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SOME NOTES FROM AN INQUIRY INTO THE ACTION OF DINITRO-BENZENE UPON THE URINE OF MAN,

AND EXPERIMENTS PROVING THE INNOCUOUSNESS OF DINITRO-TOLUENE UPON ANIMALS.

By R. PROSSER WHITE, M.D. EDIN., M.R.C.S. ENG.,
HONORARY MEDICAL OFFICER TO THE ROYAL ALBERT EDWARD INFIRMARY, WIGAN;

JOHN HAY, M.D. VICT., M.R.C.S. ENG., &C.,
MEDICAL TUTOR AND REGISTRAR AT THE ROYAL INFIRMARY, LIVERPOOL, AND ASSISTANT PHYSICIAN TO THE STANLEY HOSPITAL, LIVERPOOL;

AND

W. J. ORSMAN, F.C.S., F.I.C.,
LECTURER ON CHEMISTRY AT THE WIGAN TECHNICAL COLLEGE AND ANALYST TO THE COUNTY BOROUGH OF WIGAN AND SOUTHPORT.

IN this inquiry we find that a dose which is immediately fatal or fatal within 24 hours does not exhibit its presence in the urine of man or animals. On the other hand, animals fed upon continuous doses—that is, doses which cause serious and dangerous symptoms or death in a few days—show well-marked pathological features in their urine. These consist of tube casts, brown flakes, and hæmoglobinuria. This latter point has been well worked out by Strassmann and Stecker. In our experiments the dinitro-benzene was administered either hypodermically, or by inunction through the skin to cats. None of the urine of cats so killed showed any perceptible change of colour and in only one which had died from slow chronic poisoning did we find an indication of free dinitro-benzene.

In no fatal case of poisoning amongst the workmen have we

ever discovered any evidence of blood corpuscles or hæmoglobin in the urine. In chronic and subacute cases the typical dark tawny colour of urine is always well marked, which is probably due to some pigmentary derivatives, not to free hæmoglobin. No doubt large and long-continued doses given by the mouth to men would produce, as in animals, hæmolysis, broken-up blood-clot in the intestines, and the exudation of blood into the tubules of the kidneys. But we find that neither in the inhalation of dinitro-benzene vapour, its absorption through the skin, nor when given hypodermically to man or animals, are the grosser lesions observed, even in fatal cases. This fact strengthens us in the belief that it is chiefly through absorption by the skin that cases of poisoning occur during the industrial manipulation of this substance.

We have tabulated below the results of the analysis of the urine of men who were constantly working with dinitro-benzene. Each case was of an exceedingly mild character. The frequent presence of urobilin has not been recorded previously and points to the powerful hæmolytic action of this poison even when absorbed in very minute doses.

slight indication was found. This was in the case of a man who showed indications of poisoning and who had to leave off working.

A second question which has claimed our attention, and also a large proportion of the chemical trade interested in the practical manipulation of the toluene and benzene group of the nitrated aromatic series, is the comparative danger of these two groups. Commercially it is found that some of the toluene group can be substituted for the benzene in the manufacture of certain explosives. The employment of the benzene group is surrounded by a number of technical precautions. It is largely and widely becoming the custom where possible to substitute those of the series which are less harmful for those which experience has shown to be the more dangerous.

In an article in THE LANCET of August 31st, 1901, p. 582, a statement was made by one of us that dinitro-toluene is considered highly deleterious and is dreaded by the workmen who are engaged in its production. This settled belief has been repeated to us and it appears to express the general consensus of the opinion of the employés and

A TABLE SHOWING THE RESULTS OF THE ANALYSIS OF THE URINE OF MEN WHO WERE CONSTANTLY WORKING WITH DINITRO-BENZENE.

