

with regard to the latter that there is most uncertainty. Schäfer<sup>1</sup> says: "With regard to the angular gyrus the experiments with Sanger Brown were entirely contradictory to those of Ferrier and Yeo. In animals in which the grey matter of this convolution was destroyed on one or both sides we could discover no defect of vision." He instances, too, the observations of Flechsig on the course of the fibres of the optic radiation. Tracing these during the process of myelination that observer found that none went to the angular gyrus and he therefore excludes this portion of the cortex from the "visual area." Other observers, reasoning chiefly on clinical evidence, take an opposite view. Sir W. R. Gowers<sup>2</sup> says: "The two half vision centres are probably blended in a higher visual centre in front of the occipital lobe. The arrangement is, however, complex. In each centre both fields are represented, but chiefly that of the opposite eye."

This region is also regarded as the mind vision-centre, and a lesion here is believed to cause therefore crossed amblyopia with some impairment of vision on the same side and mind-blindness. "In the very few post-mortem examinations in cases with crossed amblyopia the posterior and inferior part of the parietal lobe—i.e., the angular gyrus in its widest sense—has been involved in the disease." As the higher centre is supposed to be connected to the retina it is supposed that a lesion on one side may be to some extent compensated by the opposite hemisphere.

The part of the visual cortex which represents the macular region is generally believed to be that lying on either side of the fore part of the calcarine fissure. Schäfer found that in the monkey "bilateral injury of both mesial surfaces of the occipital lobes appeared to cause loss of central vision, peripheral vision being intact." The cortical representation of the macula, however, appears to be not truly hemianopic but to represent more than the corresponding half of each retina, for generally in cases of hemianopia due to cortical lesion the line of demarcation skirts or goes through the macular region and not through the fixation point.

The case under discussion, tends, I think, to show that in man both sides of both retinae are represented to some extent on one side of the brain. The lesion in the occipital lobe would account for the loss of vision in the left side of the visual fields, and to those who regard the angular gyrus as representing both retinae, especially the opposite one, the destruction produced by the abscess beneath the angular gyrus would account for the loss of vision in the remainder of the fields. That both macular regions should have escaped, partially at any rate, is possibly to be explained by the bilateral representation of portions of both maculae. It is difficult, however, to see why the loss of vision in the right side of the visual fields should have been so great. Possibly a gradual recovery will take place in this respect. On the whole, then, I think that the case tends to support the opinion of those who regard the angular gyrus as part of the "visual cortex" and may be described as one of left hemianopia due to the damage to the occipital lobe, with concentric contraction of the fields of vision on the same side as the lesion, due to destruction of fibres of the optic radiation beneath the angular gyrus and to the injury to that convolution. It is, however, of interest to note that there was no evidence of mind-blindness. The patient was unable to read, but he could spell out printed letters and never failed to recognise objects.

For assistance and guidance in the treatment and for permission to publish an account of this case I have to thank Lieutenant-Colonel G. H. Sylvester, R.A.M.C., the officer in charge of No. 2 General Hospital.

<sup>1</sup> Text-book of Physiology, p. 753.

<sup>2</sup> Diseases of the Brain, vol. i., p. 143.

**LYNTON COTTAGE HOSPITAL.**—The working men of Lynton and Lynmouth, Devon, for the past two years have held an industrial fair in aid of the funds of the Lynton Cottage Hospital. The fair which was held last week resulted in a sum of £90 being handed over to the institution; in 1900 £65 were obtained.

**VACCINATION RETURNS.**—At the meeting of the Uxbridge Board of Guardians held on August 20th it was reported that during the six months ended Dec. 31st, 1900, there were 457 births in the several parishes of the union; of these children 179 were successfully vaccinated and 108 were exempted.

## SOME RECENT INQUIRIES AND RESEARCHES INTO THE POISONOUS PROPERTIES OF NAPHTHALENE AND THE AROMATIC COMPOUNDS.

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THE manufacture and employment of naphthalene and of the aromatic series of compounds constitutes a comparatively large industry both in this and other countries, and especially is this the case since they form necessary and essential ingredients in what are now known as the "high explosives." In the short time at my disposal it will be quite impossible for me (R. P. W.) to give a detailed account of the symptomatology, pathology, and precautions to be used when handling these substances. These points were considered by me in 1892,<sup>1</sup> also more recently in an article which will shortly appear in Dr. T. Oliver's book upon "Industrial Occupations." This paper deals solely with their dosage and their relative poisonous actions, and then some recent investigations upon the absorbability of the dinitro-benzene compounds through the skin. This last point is the more important as Strusmann and Strecker<sup>2</sup> in a recent paper upon the subject of dinitro-benzene rather seem to infer that there is no absorption by the skin.

