few hours, The intestine above the obstruction also contained fluid.

46. Case is recorded by Mr Pearce Gould, in the British Medical Journal Dec. 18, 1897 p. 1795, of death after successful operation for Obstruction due to intestinal toxaemia.

47. Case is recorded by Mr Silcock, of acute obstruction from peritonitis in which the patient during the operation was supposed to be actually dead, but the Intestine having been opened and a large quantity of faeces drained away rapid recovery took place.

Clinical Society April 27 1894.

At the same meeting Dr Lauder Brunton & Mr. Watson Cheyne related cases to the same purport.

48. Case is mentioned by Mr. Treves in British Medical Journal March 10. 1894 p. 557. in which he writes forcibly upon this "treatment of acute

" obstruction by the evacuation of the bowel before
" all things" and he attributes the introduction
of the practice to Benj Travers.

49. Fred. Goer 56. Chronic Bright's disease, Heart very
badly affected also, Passed much albumen
up to 15 parts per 1000 by Esbachs albuminometer.
Though I examined his urine many times I
only found more than a trace of Indican on
one occasion and that was after a hearty
meal.

50. James P. oct 27. Acute nephritis after Scarlet
fever. Albumen 5 parts per 1000. no Indican.

51. Mary St. oct 64. Chronic Bright's disease and
failing heart. Albumen 10 parts per 1000 no
Indican found.

52. Frank W. oct 49. Chronic Bright's disease
Albuminuric retinitis well marked, Albumen
13 parts per 1000. No Indican found.

It will be seen that cases № 1, 2, 3, 4, 5, 6, 7 suffered
from some mental lesion,
Case 5 was not a true epileptic but a patient
who had been drinking hard, and the Indican
was only temporary, this might be due to
vaso motor changes, which in the same way

way as glycosuria occurs for a short time, the vascular supply of the alimentary canal being in some way deranged, and the Indican forming substance being thus allowed to be absorbed.

Case No 4 only suffered from dyspeptic symptoms but these were severe, of over four years duration and accompanied by much flatulence. No doubt there was much putrefactive change taking place along the alimentary canal, and as I have explained this gives rise to the formation of much Indol, and thus the excess of Indican which appeared in the urine is accounted for.

Cases No 1. 2. 6, had undoubted ulceration of the Intestine, thus affording a good surface for the absorption of any Indol present, and case 6 had an obstruction as well as an ulceration, accounting for the marked excess of Indican.

In case 3, acute obstruction existed without as far as I could discover any ulceration, and this obstruction alone, without any attendant ulceration would account for the excess of

Indican in the urine, because as the obstruction passed away the excess of Indican disappeared, thus showing strongly that in this case the obstruction was the cause of the excess of Indican. This also applies to cases 45 and 9.

Unless case 4 be considered one of dysentery, and she certainly had some intestinal lesion to account for the blood and slime in the stools which disappeared, as did the Indican, I have had no cases of dysentery to examine unless case 14 be taken also as one of dysentery.

I have observed with respect to Indican that there is no excess to the ordinary methods of examination in cases of Typhoid fever. I have examined many ~~cases~~ urines from such patients and failed in every case to detect an excess of Indican excepting in case 35 when it was found during a relapse. I have not found it even in cases of Typhoid with constipation, as cases 32, 33. which are quoted as examples, though many more have been examined.

In case 34 a trace of Indican was found but not in excess.

Dr. Macnuma states that in a case of his of "typhoid with constipation Indican was present in great excess. Dr. Church has told me, on the other hand, that in his cases of "typhoid fever at the Leeds Infirmary, Indican is seldom found in excess, even when constipation is present. He has found traces of it and treats it when found, by daily washing out the colon and administering small doses of calomel. With Dr. A. E. Pearson of the Leeds City Hospital I examined twelve urines taken at random from typhoid patients and in no case was Indican found.
"This absence may be accounted for in one of two ways, either that the diarrhoea carried off the contents of the intestine before any Indol formed, especially as in any case owing to the acid of typhoids would be present, or else that the condition of the intestines in typhoid is such that no Indol is formed, digestion probably not going far enough to admit of this, although on the contrary it is well known that putrefactive changes are marked in typhoid stools.
Cases 36 and 37 were both Tubercular and

here again was an absorbing surface, and much Indican was found.

