which can be trusted to do well is acetyl-salicylic acid, and it is well borne by the pregnant woman. The interruption of the pregnancy is not to be thought of; in fact everything should be done to prevent the premature expulsion of the child. It will be advisable to forbid maternal nursing, particularly when the fever is of recent origin and may therefore be expected to persist for a long time.

Dr. E. M. Williams’ case would seem to be the only one recorded (Journ. Roy. Army Med. Corps, 1907, vol. ix. p. 59) in which the newborn infant had Malta fever at the time of birth. The evidence is almost, if not quite, convincing; for on the day following its birth the child’s temperature was found to be 103° F., and four days later its blood gave the positive reaction for Malta fever. It is true that the mother’s colostrum contained numerous colonies of the micrococcus melitensis; but then the child had not been put to the breast, for the mother had been known to be suffering from the malady. About three weeks previous to the child’s birth, when the mother had her second rise of temperature, she had felt violent foetal movements, and Williams thought that at that moment, perhaps, the foetus became infected. This conclusion seemed to Williams to be justifiable, and Dr. Laffont brings forward in support of it the case of a five months’ foetus from a woman suffering from Malta fever which showed the positive reaction six hours after its expulsion. This case was reported by Dr. Samut (Lancet, 1911, vol. ii. p. 878).

J. W. B.

PATHOLOGY.

UNDER THE CHARGE OF

THEODORE SHENNAN, M.D., AND JAMES MILLER, M.D.

CULTIVATION IN VIVO OF VACCINE VIRUS.

Noguchi has succeeded in obtaining pure cultivations in vivo of vaccine virus, free from bacteria (Journ. of Exper. Med., 1st June 1915).

The addition of glycerine to fresh vaccine lymph results after a time in a great reduction both in the number and in the variety of the contaminating micro-organisms, without seriously impairing the activity of the virus itself. In vaccines prepared in this way, however, organisms such as staphylococci, streptococci, B. coli communis, B. Welchii, B. xerosis, B. subtilis, and some other aerobes and anaerobes have been found. Glycerine has almost no action on bacterial spores.

Noguchi employed cultivation in the rabbit’s testicle, but, as the vaccine virus multiplies quickly and the inflammatory reaction and necrosis of tissues which ensue quickly suppress the bactericidal
powers of the testicular tissues and place them in a favourable state for bacterial development, the virus must first be freed from bacterial contaminations.

Glycerinated virus, free from sporogenous bacteria, is incubated at 37°C in order to destroy practically all the bacteria present. The skin of a rabbit is then inoculated, and after four or five days the eruption is scraped and the scrapings emulsified in saline. This emulsion is shaken up with ether, at room temperature, and cultures made from it at intervals. When spores are absent sterility is usually attained in twelve hours. The vaccine emulsion so prepared is employed for the intra-testicular inoculation of rabbits.

For a successful result, the virus has to be transferred several times from rabbit to rabbit, and it may also be cultivated in the testicles of young bulls. The testicular viruses were found to be free from bacteria, and appear to be capable of indefinite transfer from one animal to another.

The vaccinal lesions produced on the skin of the calf are identical with those produced by ordinary viruses, and human beings react in an entirely typical manner.

**Pathogenic Importance of B. Proteus Group.**

W. P. Larson and E. T. Bell suggest that the proteus group of bacilli probably plays a more important part in human pathology than is generally believed (*ibid.*, 1st June 1915).

Some strains of B. proteus obtained from human lesions are pathogenic for rabbits, rats, and guinea-pigs. There is strong evidence that these strains are also pathogenic for man. A non-pathogenic strain may be made pathogenic by the use of aggressins or by inoculation into the anterior chamber of the eye. Cultures lose their virulence rapidly. The lesions produced in animals are either simple abscesses, proliferative lesions, or mixed exudative and proliferative lesions.

**Sero-Diagnosis of Tuberculosis.**

E. Dubains and F. Jupille (*Ann. de l'Institut Pasteur*, April 1915) find that Besredka's tuberculin fixes complement in presence of the serum of tuberculous patients, in almost all forms of the disease. The reaction corresponds to lesions in process of involution, or which had presented previously a certain degree of activity. It is not sensibly influenced by intercurrent affections. When compared with the cuti-reaction it possesses great clinical value, and verifies the diagnosis of tuberculosis even though the clinical signs are absent or doubtful.