In large doses the nitrated aromatic compounds act powerfully upon the higher centres, producing coma and death. In smaller doses their effects are noticed upon the sympathetic and peripheral nerves, inducing loss of vaso-motor tone and the symptoms of multiple neuritis. Their action upon the blood is in most cases definite and characteristic; many of them seem to form chemical compounds with the hæmoglobin, producing cyanosis, deficient oxidation, and breaking up of the blood cells. With some of these poisons hæmolysis occurs and much degeneration takes place in the tissues of certain organs. The following conclusions we have drawn partly from my own experience with workmen employed in the manufacture of high explosives, partly from experiments upon animals, and partly from the experience of others. The naphthalene group, which is largely used, is probably much less dangerous than are the benzene and toluene groups. Of the naphthalene compounds it is probable that the dinitro-benzene naphthalene is more poisonous than the mono-nitro preparation.

Coming to the benzene group, mono-nitro-benzene when given by the mouth to cats does not seem to affect them at all; they rather seem to thrive and grow fat upon it. The dinitro-benzene is, on the other hand, exceedingly poisonous both to animals and men. The smallest lethal dose of dinitro-benzene for a cat of six pounds is 0.08 gramme if given by the mouth in one dose. In one instance a dose of 0.06 gramme of dinitro-benzene was not fatal but almost so. 1.2 grammes given to a cat by the mouth was fatal in about three hours. In the same ratio the lethal dose for a man of 10 stones would equal 1.82 grammes, but in all probability a smaller dose would be fatal. A lethal dose when divided up and given over a consecutive number of days does not kill—for instance, in a case where we gave 0.09 gramme of dinitro-benzene to a cat in doses of 0.04, 0.02, 0.01, and 0.02 gramme over a period of four days without causing death. It has been stated that dinitro-benzene when taken into the stomach shows a latent period before exhibiting its action. In our experience of experiments upon animals we find that if an animal survives a given dose of the poison for 24 hours it will recover entirely. This in all probability applies also to man. The vapour when inhaled acts immediately and the other preparations are readily absorbed if in a suitable solution. Hypodermically a dose of 0.04 gramme of dinitro-benzene was not fatal to a cat. From experiments with

<sup>1</sup> Provincial Medical Journal, Sept. 1st, 1892.

<sup>2</sup> Friedrich's Blätter für gerichtliche Medicin, July and August, 1901.

trinitro-benzene we found that it was distinctly not very much more poisonous than dinitro-benzene. Mononitro-toluene is quite inert when administered to cats. Our personal experience of nitrotoluene is small, but on inquiries from the places where it is manufactured we were told that it was much too dangerous to work with—in fact, it was described as “simply hellish.” The trinitro compound of toluene appears less poisonous than its dinitro-benzene equivalent. For comparison: 50 minims of a 1 per cent. solution of trinitro-benzene were hypodermically injected into a cat, causing death in a few hours. In another cat an injection of 60 minims of a 1 per cent. solution of trinitrotoluene produced only slight symptoms of cyanosis. The comparative harmlessness of trinitrotoluene is a very important fact, especially if, as we believe it does, it applies to man. Trinitrotoluene has been occasionally substituted for dinitro-benzene in some manufacturing processes with great benefit to the workmen. If it can be found practically possible to replace the benzene compound by the toluene compound in all these industries it will be a very valuable step.

