

for this function. I have recently had under my care two patients with extreme and persistent conjugate deviation of head and eyes lasting for weeks. In one case a large glioma almost completely excavating the left frontal lobe, but not involving the cortex, was found. In the second case, in which the lesion was right-sided, the presence of complete hemianopia and astereognosis with marked hemianalgesia and very little hemiplegia made it certain that the lesion was in the posterior half of the hemisphere. I may, however, go so far as to say that conjugate deviation, when persisting in the absence of other localizing signs, may indicate either a frontal or a temporal location, but it will not distinguish between the two, for Kolodny found it well marked in 6 out of 38 cases of temporal tumour. When present it is of certain lateralizing value for tumours in any part of the hemisphere. It may be seen in the form of persistent deviation to the contralateral side, or of weakness and unwillingness in deviation to the ipsilateral side.

Loss or diminution of the trunk reflexes may be of great lateralizing value, and is said to be valuable in frontal location. But I hold that it is much more characteristic of the temporal tumour, and I have several times located a temporal tumour and had it successfully removed when this was the only localizing sign present. In one-half of Kolodny's temporal cases the trunk reflexes were completely absent on the contralateral side. The presence of these reflexes has no negating significance. In both frontal and temporal tumours it is probably a contiguous sign of pressure upon the pyramidal mechanism.

Incontinence is sometimes very marked in frontal tumours, even when the mental aberration is inconspicuous. I think I have seen it more often in temporal tumours. It was present in 20 per cent. of Kolodny's cases of temporal tumours.

Papilloedema was said by Leslie Paton to occur earlier and more severely with tumours of the hemisphere the farther forward these were situated. Recently Stopford has analysed another series of cases, and comes to the conclusion that the farther back the situation the earlier and more intense the papilloedema. I am inclined to agree with Stopford, though I do not think papilloedema is of any value, either in localization or in lateralization. Horsley affirmed that it was greater on the side of the tumour. With frontal tumours one might reasonably expect it to be less on the side of the tumour, since major local pressure at the back of the orbit tends to delay the onset of papilloedema. I have seen a good many very large frontal tumours come to autopsy without having developed papilloedema.

Lethargy of a deep but rousable kind has occurred many times in frontal tumour, and when existing without headache or papilloedema it has caused several cases at the National Hospital to reach the post-mortem room with the label "lethargic encephalitis." One patient came under my care with deep lethargy following immediately upon an attack of influenza. I cured this patient at St. George's Hospital with injections of collosol iodine and salicylates, and she remained quite well and at work until fifteen months later, when a second attack of lethargy proved fatal, and I found a very large right-sided frontal tumour. This patient had no headache and never developed papilloedema. I am well aware of lethargy as occurring with pineal tumours and tumours of the upper brain stem, but I have only seen lethargy of this nature in tumours of the frontal region so far as the hemispheres are concerned.

Fits of many kinds occur with frontal tumours. I have seen characteristic minor attacks occurring frequently as the sole epileptic manifestation. Hughlings Jackson spoke of convulsions with bilateral commencement as indications of frontal location, but perhaps this was more from theoretical considerations than from practical experience. The convulsions I have seen have always commenced with conjugate deviation, which deviation has been a sure lateralizing sign. Status epilepticus is an interesting frontal symptom. I have records of two cases which were in hospital under treatment for fits, and in which no signs of local lesion of the nervous system were found. These patients developed status epilepticus and perished, and in

both cases a frontal tumour was found. I have no knowledge of any other region of the brain in which a tumour has produced status epilepticus.

There remain for consideration certain phenomena, such as Mayer's reflex, Leri's reflex, and Hoffman's reflex, which are said to be absent in prefrontal lesions, and Wessenberg's sign, which is supposed to be found only when a prefrontal lesion is present. Of these signs I have not much experience.

Signs Peculiar to Lesions of the Anterior Fossa.

The signs peculiar to the anterior fossa of the skull are those of pressure upon the olfactory tract, the optic nerve or chiasma, or upon the nerves and vessels passing through the sphenoidal fissure, and those of bony involvement. These are always certain localizing and lateralizing signs, but they only obtain with a hard tumour coming to the surface of the orbital lobe or with a growth of meninges or bone.

Signs Revealed by Ventriculography.

