zone was withdrawn 5 days after the last injection. Zones of 2 mm. have been observed after 9 and even 11 days, but their significance is doubtful, since pus containing no penicillin has been observed sometimes to produce this degree of inhibition.

Specimens of fluid from other lesions examined in this way total 192. Some of these were from abscesses treated by aspiration and injection with results comparable to those in empyema. The majority were withdrawn either from sinuses or from recent operation wounds sutured over a tube. Table II records the penicillin content in 106 such specimens; only those obtained one day after treatment are included, and others are excluded in which it appeared that penicillin was being destroyed by coliform bacilli.

TABLE II.—Zones of Inhibition produced by Fluids withdrawn One Day after Local Treatment with Penicillin Solution (usually 1,000 Units per c.cm.)

	No. of Cases giving Zones (in mm.) of					
	0	1-3	4-6	7-10	11-15	16-21
Sinuses ..	10	2	3	5	4	1
Wounds ..	18	11	5	5	10	32
Totals ..	28	13	8	10	14	33

Mechanical factors favouring retention again appear paramount in determining results. It is possible that the vascularity or other properties of the tissue bordering a cavity have also some influence, but clear evidence of this has not been obtained.

Estimations of Penicillin Content of Blood

During systemic treatment the penicillin content of the blood should be estimated. This is possible only by determining the bacteriostatic power of the serum either for the patient's own organism or for the standard staphylococcus. All methods for doing this depend on using the undiluted patient's serum and dilutions of it in normal serum as a culture medium; a small inoculum of staphylococci grows in serum in the form of colonies, which may be counted if such cultures are made on slides, the cover-slip being sealed with petroleum jelly. Inhibition of growth in any given dilution may be either complete (no colonies) or partial (fewer colonies than in a normal serum control).

Dosage in this series of cases was uniform, 120,000 units a day being given to adults and a correspondingly smaller dose, approximately related to body weight, in children. The penicillin content of 37 specimens of blood from 13 patients receiving penicillin by intravenous drip or other continuous method of administration is stated in Table III.

TABLE III.—Numbers of Serum Specimens Bacteriostatic to Oxford H Staphylococcus in Different Dilutions

Bacteriostasis:						
Nil in pure serum ..	..	..	..	..	..	1
Partial in pure serum ..	..	..	..	..	..	5
Complete in pure serum ..	..	..	..	..	..	11
Partial in 1 in 2 serum ..	..	..	..	..	..	3
Complete in 1 in 2 serum ..	..	..	..	..	..	7
.. " 1 in 4 serum ..	..	..	..	..	..	5
.. " 1 in 8 or over ..	..	..	..	..	..	5

These variations cannot be fully explained, although one cause of a high titre may certainly be retention due to renal inefficiency; 3 of the 5 specimens listed as "1 in 8 or over" came from the case referred to also by Morgan, Christie, and Roxburgh (p. 515), in which repeated estimations (not listed here), after administration was stopped, showed long delay in excretion. A concentration giving complete inhibition in pure serum is probably adequate for full therapeutic effect, and *in vitro* tests (to be published later) have shown that the rate of death of staphylococci in blood containing penicillin is not accelerated by increasing the penicillin concentration within the range of 0.1 unit to 10 units per c.cm.

When three-hourly intramuscular injections are given, the blood concentration is known to rise rapidly after each injection, then to fall progressively until the next. Specimens obtained immediately before a dose was due gave no inhibition at all in 6 and partial inhibition in pure serum only in 3. A much greater number of such estimations must form the

basis of any judgment on this method of treatment; but to gain an idea of whether dosage is adequate must clearly be more difficult, and on theoretical grounds the maintenance of a steady level by continuous administration seems to me more likely to achieve full therapeutic effect.

Comment

This condensed account of laboratory work on cases some of which are described by foregoing authors is no more than an interim report on a study still in progress. It is intended to present a picture of the nature and volume of work which is called for from the laboratory if penicillin treatment is to be directed intelligently and, still more, if its efficiency is to be improved. At the same time a few minor original observations are briefly reported which may be of some service to other workers.

