

close to the electric station it was hardly affected at all. The electricians account for this by the fact that the difference of potential between the pipe and the earth would become greater the farther away one gets from the source of leakage. The old portion of the pipe was also examined where it passes beneath the cable but was not at all affected, owing, it was supposed, to a protective coating of oxide having formed. Only the inside of the pipe was affected, the outside showing no sign of deposit or corrosion.

Needless to say, numerous samples of water were tested from other houses in the neighbourhood, including one from a cottage a few yards away from the electric station, but no lead was found. If a small leakage of electricity (1.8 volts) can produce electrolysis in this way, it seems to me that in towns which have large electric installations, with networks of cables and water pipes, such a thing should be more common. I am told that the Board of Trade regulations for earth return on tramways allow a difference of potential on the return circuit of 7 volts. Also, is it not a common thing to use a water pipe as an earth for telephones and electric bells? On placing a voltmeter between the cut ends of the lead pipe I obtained a deflection of about  $\frac{1}{10}$  of a volt; this amount I could also get in my own laboratory by connecting the gas and water pipe, as also in a town ten miles away supplied with the same water.

## THE ACTION OF TRYPSIN UPON THE LIVING CELLS OF JENSEN'S MOUSE-TUMOUR.

A PRELIMINARY NOTE UPON A RESEARCH MADE (WITH A GRANT FROM THE CARNEGIE TRUST)

By J. BEARD, D.Sc.,

UNIVERSITY LECTURER IN COMPARATIVE EMBRYOLOGY,  
In the Research Laboratory of the Royal College of Physicians,  
Edinburgh.

THE experiments were undertaken to determine in the first place three points—(1) the action of trypsin upon the living cells of a carcinoma such as Jensen's mouse-tumour; (2) to test the truth of the conclusion advanced by me in 1902<sup>1</sup> that cancer was an irresponsible trophoblast; and (3) the length of treatment and number of injections of trypsin necessary to destroy the tumour.

The inoculations from a Jensen mouse tumour were made by Dr. H. Wade on October 10th, 1905, and the first injections (into the tumour mass) were commenced on November 15th.\* By this time some seven or eight mice had well-marked tumours. Of these, two were taken for treatment, and along with them was placed a "control mouse," which was living when the second "trypsin mouse" was killed. The remaining stock of mice with the tumour may also be regarded as controls. The preparation of trypsin employed (Fairchild Bros. and Foster's) was that originally dispensed to Dr. John A. Shaw-Mackenzie's prescription by Mr. F. W. Gamble, and it was with great generosity supplied gratis by Messrs. Allen and Hanburys for these experiments. This firm sent the solution in two strengths—3 per cent. and 5 per cent.—containing no antiseptic such as phenol.

The first difficulty was to decide upon some dose to be tried, and after one injection into each mouse of 2 minims of a 2½ per cent. solution—made by dilution with sterilized distilled water—all the later ones were of 2 minims of a 1½ per cent. solution. The reason for the change was that on the day after the first injection both mice were found in coma and quite cold, with legs in the air. In a warm incubator they recovered, and we did not experience the like result in them again or in the control mouse at any time. After this alarming experience—due, perhaps, to auto-intoxication by some other of the products of the tumour (? an alcohol), as "extracted and digested" by the large dose of trypsin—it was decided to reduce the dose by more than one-half, for in the first instance the amount of the trypsin

solution had exceeded that of water. One of the mice weighed 17 grams, and, taking the weight of an average man at 70 kilos, or 154 English pounds, one hundred times the maximum dose (30 minims) ever employed by Shaw-Mackenzie or any other physician in cases of inoperable cancer in man had in the first instance been given to the two mice! The minute size of the "patients,"  $\frac{1}{4000}$  of a man, must be the excuse for this error.

After ten days, when four injections in all had been made into each mouse, one of them was found dead by the laboratory servant. The *post-mortem* examination made by Dr. Wade revealed no cause of death. But for the presence of a tumour mass the mouse appeared to be quite healthy. The laboratory attendant thought that it had got caught between the cage and food vessel, and so (? when intoxicated) had caused its own death. The microscopical examination demonstrated that every single cell of the tumour was in degeneration, fully half of them being represented by shapeless masses of particles, probably remains of nuclei, and all the rest were mere skeletons of cells. Even these seemed in very many cases to be crumbling and falling rapidly away, as though in a hurry to quit the scene. The somatic tissues of this mouse, as represented by the leucocytes and connective-tissue stroma cells, were quite normal, and in the following instance also.