There remains the method of ventriculography, which in skilled hands has resulted in many brilliant successes in this and in other difficult regions of the brain.

I hope that in introducing this subject to you I have said nothing that is dogmatic and nothing that is antagonistic to the feelings of any of you. If I have done so my fate will surely be that of all who are too sure about so delicate a subject as location within the cerebral hemispheres. May I tell you a story of one who did dogmatize? It concerns no less an observer and fine neurologist than Albert Knapp, who, in his monograph on *Tumours of the Temporal Lobe*, wrote: "Paralysis of the sixth nerve, so common in tumours of the hemispheres elsewhere, is practically unknown with temporal tumours, and its absence is of localizing value. I have myself recorded the only case in the literature of the subject." I am informed that after publishing this monograph the six consecutive cases of temporal tumour which came under Professor Knapp's care all had sixth nerve paralysis.

INCIDENCE OF DISEASE OF THE BLADDER IN WORKERS IN CERTAIN CHEMICALS.*

BY

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I HAVE lived in the vicinity of a chemical works for nearly thirty years, and for the period 1900 to 1910 had, as patients, many men who had worked at this factory for several years. Since 1918 I have held the position of appointed surgeon for the factory, and have had, at all times, perfect freedom of access and much help from the managers and staff chemists in all problems that arose.

In the early periods (1860 and on) of the making of certain dyes from coal-tar products arsenic was largely used (As_2O_3); workers were not protected in any way, and cases of toxæmia were only beginning to be observed. At these times any man who offered himself got a job, if such were available. Cases were sent to the doctor simply as they happened, and no records were kept. No other system was thought necessary. Now we only take mature men below a certain age; they are examined as to indications of good health and evidences of skin trouble. A well-fitted first-aid station and a competent nurse are provided, and all cases are seen medically on the spot as soon as possible after report. Also, men are encouraged to report on any deviation from general health, and such cases are investigated, there being an attempt to promote good feeling always between doctor, nurse, and men, so no trivial report is ignored, and all cases are recorded. It is, however, not easy to give percentages of incidence of disease in chemical workers, because usually a man's job is not the same over a long period, and prior to coming

* Read in opening a discussion in the Section of Occupational Diseases at the Annual Meeting of the British Medical Association, Manchester, 1928.

to this factory he may have worked on pitch, tar, etc., or at a similar dye-making works. Chemical plants do not employ the same number of men constantly, and in the dyestuffs industry there may be such a large number of products chemically different that the works atmosphere is a mixture of various odours, and so, day after day, one inhales something from everything going on.

Again, quite a large percentage of the men employed are lead-burners, plumbers, joiners, mechanics, electricians, and other artisans, so that unless we had a steady number of men constantly on the same chemical process over many years, percentages would be of little value.

In a chemical works manufacturing dyes one might expect men reporting, occasionally, pigmentation of urine, because sometimes, in spite of muzzles, air-draughts, washing, etc., face, hands, tongue, and mouth are freely coloured, and ingestion, or perhaps absorption through the skin, occurs. This pigmentation of urine rarely happens, but we must impress upon men the necessity of reporting such changes. Of course, the object of this desire for a report from men is to see quite early any alteration of urinary colour in order to eliminate pathological pigmentation.

It is well known that reaction to dyestuffs varies with individuals, and with age and habits, blonds being more susceptible, and alcoholics also.

Primarily, certain chemical groups are known to cause forms of acute dermatitis and conjunctivitis, or bronchial and nasal troubles; others—for example, aniline—by absorption, ingestion, or inhalation, in acute cases produce illness, and pigmentation, visible on face, hands, and ears, as well as general bodily weakness, dyspnoea, and possibly blood in the urine, owing to the production of methaemoglobin in the blood. Such cases, seen early and treated, recover health, and I have not heard of any subsequent growths from acute illnesses of this type.

During 1919 a number of men working on a reduction process reported alteration in urinary colour, and some, not even feeling ill, were found passing blood in the urine; there were about 23 cases in all. This was traced to the effects of AsH_3 . Many of the men were sent to hospital, and all recovered their health. After the war, and the change over to peace conditions, many of these men left the works, and their subsequent history is not known. The source of the arsenic was in the acid employed, and only pure acid afterwards was used. Lead-burners using hydrogen produced from impure acid containing arsenic were liable to be affected as the result of inhalation, and two cases were known. With improved conditions no further case of this type has been seen.