So much, then, for the comparative poisonous properties of naphthalene and the aromatic series of nitro compounds. These all refer to their action when introduced into the system either hypodermically or by the mouth. I (R. P. W.) have long felt that dinitro-benzene, with which I am specially familiar, is very largely absorbed by the skin, but up till quite recently I could find no conclusive evidence that this substance was capable of being directly absorbed. The only experiment pointing to its possibility and probability occurred some years ago in the case of a German firm who were working with this substance. In order to eliminate the danger due to the inhalation of the vapour and the fine powder suspended in the air the following experiment was carried out and was narrated to me by an eye-witness. It consisted in applying to the men an oro-nasal mouthpiece fastened on to the face with an outlet and inlet tube carried to the outer air. This was fitted with valves through which the wearer inspired the fresh air and exhaled the vitiated breath. Under these circumstances it seemed that there was no possible chance of the dinitro-benzene vapour or powder obtaining access to the mouth or nose, but even with this precaution the incidence of sickness in the factory was not affected, and the only other channel by which the poison could get to the blood if this experiment was properly carried out must have been the skin. The possibility or impossibility of absorption by the human skin of drugs in any large quantity seems to be a very difficult problem, and Schäfer<sup>3</sup> says that literature extending over a century indicates that the production of impartial testimony on either the affirmative or negative side has proved of no little difficulty. He says that watery solutions are not absorbed. Krause maintained that ethereal and alcoholic solutions can be absorbed, but Fleisher, Ritter, and Winternitz, on the other hand, have stoutly denied the possibility. The application of oily solutions of certain drugs, veratrine, aconitine, potassium iodide, morphine, quinine, and salicylate of soda are probably quite inert, and the only exception appears to be mercurial ointment, which is undoubtedly absorbed. The fine globules of mercury in mercurial ointment are forced under the skin; the black oxide by the action of the chloride of sodium forms calomel, and this in the presence of oxygen is further changed into corrosive sublimate, which in this state is readily taken up into the system. This negative evidence made me somewhat sceptical as to the absorbability of the aromatic series of compounds, but when discussing the question with Mr. Orsman, our chemist, he said that on one occasion when working with toluidine he accidentally spilled some on his fingers, and he narrated how he at once felt the physiological effects, such as faintness and giddiness, which he considered due to absorption. Another point is that workmen engaged in working amongst these higher fluid distillates are always very careful not to subject their hands to any prolonged immersion in them, fearing the results. I therefore asked Dr. John Hay of Liverpool to kindly undertake the following experiments for me.

CAT 1.—In the afternoon of Oct. 10th, 1900, the back of a female cat was carefully shaved whilst the animal was under an anæsthetic. An ointment composed of anhydrous wool fat, containing 25 per cent. dinitro-benzene, was applied to the skin over an area of three square inches. A piece of lint was laid over the anointed skin and the whole was covered and sealed with a gauze and collodion dressing.

The next day, at 10 A.M., the cat was noticed to be somewhat stupid, but if startled in the slightest it jumped up in its cage and fell down stiff and rigid with its limbs extended. At 1 P.M. on this day the cat was dying. Its respirations were gasping, with long intervals of quiescence. The tongue was a livid blue, as were also all the mucous membranes. On opening the thorax after death the lungs were observed to be pale. The blood was collected. It was of a dull chocolate brown tint and coagulated readily. Spectroscopically it gave a dark absorption band corresponding with the meth-hæmoglobin band. On microscopical examination of a fresh specimen many of the red corpuscles appeared small and misshapen. It was not possible to find dinitro-benzene in either the blood or the urine.

As a criticism on the above experiment it might be advanced that the dinitro-benzene entered the circulation through cracks and small cuts almost unavoidably produced whilst trying to free the cat's back from its down. Therefore it was decided to shave the fur off three or four days before the anointing, so that any chance abrasion or cut might have time to heal.

CAT 2.—On Oct. 12th the fur was shaved off from the back of a fine large tabby cat, an anæsthetic being used to keep the animal quiet during shaving. On the next day the skin appeared quite clean and practically free from abrasions or cuts. On the 15th a 25 per cent. dinitro-benzene ointment was applied to an area of one and a quarter square inches and was carefully sealed with a collodion dressing as before. On the next day distinct but slight cyanosis of the mucous membrane was observed. The cat appeared to be otherwise normal. On the 19th the tongue and lips were markedly blue. The reflex excitability of the cat was noticed to be distinctly increased. On examination of the urine it was found to contain blood. The cat died on the next day whilst under an anæsthetic. On examining its blood spectroscopically absorption bands similar to the meth-hæmoglobin absorption bands were observed. The liver showed the naked-eye appearances of fatty degeneration.