Osler's statement that Indican is not found in cases of constipation is contradicted in cases 13 + 19, the large meat diet in case 13 may have accounted for the excess of Indican.

Case 10 shows that the presence or absence of Indican in the urines of comatose patients is of importance, though it is by no means always found, as in case 11.

I have rarely found Indican in albuminous urines, cases 49 to 52 are given as examples, though there was some in case 10.

It is not usually found in urines of low specific gravity. It is often absent in gouty cases, at the same time cases 12. 13. 14. 15, 24a, show that Uric acid removal is of benefit to the patient.

Since Uric acid and Indican are both manufactured by the renal epithelium, their absence in some cases in the urine suggests a functional paresis of the cells.

In acute cases where Indicanuria is a complication cases 16. 18, 20, 24. 25. 26. 27. 28, 38, 39, 42, 43, 44, as in specific fevers, Pneumonia. Pleurisy, Bronchitis,

The treatment is always arranged so as to alleviate this symptom, and its removal serves often to turn the scale in favour of the patient and against the disease.
In rheumatic fever especially my first step is to examine the urine for Iodides, if it is found I give a dose of calomel. If it is urgently needed to commence salicylic treatment, I give or order a copious enema of boracic acid lotion, and give same or potassium in addition to the salicylates as long as the Iodides persists.
In the cases of Eczema 40, 41, I communicated that the removal of the Iodides, did much to alleviate the disease, this is probably the action of the Harrogate treatment of the hot strong sulphur water, 24 to 36 being prescribed daily.
Case No 20, is of interest as showing marked toxic effects which disappeared on removal of the Iodides; as also in case No. 21.
Case No 22 partakes of a similar character.
Cases 23. 24 are of great interest inasmuch as they show the peculiar effects of minute doses

dietary, when the patients are suffering from disordered digestion, and the almost instantaneous cures on the principal of Indican.

My cases collected 45. 46. 47. 48 inclusive with operations are very limited, and not the result of any an experience. This I much regret, but the examinations of some 80 to 90 urines of patients on whom I have operated for various reasons, have shown nothing in the way of imparting any knowledge on this subject. I am of opinion however that it has long been believed that cases of intestinal disease treated by operation may be lost by absorption of toxines from the interior after the operation has been successfully performed. Surgeons are however naturally unwilling to add to the length of such an operation performed as is very often the case, in prostrate patients, but, if subsequent investigations should prove that no patient is likely to recover from operation for intestinal obstruction if Indican is present in great excess in the urine, unless the source of this is

washed away or withdrawn through an opening in the gut. The additional procedure will not only be justified but will be compulsory.

Inferences from the presence of Indicanuria.

That there is an excessive formation of products of putrefactive fermentation in the intestinal canal due to a deficiency of Hydrochloric Acid in the gastric juice, either absolute, or in relation to the quantity of food, ingested, and hence unrestrained multiplication of the putrefaction microbes afterentering the intestines, or, that there is putrefactive decomposition in an abscess somewhere in the body.

Indicanuria may usually be regarded that there is a putrefying material in the intestine which must if possible be removed, and that there are microorganisms in it which must be destroyed or checked. It is possible of course that microorganisms are reinforced from without whenever the gastric juice fails. Cultures of cholera bacilli may be swallowed with impunity but only if

the gastric secretion is normal, if it is neutralized or absent and the bacilli thus reach the intestines in numbers, cholera results. It also seems probable that this reinforcement of the intestinal microbes is greater at some seasons or in some conditions than others.

Toxic effects of Indol.

Indol itself does not appear to be very injurious. It has been given freely to animals and has been subcutaneously injected, but though Indican was found in great excess in the urine, according to Jaffé no symptoms of toxaemia are manifested. In some fermentations however in which Indol is produced, highly poisonous substances, alkaloids or albumoses are also produced; the filtrate of Klein's broth culture of a variety of Bacillus coli was extremely fatal to guinea pigs. Some microbes as Tetanus and perhaps also Typhoid are inert and cannot elaborate their poisons except when the products of putrefaction are present. British Medical Journal. April 21. 1894. p. 870. Indicaemia may therefore