**Distribution of Diphtheroid Bacilli.**

Wm. Harris and H. W. Wade discuss this subject (*Journ. of Exper. Med.*, 1st May 1915). They mention many instances from
the literature in which organisms of this group have been isolated from pathological conditions to which they have been believed to possess etiological relationship, and they also refer to reports of their occurrence as saprophytes. They conclude that diphtheroids are widely distributed in nature, being present in the air, on the body surfaces, and at times, through contamination or indigenous, in the deeper tissues. They constitute a wider field of saprophytism than is generally appreciated. While some strains may represent pathogenes, their aggregate is patently not of the disease-producing variety. They can be cultivated from various pathological tissues to which they bear no etiological relationship, such as the lesions of tuberculosis, leprosy, blastomycosis, tertiary syphilis, and tumours of various types.

**Chorionepithelioma of Testicle.**

Dr. J. V. Cooke describes a case of chorionepithelioma of the testicle, with secondary growths in the brain, liver, kidneys, stomach, peritoneum, and thyroid, and has collected 46 other cases from the literature (*Johns Hopkins Hosp. Bull.*, June 1915).

The ages of the patients varied from 16 to 46 years, but the large majority of the cases occurred in individuals between 20 and 40 years of age. The right testicle was slightly more often affected than the left. In 2 cases an undescended testicle was the seat of the new growth. The duration of the disease varied from 2 months to \( \frac{2}{3} \) years. In 29 cases a fatal termination was specifically mentioned. One patient appeared to be well 5 months after the operation. In 17 other cases operated on the result was not given.

The most common symptoms were referable to the secondary pulmonary growths—haemoptysis and dyspnœa. Abdominal nodules were commonly felt. In several cases fatal haemorrhage occurred from metastases in the lungs, stomach, or intestines. In 2 cases hypertrophy of the breasts with secretion of colostrum-like fluid was observed. Cachexia, with loss of weight and strength, was remarked in the terminal stages of all the fatal cases.

**Biological Methods for the Diagnosis of Malignant Tumours.**

Dr. G. Mioni publishes a long article on the above subject (*Tumori*, May-June 1914), from the laboratory of Professor Alessandri.

Following a long introduction, in which he traces the development of our knowledge of immunity in general, the author goes on to describe his own observations, which are of great interest.

His investigations have to do with isohæmolysins, Elsberg’s test, the antitryptic reaction, the deviation of complement reaction, and the meiostagmine reaction of Ascoli and Izar.
Isohaemolysins.—The author employed exclusively Crile's method, as it seems to have given most general satisfaction.

The blood of the patient is taken from an arm vein, and collected in two or three tubes. One sample is defibrinated, and to it is added a quantity of saline; the others are allowed to coagulate. All are placed in the ice-chamber for 24 hours.

The clear serum is separated from Nos. 2 and 3, and the corpuscles from No. 1 are washed and emulsified in saline.

A series of 16 haemolysis tubes is put up, in each of which 0·5 c.cm. of serum and 0·5 c.cm. of corpuscular suspension are placed. These are incubated at 37° C. for two hours, and then placed in the ice-chamber for 20 hours, before reading off the results. In this manner a serum suspected of containing isohaemolysin is not only tested against its own corpuscles and against those of three other individuals, but also it is possible to ascertain the resistance of the corpuscles of the suspected blood to the action of three other serums. In the first case "the serum is pathological which dissolves the normal erythrocytes; in the second the serum is normal which dissolves pathological erythrocytes."

In 35 cases of malignant growth, in which the diagnosis was confirmed by autopsy, the first reaction (active haemolysis) was positive in 21 (62 per cent.) and negative in 14 (38 per cent.), the latter series including 8 visceral cancers, 1 mammary cancer, 1 squamous epithelioma, and 4 sarcomata. The second reaction (passive haemolysis) was positive in 17 cases (48 per cent.) and negative in the remainder.

In 35 control cases the first reaction was positive in 10 and negative in 25, while the second reaction was positive in 9 and negative in 26, the positive cases being cases of suppuration, acute febrile conditions, or cases of surgical tuberculosis. The practical value of the test was confirmed up to a certain point.

Elsberg's Reaction.—For the study of haemolysis in the living patient the author followed exactly the method advised by Elsberg, injecting under the skin of the forearm or shoulder 1 c.cm. of a 10 per cent. suspension of washed red blood corpuscles. In 5 cases only, out of 35 cases of malignant disease, a nodular reddish swelling appeared, and in 4 out of 35 controls a similar result was obtained. No better results were obtained with various modifications of Elsberg's technique, and Mioni concludes that this test is not of practical value.

Antitryptic Properties of Serum.—In carrying out this test the author employed the method advised by Marcus. This author prepares the test-fluid as follows:—5 c.cm. of pure glycerine and 5 c.cm. of distilled water are shaken up with 0·1 grm. of Grübler's trypsin. After incubating for 30 minutes at 55° C. it is again shaken, and then filtered, furnishing a clear, colourless, slightly viscid, and weakly
alkaline test-fluid. The observation material is Loeffler's serum, coagulated in Petri's capsules.