Quite a number of intermediates, as well as finished dyestuffs, can produce in some persons, varying with idiosyncrasies—for example, sweating, colour of hair and skin, seasons—extensive acute dermatitis, and this often recurs in the same individual if re-employed.

Although I have had many such cases, I have only met one case of surface epithelioma which might follow this irritation, and I have not seen any undue development of warts on hands or other parts affected, and no rodent ulcer of the face. I am not certain that the cause of the case now related is true.

A man about 48 years of age, with twenty years' service, alleged that three months before seeing me a piece of Na_2S had slipped down his waist belt and caused a sore on one side of the scrotum. At my examination he had a well-defined epitheliomatous ulcer, with deposits in the groin. He was sent to hospital, no operation was performed, and he died six months later from systemic invasion. The cause in his case was doubtful. I do not think his statement was reliable.

I have no records of malignancy in nose, throat, larynx, or lungs resulting from inhalation of $CoCl_2$, H_2S , AsH_3 , or other toxic gases, and no permanent eye trouble; and I have not any indication of ulcer or growth in stomach or bowels being more common in the chemical dye industry than in other occupations.

Up to 1900 various preparations were produced in the manufacture of which arsenic acid was used. Considerable quantities of α -naphthylamine were also produced, and normally in this no arsenic would be used. The number of workmen then employed varied from 100 to 200, and

of men are available, but W. F. Dearden in 1902 had some experience with acute aniline poisoning occurring in other workmen on fast aniline black, and this was reported in the *British Medical Journal*. Up to 1910 I had personal knowledge of three men working on α -naphthylamine who died from urinary trouble due to neoplasm, and I know the names of more, but having no personal proof they cannot be included. It is possible these men might have suffered from arsenical poisoning, as we know that surgical diagnosis and treatment was then less precise.

Since 1918 α -naphthylamine has been in fairly continuous production save for a period of some months. All the men engaged on those parts of processes where there is risk in handling the material wear gloves; they are not in the open air. Others, working on distillation, are in the open air, and ordinarily do not handle the product, because pipe lines are used to transfer from one vessel to another by pressure. All the men are provided with baths, which they certainly use daily. There are good facilities for washing hands before meals, and separate lockers for working clothes and day clothes; they do not go home in working clothes; there is a canteen away from the plant for food, etc., and milk is given to each man daily.

Moreover, α -naphthylamine does not cause acute cyanosis, or any irritation of skin, nose, fauces, larynx, eyes, or stomach. For a period of six months a weekly examination by a competent analyst of carefully obtained specimens of urine yielded no indications of abnormal contents. Whereas, on another plant—distillation of nitro-toluol—workers were found passing nitro-bodies, and yet feeling quite well. This observation could not be followed up for a prolonged period for various reasons. After many years' service on plants men report a frequent desire to micturate, with possibly strangury and blood. Competent examination at hospital perhaps reveals a neoplasm at the ureteric orifice in the bladder. Some of these men have been treated by diathermy endovesically, others by incision, and have returned to work, their job being changed where possible.

I will report now the cases known amongst workers on the α -naphthylamine plant, and it is curious that cases only seem to occur amongst workmen, for staff chemists on the plant with service equally as long, and always in the odours and dust, have not so far been affected. Moreover, large amounts of this crude stuff have been used for experiments on mice by cancer research authorities, and, taking the whole length of life in a mouse in comparison with man, no pathological results were found. This stuff, when new, has a faint aromatic odour, like naphthalene. As it becomes older, or if in contact with human clothes, skin, etc., it develops an intense faecal odour similar to skatol.

URINARY DISEASES IN WORKERS CONNECTED WITH α -NAPHTHYLAMINE AND DYES PRODUCED WITH ARSENIC AS AN AGENT.

From 1880 to 1910.

During this period there were eight men who were said to have had pronounced urinary trouble. All are dead, but their history was not known to me personally. Three others, who were engaged chiefly on α -naphthylamine, are also dead—one after about fifteen years' service, one after twenty years' service, the other for an unknown period. These men were known to me and were at times treated by me. The average number of men on the job before 1910 is not known—probably 150 to 200.

From 1918.—Production of α -Naphthylamine.