No.	Specific gravity water = 1000.	Appearance.	Colour.	Reaction to litmus.	Urea per cent.	Albumin.	Bile pigments.	Sugar.	Urobilin.	Dinitro-benzol.
1	1029	Clear.	Red-brown.	Acid.	2.6	Nil.	Nil.	Nil.	Nil.	Nil.
2	1030	"	Yellow.	"	—	—	—	Present.	—	"
3	1024	Slight precipitate mucus.	"	"	—	Nil.	Nil.	Nil.	Nil.	"
4	1021	" "	Red-brown.	"	—	"	"	"	"	"
5	1025	Heavy red precipitate.	" "	"	—	"	"	"	Present.	Trace.
6	1027	Clear.	" "	"	3.3	"	"	"	Nil.	Faint trace.
7	1026	Thick white precipitate.	Pale yellow.	"	2.9	"	"	"	"	" "
8	1026	Red deposit.	Red-brown.	"	3.1	"	"	"	Present.	Nil.
9	1022	" "	" "	"	3.0	"	"	"	"	"
10	1022	Clear.	Yellow.	"	2.8	"	"	"	Nil.	"
11	1027	Red deposit.	Red-brown.	"	3.1	Trace.	Trace.	"	Present.	"
12	1025	" "	" "	"	2.9	Nil.	Nil.	"	"	"
13	1024	" "	" "	"	2.8	"	"	"	"	"

It will be noticed in the above table that all the samples are acid, many being strongly so. Nearly all are dark-brown in colour and generally precipitate out a red deposit, principally urates. In most of these urobilin is present and can be easily recognised by the following test. 100 cubic centimetres of the urine are acidified with 10 drops of strong hydrochloric acid and are then shaken with 20 cubic centimetres of chloroform. The chloroform which falls to the bottom is separated by means of a separating funnel and filtered into a test-tube. Four cubic centimetres of a solution of one gramme of crystallised acetate of zinc dissolved in a litre of 95 per cent. alcohol is then poured gently down the side of the test-tube and at the junction where the liquids meet a green fluorescent ring characteristic of urobilin will appear, and on shaking the solution will become fluorescent, being green by transmitted light and rose-coloured by reflected light. This pigment can also be detected by means of the spectroscope.

No experimental evidence has yet proved that reduction takes place in the body in case of the nitro compounds of benzene to aniline or phenylene-diamine. In several samples of urine tested both nitrates and nitrites were present, so that in the case of phenylene-diamine being present the pigment Bi-marck brown would be formed and would give the urine a brown tint. The samples of urine were tested for free dinitro-benzene by the following method. The urine is treated with zinc and hydrochloric acid for some hours. Any dinitro-benzene that may be present is reduced by the nascent hydrogen into phenylene-diamine. The urine is then alkalisied with caustic soda and well shaken up with ether. The ether is then separated, filtered, and evaporated. The residue is treated with diluted acetic acid and nitrite of soda, when a yellow or brown colouration shows the presence of dinitro-benzol in the original sample. In three cases a

officials at certain works. Dr. T. M. Legge, H.M. medical inspector of factories, from his large experience of such industries, thought there might be some doubt on this point. We therefore deemed it advisable to experiment upon animals, with the following results. To two cats were administered a 1 per cent. solution of dinitro-toluene in cod-liver oil. The quantity given was two cubic centimetres in the morning and two cubic centimetres in the evening daily until each had partaken of 24 cubic centimetres. Neither cat exhibited any symptoms of poisoning. Two weeks later one of the above cats and a second fresh cat were each dosed with a 1 per cent. solution of dinitro-toluene in cod-liver oil, four cubic centimetres in the morning and four cubic centimetres in the evening until each cat had received 24 cubic centimetres, with no result except a very slight change in the colour of the mucous membrane.

These experiments prove that to cats dinitro-toluene is rather a harmless drug and if we compare it with the results published in the article in THE LANCET already alluded to where similar doses of dinitro-benzene were administered to cats the contrast is most marked. It must be remembered that these experiments deal with animals, but our experience with allied groups of the aromatic series show a close similarity of action when they are exhibited to animals and men and further industrial experience strengthens our belief that mono- di- and tri-nitro-toluene can be safely manipulated with ordinary precautions.

NOTIFICATION OF CHICKEN-POX —At the meeting of the Falmouth Corporation held on May 8th it was decided, on the recommendation of the Sanitary Committee, to make chicken-pox a notifiable disease for six months.