CAT 3.—On Oct. 20th the back of a cat was shaved and any abrasions of the skin were allowed to heal. On the 23rd a piece of parchment three inches by one inch covered with 25 per cent. dinitro-benzene ointment was applied and sealed with collodion and gauze dressing. By the 24th the collodion and gauze were quite firmly fixed and it would have been quite impossible for the cat to have transferred any of the ointment into its mouth. The nose and the mucous membrane of the mouth and tongue were, however, pale and cyanosed. On the next day the nose and mucous membrane were still pale and bluish, but the cat otherwise appeared healthy. The cyanosis was still more marked on the 26th and there was quite a deep blue colour at the sides of the tongue. It was noticed to be salivating freely and there was a definite alteration in its voice. On this date an anæsthetic was administered and another strip of anointed parchment was sealed on to its back. On examining the blood it was found to be altered; irregular and refractile bodies were found apparently on the red corpuscles and the corpuscles were altered in shape. The corpuscles did not run into rouleaux as in normal blood. The pseudometh-hæmoglobin absorption bands were distinctly present and the blood was definitely brown to the naked eye. At 1 P.M. on the 27th the cat looked distinctly worse; there was marked salivation, the nose was very pale, and the tongue was even more cyanosed. The cat was constantly crying out and lying curled up at the back of its cage. It was not resistive in any way and walked with some stiffness. There was distinct increase in the patellar reflex. The urine was highly discoloured, but there was no bile. The blood was difficult to obtain as the ear almost refused to bleed. It was chocolate brown. The alteration and irregularity in shape of the corpuscles was even more marked than on the 26th. Some of the small glittering bodies were seen floating free in the plasma. The cat was still alive on the 29th but looked very ill. The symptoms previously mentioned were aggravated, the gait was more reeling, and the cat showed a tendency to fall on to its side. There was distinct spasticity of the hind legs which were lifted high up as it walked. The patellar reflex were increased. On the 30th the cat was apparently dying, it was unable to walk and lay on its side. There was marked twitching of the head and paws. The patellar reflex was still increased. The cat was killed. Its blood was a very rich chocolate brown, and the pseudo meth-hæmoglobin band was demonstrated in it. The

<sup>3</sup> Text-book on Physiology, 1893.

urine was almost as dark as blood and contained both meth-hæmoglobin and also oxyhæmoglobin. No dinitro-benzene could be demonstrated in the urine or in the blood. On making a microscopical examination of the kidneys they were found to be in a condition of inflammation, probably a toxic nephritis.

Dr. Hay gives the following account of an experiment performed upon himself: "On Oct. 8th, before dressing, I anointed my groins with a small portion of the 25 per cent. dinitro-benzene ointment, weight 400 milligrammes, containing 0.1 gramme of dinitro-benzene. I repeated this in the evening before going to bed. On the 9th I noticed very marked blueness about the lips and the finger nails; the tongue was also markedly blue. There were no subjective sensations. Before dressing I anointed my groins again with a similar quantity, but at 12 noon, owing to the cyanosis increasing in intensity, I carefully washed off all the ointment. At 1 P.M. the lips were a livid blue and the nails and skin generally of a deadly hue. The pulse was 100 to 120; it was regular in time and force and with its tension apparently raised and fuller. There was a feeling of fulness in the head and some throbbing headache, increased by movement. There was no obvious alteration in the urine. On cutting the thumb the blood appeared of a distinctly brown and darker colour than is normal. There was definite blurring of the oxyhæmoglobin bands, but no absorption bands with red. An examination of the urine gave negative results. Three ounces were sent to Dr. White. [The examination of the urine of Dr. Hay gave no reaction of the dinitro-benzene test. This is easily explained, as in no instance with which I (R. P. W.) am acquainted has so short an exposure to the dinitro-benzene poison ever given a reaction either in man or any animals.] At 6 P.M. the pulse was still full and bounding, from 96 to 98, regular in time and force. There were a rather metallic taste in the mouth and frontal and orbital headache, accompanied by a feeling of fulness, increased by movement, especially when running up and down stairs. Oxygen was inhaled for five minutes without any relief or alteration in the appearances of the lips and skin. The veins of the hands and the ears were full and engorged. A distinct tremor of the hands was present. On the 10th there was still some cyanosis of the lips, but not so marked as on the 9th. The headache had almost disappeared and there was no tremor. The pulse was still somewhat frequent. On the 11th my health was practically normal with the exception of a slight tendency to headache."

These experiments prove most conclusively the ease with which dinitro-benzene when in close contact with the skin becomes absorbed. It is, however, common knowledge that the skin of a cat is thinner, more vascular, and less horny than that of a man, and therefore this personal experience is of great value. Facts like these, which are important, suggest the necessity of instituting experimental inquiry into the methods of operation of many of the industrial poisons—i.e., plumbism, phosphorism, mercurialism, &c.