In the case of the second "trypsin mouse" the treatment was continued until Thursday, December 7th. In this period of twenty-two days in all nine injections of trypsin were made. On this date one of the other control mice, but not that living with the "trypsin mouse," died of its tumour, and it was then resolved to kill the "trypsin mouse." The tumour was at once exposed, an incision made into it, and the whole with a piece of skin preserved in 5 per cent. corrosive sublimate. Before the mouse was killed it was noted that the skin over the tumour was in necrosis. At the time this was set down to phenol in the trypsin solution, but afterwards it was ascertained that the solution contained no antiseptic of this kind. In the case of the control mouse, which died of its cancer, the tumour was quite as large as the terminal phalanx of a man's thumb, while in that of the second "trypsin mouse" it was only as big as a lentil. Microscopically, this latter apology for a tumour was in advanced degeneration, shrinking away to nothingness, and quite harmless. It appeared probable to us that, at the time we killed it, its "cure" from cancer was not far distant, and the microscopical examination confirmed this opinion. Even without further treatment the tumour would in all probability have been absorbed shortly or its remains cast out.

The experiments will be resumed as soon as the stock of mice with tumours has been replenished.

Though the number of experiments is small, already they have established what in advance I knew that they would. This degeneration of an asexual structure (a malignant tumour or trophoblast) under intestinal (tryptic) digestion I have witnessed again and again in past years.<sup>2</sup> The experiments were not needed to convince me that trypsin would cause a cancer to degenerate in the same way that it does that of the trophoblast, etc., in normal development. How such a conclusion can be arrived at is, I know, a mystery to many. It is solely by the use of the comparative morphological and physiological method, of which my departed friend, Professor George Bond Howes, was so ardent an exponent.<sup>3</sup>

In advance I know that, no matter how often we repeat this experiment, even with much smaller doses, the like results will invariably be obtained. In the nature of things it must be so, for in the cancer ferment, malignin, and in trypsin we have an antithesis of ferments, of which the latter is the more powerful. For reasons which cannot be entered upon now, it appears to be certain that the action of trypsin upon the cancer cell is to pull down the cancer albumin—a living substance—and the cancer ferment—malignin—produced by this. Apart from its origin and apart from the parasitic theories proper, the extant theories of the nature of cancer come under three headings—germinal or gametoid, trophoblastic or asexual generation, and embryonic or somatic. In addition to their confirmation of the conclusion that trypsin is the substance which will destroy the cancer cell with ease, and without danger to the individual (Beard and Shaw-Mackenzie), these experiments go far to prove that in its

\* My sincere thanks are due, and are hereby rendered, to Dr. H. Wade, F.R.C.S.E., for his great kindness in making the successful inoculations with the Jensen mouse adeno-carcinoma, and for performing the injections on my behalf. It is right to add that, in spite of my entreaties to him to agree to a joint authorship of the research, he declined for private reasons, which I can fully appreciate, while not admitting their cogency.

nature cancer is neither germinal nor somatic, for trypsin, the architect of the soma, does not in life destroy the soma or sexual individual or its sexual products, whilst its action is direct and utterly ruinous upon trophoblast or asexual generation.

## REFERENCES.

<sup>1</sup> *Lancet*, June 21st, 1902. <sup>2</sup> The Cancer Problem, *Lancet*, February 4th, 1905. <sup>3</sup> See G. B. Howes's Belfast address, Section D, Brit. Assoc. Adv. Sci., 1902.

## MEMORANDA:

## MEDICAL, SURGICAL, OBSTETRICAL.

## FOOD POISONING AND COMA.

A CASE very similar to that reported by Dr. Kennard<sup>1</sup> came under my notice a few years ago. A lady had given a luncheon party, the viands for which had been prepared by a confectioner. None of the persons who partook of the lunch were ill after it. At supper the same night the lady had some of the viands left from lunch. She was a very moderate and fastidious eater, but may perhaps have supped more heartily than usual. When her husband went to bed he found her comatose. In great alarm he telephoned for her doctor, and on his return to her bedside found her writhing and heaving in a strange manner, but still comatose. Suddenly her writhings and heavings culminated in most violent vomiting, so violent that some of the vomit flew out of the open window, about 4 ft. distant. As soon as the vomiting ceased she returned completely to her senses, and suffered no further ill-effects. What was the *rationale* of the coma? It seems that it can scarcely be attributable to any presence of ptomaine or other poison in the blood, but must have been due to the mere presence of indigestible food in the stomach. Was it an exaggeration of the drowsiness we are all apt to experience after a full meal? Sleep pushed to excess is coma.

London, W.

CHAS. MERCIER.

## IMPACTION OF A HAT-PIN IN THE MALE URETHRA.

THE cases reported by Dr. C. Hamilton Whiteford (p. 20) and Mr. W. F. Brook (p. 80) recall to me a similar one that I located about twelve years ago, when Senior House-surgeon to the Royal Portsmouth Hospital. The patient, a young man about 25 years of age, introduced the pin to try to overcome a spasmodic retention of urine. Before admission to the hospital an attempt had been made, under an anaesthetic, to remove the pin with a pair of forceps, failure resulting from the pin point penetrating the urethral wall, as soon as any traction was made. On admission the penis was partly erect, and the head of the pin could be felt well back in the perineum, while the point was about an inch below the corona. Removal was easily effected without an anaesthetic by the simple expedient of passing the reverse end of a metal catheter, which had no eyelets on its side, down the urethra far enough to cover the point of the pin. No difficulty was then experienced in pushing the pin upwards by means of the head in the perineum. I should think that the case of a clinical thermometer might be used with equal success. The pin measured just 6 in. in length.