R. H., aged about 56; nearly thirty years' service. Primary operation 1906; again operated on in 1911. Worked on stills, and sodium naphthionate. Died December, 1924—inoperable carcinoma of the bladder.

T. B., aged 58. Employed as farm labourer in Shropshire to 1894; in tar works to 1900. Distillation of naphthol for eight years, then charge-hand on distillation of α -naphthylamine for twenty years. Neoplasm of bladder; operation in 1927. Died in December, 1928, with extensive carcinoma of the bladder.

F. G., aged 54. In 1914 was engaged in production of α -naphthylamine. In 1915 had papilloma removed at the Royal Infirmary, and since then has been employed on other processes and work as a foreman. In 1929 he had urinary difficulty; is now under Mr. Macalpine. Not yet diagnosed as growth.

J. W., aged 56. Thirty years' service on plant (reductions chiefly). Had urinary trouble about 1917. Papilloma removed at the Royal Infirmary by Mr. Burgess. In October, 1928, had recurrence of blood in urine, pain, etc. Seen at Ancoats Hospital. Had papilloma which was treated by endovesical diathermy. Is now under Mr. Macalpine at Salford Royal Hospital. He has extensive

Urinary Cases in Other Departments.

1914. M. J., aged 54. Twenty-five years in works. Had urinary trouble, and was sent to Ancoats Hospital and later to the Radium Institute. He died, and at necropsy was found to have had a malignant growth of the prostate.

1926-27. K., aged 56. Twenty years' service: metaphenylenediamine, di-nitro-toluol, benzidine. Had neoplasm of the bladder, and died in 1927. H. was employed at the same place, and same service. He also had neoplasm of the bladder and calculus. He died in 1926. W. had the same twenty years' service as K. Was in hospital for five weeks in 1919 with acute benzidine toxæmia. Died in 1927 with growth of the bladder.

1927. W. T. was engaged for nearly thirty years in the same service as the last three cases. He complained of pain, and blood was present in the urine. He was admitted to Crumpsall Infirmary, and died. Post-mortem examination disclosed lymphosarcoma of the abdomen invading the bladder. N., aged 56, had nearly thirty years' service; at first for some years in the warehouse at the works. He was for ten years on the sulphuric acid plant; later on metaphenylenediamine. For the last ten years he was weighing barrels of finished dyes. At necropsy he was found to have extensive growth of the bladder.

1924. W. and D., young men of 25 to 30 years of age, of short service; employed in grinding diphenylguanidine. They had serious urinary pain, but no hæmorrhages. They left the works, and their further history is not known.

1924. R. J., aged 42, was employed in the works for five years. He died in Crescent Road Hospital with malignant growth of the bladder. S. was employed for many years in drying finished dyes in stoves, mainly of triphenylmethane type. He had dysuria and blood in urine in 1925. Was operated on for papilloma at the Royal Infirmary. He is still living, but not at work.

1926-27. W., a big, 16 st. man of 30. Was employed on naphthalene intermediates—sulphonations, nitrations, and reductions. Had pain, and blood was present in the urine. He was seen and treated

by Mr. Macalpine. No neoplasm was found. He is now working as a mechanic, and is well.

1927. A. had dysuria and blood in urine. He was working on cyanide crushing; no connexion established. He is quite well.

1928. T., aged 60, has had fifteen years' service on azo colours. He had blood in the urine and was treated by his own doctor. He is well and still at work.

The urines of several of the above employees were analysed, but yielded no evidence of toxic bodies.

Non-urinary Cases.

1920. Incog.; employed on various products; had carcinoma of the caecum.

1924. R. H. was employed on various products—intermediates and triphenylmethane; also, prior to this engagement, for many years on phenol distillation. He had carcinoma of the pylorus and died.

1927. K. C. suffered from epithelioma of the scrotum, said to be due to Na₂S; deposits in abdomen. He died.

Owing to the fact that many of the men previously had worked on processes other than α -naphthylamine, and some never on α -naphthylamine at any time, it is, in my opinion, impossible to assume this to be the most potent agent. If it were possible to have men under medical observation for a long period of years in works solely concerned with the making of α -naphthylamine, and not near any contaminating plant, and a staff of men with no previous chemical history, we might be able to trace the irritant. So far we cannot arrive at any true percentage of cases in general, owing to the following facts: (a) men sometimes employed on one job, then on another; (b) irregular operation of the plant owing to trade; (c) no proper history of men after leaving the works.