Passing to the subject immediately before us, it would appear that given the manipulation of a certain strength of poison a corresponding amount of sickness will ensue and that the incidence of sickness among those manufacturing explosives varies with the proportion of dinitro-benzene. Handling, grinding, heating, and otherwise manipulating pure dinitro-benzene are at all times most risky and dangerous to the worker. If the process involves any possible personal contact the strictest precautions must under such circumstances be carried out. With a less percentage of dinitro-benzene in the material manipulated we have often associated a marked amount of sickness; for instance, when working with 14 parts of dinitro-benzene to 100 parts of the other ingredients our experience has given a ratio of sickness varying from 5 to 40 per cent. of the workmen immediately employed. The amount of sickness is largely affected by atmospheric conditions, such as temperature and moisture, also by the hours of work. Our experience is that with percentages under 10 and preserving the ordinary strict precautions acute cases should be non-existent. In the early days of association with the use of dinitro-benzene the dinitro was very largely contaminated with the mono-nitro-benzene and also probably with some of the toluene compounds. In recent years, with a much more carefully prepared dinitro-benzene, but with almost the same percentage of it, the incidence of sickness has been markedly lessened. The following consideration may partially explain this fact. Pure dinitro-benzene consists of colourless crystals, but through impurities the commercial dinitro-benzene is often of a darkened colour,

especially when mixed with mono-nitro-benzene, and under these circumstances the men frequently object and will even refuse to work.

In a previous part of this paper it has been shown that the mono-nitro-benzene is practically innocuous to animals; it is probably also innocuous to man and if so we can only suppose that the liquid greasy mono-nitro-benzene may assist in a material degree to render the dinitro-benzene more adhesive and thereby more easily absorbed through the skin. The mono-nitro-benzene acts as a powerful solvent of dinitro-benzene just as do the fats and oils. Acting upon this thought 0.1 gramme of chemically pure dinitro-benzene crystals alone was applied to the skin of a cat sealed as in the previous manner, yet after three days no alteration had taken place in the animal. In a second experiment 0.1 gramme of chemically pure dinitro-benzene dissolved in mono-nitro-benzene was applied to the skin of another cat at the same time. In this latter cat after the same number of days' exposure to the poison cyanosis became visible. The area of exposure of both of these poisons to the skin was identical—viz., a space of two square inches. These experiments emphasise the necessity there is of some solvent to enable the poison to be carried through the skin, for had the same dose of poison been suspended in an animal fat symptoms of poison would have been very marked. It also rather suggests that the numerous oxidising ingredients associated with the dinitro-benzene in the manufacture of high explosives may have some influence upon absorption. It must not be forgotten that in the practical working of these substances particles alight upon the body where they undergo friction and pressure and are moulded into the coil and sebaceous ducts. Recently it has been proved that not only the sebaceous but also the coil glands excrete a certain amount of oil which acts as a ready solvent to the dinitro-benzene. The presence of oil on the hands, where there are no sebaceous glands, has an important bearing upon the necessity of frequent washings of all exposed surfaces of the skin. No part of the skin, except absolutely necessary, should be left uncovered by the special clothing ordered. The hair of the head should be cut close and the face have as little hair on as possible. Caps should be tight-fitting and cover as much as can be conveniently arranged.

In conclusion, we should like to advert to the necessity which exists for instituting a Government laboratory in which experiments such as we have carried out can be performed instead of leaving these points to the energy and enthusiasm of private workers.

## ON THE PROPHYLAXIS OF CARCINOMA.

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If we grant that the *materies morbi* of carcinoma is most likely a living organism, the situations generally attacked by carcinoma suggest (1) that its specific cause flourishes in either the secretions or the cells of the skin-glands, including the mammary gland—e.g., milk, butter, cheese, sebaceous material, and sweat; and (2) that before milk, butter, and cheese are allowed to rest in contact with weakened parts—e.g., ulcerations—either inside or outside the body, such articles should be sterilised by heat, while the secretions of the glands of the skin should be kept away by cleanliness. It is assumed that everyone will agree that chronic inflammations of parts liable to primary cancer should be cured, if possible, and that ulcerations and cicatrices in such localities, unless there are predominating reasons to the contrary, should be removed.

Almost all primary carcinomata are seated in the breast, the alimentary canal, the skin, and the uterus, or in canals, ducts, and glands subsidiary to those parts or directly opening into them—e.g., the larynx, liver, pancreas, vagina, and urethra. The majority of those which have come under my own observation have occurred in either the breast or in the alimentary canal (including in the latter the lips and the rectum).

Reflecting on what medium would be a likely or possible carrier of the essential cause of cancer (whatever that may be) to two such different localities as the breast and any