The greater part of the technical work here described was carried out by Miss P. M. Waterworth. Her services and the equipment of the laboratory used were made available by the generosity of "Bundles for Britain," which organization provided a fund under the control of Mr. Rainsford Mowlem for laboratory work in connexion with his surgical unit.

Medical Memoranda

Reliability of the X-ray Diagnosis of Early Pulmonary Tuberculosis

The case cited by Dr. Sharpe in the *Journal* of Nov. 6, 1943 (p. 579) and the series of letters which followed have brought into prominence the important question as to how far x-ray films of the thorax can be relied upon in the early diagnosis of pulmonary tuberculosis. The following is a case in which a fatal miliary tuberculosis supervened shortly after the lungs were declared to be entirely free of evidence of infection by a reliable radiologist who has had great experience in reading radiographs. This x-ray examination was made while the patient was in hospital suffering from tuberculous meningitis.

An electric welder aged 21 was admitted to hospital complaining of severe headache. Clinical signs of meningitis developed, and laboratory findings confirmed the diagnosis. The radiograph of the chest taken while in hospital was negative. Death occurred on the thirteenth day after admission. Necropsy findings were: a typical Ghon lesion about 1 cm. in diameter lying immediately beneath the pleura in the upper part of the right lower lobe, the lesion involving a vessel of medium size; enlarged caseous glands at the root of the right lung; small caseous tubercles in the cerebral meninges, spleen, kidneys, and adrenals.

The questions which arise are how frequently cases are missed by the radiologist, and what type of lesion it is which fails to show up in the x-ray film. As to the first matter, Dr. Richards, radiologist to the Toronto General Hospital, has collected the statistics of active tuberculosis developing in enlisted men in Canada during the first two years of the war. He finds (*Amer. J. Roentgen.*, 1942, 47, 66) that 16 men who had negative x-ray films on enlistment developed active tuberculosis—a percentage of only 0.004. We are informed verbally by a urologist in charge of one district in Canada, however, that he has seen no fewer than four cases of tuberculous epididymitis in soldiers who must have passed the test of a chest radiograph. This means that a percentage which is not negligible is declared free from evidence of pulmonary tuberculosis after inspection by the radiologist.

LESIONS WHICH FAIL TO SHOW UP

As to the matter of the type of lesion which fails to show up in the x-ray film, we are inclined to believe that many localized cases of primary tuberculous infection are invisible in radiographs. For the sake of brevity we may refer to this primary tuberculous pulmonary lesion as the Ghon lesion. It is situated at the periphery of the lung immediately under the pleura, usually not at the apex, and it consists of a small area of caseous consolidation later surrounded by a rampart of fibrous tissue. Spreading from it is a chain of infected lymphatics terminating in a caseous gland in the hilum of the lung. It is a moot point whether this lesion—which is usually small, often less than 1 cm. in diameter—can be demonstrated by x rays, especially if it be placed laterally and so hidden behind the ribs. When it becomes the seat of calcareous deposit it is more easily seen.

As to the matter of appearances in x-ray films which are suggestive of tuberculosis but which are not tuberculous in origin, probably every radiologist has seen suspicious lesions which disappear after a short time. Virus pneumonia of an

interstitial type and the rare condition of sarcoidosis both give pictures which may be confused with those found in tubercle.

The time which elapses between the exposure of susceptible persons to an open case of tuberculosis and the first radiological evidence of tuberculous disease is frequently three years or more in adults. This is the period of the Ghon lesion. During this interval the earliest evidence that a tuberculous focus is present in the body is the change in the allergic response to tuberculin.