THE EFFECT OF RADIATION ON THE RESISTANCE OF RABBITS TO INFECTION WITH VIRULENT STAPHYLOCOCCI.

BY

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INTRODUCTION.

THE clinical study of disease treated by general light baths suggests that the absorption of rays of light by the skin increases the general resistance of the body to bacterial infection. The curative action of light has been successful not only in surgical tuberculosis, but in certain bacterial diseases of the eye, mucous membrane, and skin. Recent research on the action of light in the cure and prevention of rickets has proved that this disease is due to deficiency of vitamin D, and that irradiation causes the production of vitamin D from ergosterol in the skin and the absorption of this vitamin. Up to the present the experimental work on the effect of irradiation on resistance to infection has been limited and contradictory. Rhode¹ found that irradiated guinea-pigs were less susceptible to inoculation of saline emulsion of tuberculous sputum than control animals. These experiments were repeated by Hase,¹ but his results were negative. Mayer² carried out a similar series of experiments, and infected guinea-pigs by inhalation; his results indicated a possible increase in resistance when irradiation preceded infection. C. M. Hill and Janet H. Clarke³ tested the effect of ultra-violet radiation on the resistance of rats to a culture of pneumococci; their conclusions signify some possible benefit if irradiation precedes infection. In their experiments shaved rats were exposed to a quartz mercury vapour lamp; the skin of some of the animals was severely burned, and this suggests that the results of their experiments may be associated with the effects of local necrosis or inflammation. Animal experiments of this nature are difficult, for it is impossible to study the effects of repeated applications of short ultra-violet rays on small areas of skin unless the hair is shaved or removed by a depilatory. This would mean that such animals would have to be almost completely shaved if the principles of "short-ray therapy" were correctly adopted.

The "minimal erythema dose" of ultra-violet rays applied to an area of skin equivalent to 20 to 30 sq. cm. per kilogram of weight increases the bactericidal power of

samples of defibrinated blood, collected one to two and a half hours following irradiation, and tested *in vitro* by the "slide cell technique" of Wright, Colebrook, and Storer.⁴ Colebrook suggests that this effect is due to increased function of the leucocytes. My own experiments⁵ on living animals suggest that following irradiation of the surface layers of the skin a photo-biochemical reaction occurs, and a bactericidal substance is first produced locally at the site of irradiation and is carried by the blood stream into the general circulation. So far experiments have failed to demonstrate bactericidal activity in extracts of irradiated skin or other tissue cell emulsions—that is, liver, spleen, testes, brain, and thymus. When defibrinated blood is directly irradiated, the bactericidal properties are diminished and the leucocytes are damaged. The intravenous injection into the living animal of irradiated blood cells and other tissue cells (testes, liver, thymus) is followed by an increase in the bactericidal power of the blood as tested *in vitro*.

The correlation of the bactericidal power of the blood so tested with the resistance to infection is so far indefinite. While some of the tests on human blood show a high bactericidal effect during acute pyrexial infections, a low haemo-bactericidal power and an impaired efficiency of the leucocytes must be regarded as giving an unfavourable prognosis. The effects of irradiation and of many chemotherapeutic substances are only of a transient nature; it has not been possible to discover an innocuous therapeutic agent which can produce a high haemo-bactericidal action for a prolonged period. The majority of the bactericidal compounds rapidly disappear from the blood stream and are quickly excreted; others are less soluble, are retained within the tissues, and are slowly eliminated. There is no suitable "in vitro technique" to estimate the resistance of the fixed cell or tissue immunity, and this increases the difficulties of assessment of resistance by experimental methods.

P. Hartley⁶ has shown that the exposure of immunized animals to ultra-violet rays is without effect on the content of diphtheria antitoxin or typhoid agglutinins of their serums. The conclusion which can be drawn is that the biologically active ultra-violet rays shorter than 3,100 A.U. appear to have some power to increase the "non-specific" immunity of the blood cells, but not the specific immunity. M. Hardy⁷ has summarized the effects of measured amounts of ultra-violet rays on the blood cell count of animals. The conclusions from her observations agree with those of Traugott,⁸ Aschenheim and Meyer,⁹ Cramer,¹⁰