Bedford Park, W.

T. H. BISHOP, M.D., C.M.

THE two cases recorded in the current and penultimate numbers of the BRITISH MEDICAL JOURNAL recall to my mind one that came under my notice at the Exeter City Workhouse six months ago. A man, 55 years of age, was in the habit of passing a large hat-pin into his urethra with the object of removing some supposed obstruction. This time the pin slipped in beyond his reach. On seeing him a few minutes later I found that the point of the pin was from 3 to 4 lines from the meatus, and was free in the canal. I could not get a firm hold of it with a pair of bow dressing forceps. On making the patient lie down, and placing the thumb just below the head of the pin in the perineum, the point was brought within the grasp of the forceps, and the pin drawn out. A little force had to be used in extracting the head from the meatus, which caused a little bleeding. No anaesthetic was necessary, and no further trouble ensued. The little

<sup>1</sup> BRITISH MEDICAL JOURNAL, January 13th, p. 80.

manœuvre of getting the patient to lie down and carrying the penis over towards the abdomen advanced the point of the pin towards the meatus, and facilitated extraction.

Exeter.

JOSEPH A. W. PEREIRA, M.D.

## HILL DIARRHOEA.

THE discussion on hill diarrhoea and sprue at the Tropical Section of the British Medical Association's meeting at Leicester, reported in the BRITISH MEDICAL JOURNAL of November 11th, 1905, is of much interest to medical men in India, and no doubt Mr. Cantlie's meat juice treatment will receive wider trial than it has yet had. Dr. Andrew Duncan's opinion as to the cause of the disease, agreeing with that expressed some years ago by Colonel Dyson, will not, I think, receive much support. In Darjeeling mica has been practically banished from the water supply, yet hill diarrhoea is still often met with. One understands also that it occurs in hill stations where mica is not a constituent of the water. Moreover, the water drinkers in Darjeeling, women and children, rarely suffer from the disease. In the nearly two years I was civil surgeon of Darjeeling and in charge also of large European schools, I scarcely ever saw the disease in women or children, though treating numerous cases in men. All must agree with Colonel Dyson that "officers on coming up from the plains at once take more exercise and so get more thirsty," not *more* thirsty, however, than after exercise in the hot plains. He might have added they get more hungry too. The drink taken, however, rarely contains any mica. The sequence of events usually is that men arrive from the hot plains with digestions impaired by the intense heat and poor food obtainable. They at once eat heartily and take severe exercise, often showing indiscretion in not wearing warm enough clothing, or in not changing at once when hot and perspiring after playing squash or polo. In this way their digestions are overtaxed and their livers become congested; diarrhoea naturally follows. If properly dieted and clothed, etc., the diarrhoea stops, but if recurring chills are not avoided, or if the patient's health has been seriously undermined in the plains, the diarrhoea continues and sprue may develop. Sending the patient a few thousand feet down usually stops the diarrhoea, but not always.

Attributing hill diarrhoea to mica seems to me likely to lead to the observance of unnecessary precautions and to the neglect of very necessary ones.

F. P. MAYNARD, M.B., F.R.C.S.,

Calcutta, Nov. 30th, 1905.

Major, I.M.S.

## EXTREME BLADDER OVER-DISTENSION.

ON September 9th, 1905, I was called to see a man aged 80 suffering from retention of urine. From his relatives I learned that up to a month ago he could pass his water readily, but that since then only a few drops had come away daily. I found him in bed propped up with pillows. He could speak sensibly, and showed no signs of coma or delirium. Pulse 90, temperature 100° F., respirations 30. Tongue covered with a brown fur; breath bad. Twitchings of the left thumb. Both legs very oedematous. He complained of much pain over the abdomen and of great thirst. There were signs of congestion at the bases of both lungs.

On examination of the abdomen a tumour was felt extending from the pubes to the xiphi-sternum. The abdominal walls were extremely tense, and the skin showed signs of cracking. The flanks were resonant on percussion. As a catheter could not be passed he was aspirated above the pubes, and 260 oz. of urine were drawn off. The urine was clear except towards the end of the operation. The patient lived four days, and a catheter was passed daily. A partial *post-mortem* examination was performed and the following conditions were noted: The bladder was found to occupy the abdominal cavity up to midway between the umbilicus and xiphi-sternum. It was firmly adherent to the abdominal wall and the surrounding viscera, and could not be separated without tearing of its walls. The walls were very thin. The ureter and pelvis of the kidneys were greatly dilated. There were no deposits or calculi in the bladder. The middle lobe of the prostate was found much enlarged and projecting over the vesical opening of the urethra. The size of the bladder, as also