be taken to indicate further, that there are associated poisons actually circulating in the tissues and that the contents of the gastro intestinal canal are a favourite culture medium for some pathogenic microorganisms. It may therefore be confidently stated that if the quantity of Indican in the urine of any person be at all considerable, he will be found to be in some way ailing, manifesting energy or subject to some discomfort or pain. Indicanuria is not commonly found in all cases of intestinal disorder, as a mere accidental result of no practical value or importance, as it does not always occur in all intestinal cases, especially in cases of strangulated hernia, as is pointed out by Chuston the presence and the quantity of Indican depending upon the nature rather than the quantity of the intestinal contents. I do not pretend that in all cases removal of Indicanuria will be followed by recovery from other disorders, it merely disposes of one depressing cause and thus

contributes to the healthier nutrition of the leucocytes and tissues.
Indicanuria may not be the chief epiphenomenon in a case and even when indican disappears the chief disease may remain, as in cases of Typhoid, malaria, Graves's disease, Pneumonia etc, hence the same it is unwise to neglect the Indicanuria
If the fermenting material can be removed from the colon either by Calomel or by enemata or both combined then it is unnecessary to remove it.

Treatment.

When Indicanuria is found to be present, then if possible a small dose of calomel from 1/2 to 3 grains should be given and repeated as often as is necessary, until the unwelcome reaction.

Pepsin and Hydrochloric acid should be given with animal food and diastase with starchy food. The food taken should be made unapt for the continuance of fermentation, any food which is known to be di-

possible by the patient may be taken, with pepsin etc as I have stated above. Salol and Sozoplen may be given likely to keep down the excess of Bacillus Coli. Aloes and Rhubarb may also be given if necessary and indicated.
The enema may be given under chloroform or other anaesthetic is necessary.
The free administration of enemata unless Diuresis or some other intestinal toxaemia is looked for is not to be advised, and may do harm.

Conclusion.

In writing this thesis I have attempted to show, from my own observations, and those of others, that the excess of Indican may at times be of great clinical importance, and if these observations be correct with regard to its non appearance in Syphilis and its appearance in Tubercular lesions of the bowels, it may help, especially in connection with other tests, on some occasions to differentiate between obscure cases of these diseases.
I cannot do better in conclusion than

quote the clinical investigations of Dr. Charles. E. Simon of the condition known as Indicanuria and given by him in the American Journal of Medical Sciences under the heading:- "The modern aspect "of Indicanuria".

1. "The gastric juice possesses antiseptic and germicidal properties.
2. These properties are referable to the presence of free hydrochloric acid.
3. A subnormal amount of free hydro-chloric acid will permit an increased degree of intestinal putrefaction.
4. The conjugate sulphates form an index of the degree of intestinal putrefaction.
5. The increased intestinal putrefaction in cases of subacidity of the gastric juice is largely referable to an increased formation of Indol.
6. The elimination of Indican in the urine may be regarded as an index of the amount of free hydrochloric acid present.
7. A normal acidity of the gastric juice

is never associated with increased Indicanuria.

8. Cases of ulcer of the stomach apparently form an exception to this rule, an increased Indicanuria being associated with hyper-chlorhydria.

9. In other cases of hyperchlorhydria a sub-normal or normal amount of Indican is eliminated.

10. Simple constipation is not always, indeed rarely accompanied by an elimination of Indican.

11. Diarrhoea referable to a catarrhal condition of the colon, often following a previously existing coprostasis, as well as diseases of the colon generally, is not associated with an increased Indicanuria.

N.B. This is open to question. N.P.I.

12. In the differential diagnosis between ileus and coprostasis a small amount of Indican excludes the former condition

N.B. This is also open to question. N.P.I.

13. In cases of anachlorhydria with much Lactic acid the Indican is not necessarily increased.

14. No Indican or but little Indican with a delayed Günsberg potassium Iodide reaction, indicates the absence of free hydrochloric acid, with much lactic acid.

15. Much Indican with a normal or anticipating Günsberg reaction is suggestive of ulcer.

16. In cases in which the use of the gastric tube is impractical or contra indicated, or in cases of mere superficial examination, the Indican reactions furnish a valuable index of the condition of the patients digestive powers.

17. By means of the Indican reaction we are enabled to follow closely the results of treatment instituted in cases of gastro intestinal disease, The following are however necessary premises:-

1. That a perception of decomposing proteids is not taking place anywhere in the body, as such a process in itself

2. is capable of producing an increased elimination of Indican.

2. That there does not exist a stenosis of the small intestine
3. A normal mixed diet, containing no excessive amounts of red meat.

Finis