Taking a series of 12 small sterile test-tubes or watch-glasses, a drop of the test-fluid is placed in each, and to the first a drop of the patient's serum is added, to the second a drop of serum diluted with equal parts of saline, to the third a drop of serum diluted with two parts of saline, and so on. From each tube or watch-glass two loopfuls of the mixture are placed upon the surface of the Loeffler's serum, arranging the successive deposits in a circle. In the centre two loopfuls of a control mixture of test-fluid and saline are placed. The plate is incubated at 50° C. for 6 to 8 hours. Thereafter the degree of digestion of the coagulated serum is noted, from the depth of the hollows produced by the test deposits. Absence of digestion indicates inhibition of the trypsin by the antitrypsin of the patient's serum. The grade of dilution of this serum, which inhibits tryptic digestion, furnishes the antitryptic index.

In normal individuals the antitryptic index varies between 1:2 and 1:4. Mioni found that it rose to 1:7 in 2 cases of suppurating hydatids of T. echinococcus. In 35 cases with malignant disease the index in 3 cases was 1:4; in 6, 1:5; in 7, 1:7; in 9, 1:8; in 3, 1:9; and in 1, 1:10. Hence the reaction was positive in 32 of the cases (91.4 per cent.), a percentage similar to that obtained by other investigators who employed different technique.

Mioni concludes that the presence of a high antitryptic index in a patient in whom one can exclude an acute infection or a focal suppuration supports a diagnosis of malignant disease.

**Anaphylaxis.** — In these investigations the author followed the technique suggested by Pfeiffer and Finsterer. He injected guinea-pigs intra-peritoneally with 4 c.cm. of serum from a cancer patient, and after 48 hours gave a second intra-peritoneal injection of tumour extract. In a second series of observations he gave the second injection subdurally according to Besredka's method. Suitable control tests were made. The results were absolutely negative when the second injection was intra-peritoneal, and positive in one-third of the cases when it was subdural. It is possible that these apparently positive results were really due to direct mechanical or toxic effects of the injected material upon the central nervous system.

**Deviation of Complement.** — In some of the deviation tests Mioni used as antigen an aqueous extract of tumour, in others an extract in pure methylc alcohol, along with sheep corpuscle amboceptor, and guinea-pig complement. The test material was the blood-serum of cancerous individuals.

In 34 malignant cases, deviation was complete in 8 cases only, incomplete in 5, and negative in 15. In 6 cases the patients' serum inhibited haemolysis by itself. In 24 normal cases the result was
negative in 15, incomplete in 5, and in 4 the serum alone inhibited haemolysis. But although the serum of some cancer patients deviates complement, Sampietro, Weinberg, and de Marchis have shown that syphilitic serum in contact with extract of carcinoma deviates complement; and as it is not always possible to exclude a syphilitic infection, the results obtained were not very satisfactory, even to the modified extent shown.

Meiostagmine Reaction.—Ascoli and Izar proposed at first an antigen prepared by means of an alcohol-ether extract of non-ulcerated tumour, but later they prepared the antigen with methylc alcohol. Micheli and Cattoretti showed that extract of the pancreas of the dog or calf formed an efficient substitute, and further experience has established the correctness of this conclusion.

The result of mixing antigen with the patient's serum is a diminution of surface tension easily appreciable by Traube's stalagmometer, which indicates the variation in the number of drops in a given uniform quantity of the mixture. Ascoli and Izar found the reaction positive in 93 out of 100 cases of malignant tumour, whereas in 103 control cases the reaction was invariably negative. Mioni, using the pancreatic antigen, obtained a positive reaction in 20 out of 35 cases. In 28 controls the reaction was negative in 26.

If the difficulty of producing efficient antigens and the ease with which these lose their activity are borne in mind, it is to be doubted whether the reaction is one which can be transferred from the laboratory to the bedside.

After removal of malignant tumours Mioni noted a progressive diminution, going on to complete disappearance, both of the isohæmolysin and of the antitryptic reaction, demonstrating that both isohæmolysin and antitryptic ferments stand in direct relationship to the presence of the neoplastic mass and are indications of the altered metabolism of the individual suffering from malignant disease.

Evidently the author considers that the antitryptic reaction is of most practical value, but he also favours Crile's test and the meiostagmine reaction, the former taken in association with the clinical data, and the latter only in the hands of experts in its employment.

A full bibliography is appended to the paper. T. S.