Another point of importance illustrated by the above case is that throughout the first few years of infection there is a tendency to bacillaemia, with resultant metastatic foci in various organs such as meninges, bone, kidney, and epididymis. It is remarkable how often necropsies are performed on cases of miliary tuberculosis without the pathologist being able to assign to one particular lesion the role of primary focus of infection, the fact being that it is a minute primary focus of the type indicated.

We are inclined to agree with Dr. Fawcitt (*Journal*, 1943, 2, 692) that there is no such thing as x-ray *diagnosis* but there is x-ray *evidence*, and that this fact is not yet fully appreciated. Nevertheless, mass radiography of recruits, schools, and nursing personnel is wonderfully reliable in spite of the occasional false negative and false positive.

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Tuberculin Jelly Patch Test

Other Tuberculin Skin Tests.—Since the introduction of the Vollmer patch test in 1937 much experience of its advantages and disadvantages has been gained. On the whole, it is a satisfactory and comparatively simple method of performing a tuberculin skin test. There is a tendency, however, for the patches to become dry and the tuberculin inactive, with consequent inaccuracies in the results. This has been especially noticeable during the war years. Compared to the Mantoux intracutaneous test, it can be said that the Vollmer patch test with freshly prepared patches is at least 95% accurate.

Tuberculin Jelly.—Recently an opportunity has arisen for the carrying out of a series of tests with tuberculin jelly, prepared as follows:

Old tuberculin (tuberculinum pristinum)	..	..	..	95%
Inert adhesive	..	..	..	5%

Method of Application.—The jelly is put up in small tubes, and after an area of skin between the shoulder blades has been carefully cleaned with acetone (for preference) a small portion of the jelly is pressed out on to the cleaned area. (I have found it more satisfactory to use a specific marking, which in my case has been the letter "V.") Without waiting for the jelly to dry, a piece of elastoplast about 1 in. wide and 2 in. long is used to cover the jelly and is allowed to remain on the back for the usual 48 hours. Meantime instructions are given that the child should not be bathed for this period, and after the removal of the plaster the back is viewed daily for several days.

Reading the Test.—A positive test is shown by an erythema or slight vesiculation of the skin in the shape of the marking used. A negative result is shown by a completely normal appearance of the skin area on which the jelly was applied.

Results.—Experience has shown that with the letter "V," the arms of which are 1/2 in. long, the reaction is equivalent to that of 0.1 c.cm. 1/100 old tuberculin (intracutaneous Mantoux test). In a recent series of 100 (specially selected) children, to whose backs the tuberculin jelly was applied, both at the Hospital for Sick Children, Great Ormond Street, and the Children's Department, Westminster Hospital, in-patients and out-patients, the following results were obtained:

Result	Vollmer Patch	Mantoux	Tuberculin Jelly
Positive ..	32	35	35
Negative ..	68	65	65
	100	100	100

Conclusions.—It would appear that in this series tuberculin jelly was a more accurate method of performing the skin test than the Vollmer patch test. No local reactions of undue severity were recorded. Other advantages appear to be: (1) the much smaller cost of the jelly in comparison with the patches, which is a considerable item in out-patient departments and clinic work; (2) the jelly will keep indefinitely in the tubes and is therefore more suitable for the general practitioner who may use this test only at infrequent intervals.

I have to thank Mr. Dreebin, of Messrs. Allen and Hanburys Ltd., for supplying me with the jelly and for his helpful suggestions.

London.

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Reviews

AN ORNITHOLOGIST ON EVOLUTION

Systematics and the Origin of Species from the Viewpoint of a Zoologist. By Ernst Mayr. (Pp. 334, 26s. 6d.). New York: Columbia University Press; London: Oxford University Press.

Darwin had a profound knowledge of systematics, palaeontology, and genetics, on all of which the theory of evolution rests. His successors cannot hope to cover so wide a field, though Dr. Huxley has very nearly succeeded in his recent *Evolution*. Dr. Mayr is an ornithologist, whose work has been largely in the present Pacific war zone, and his facts, like those of Wallace, are mainly drawn from the study of living animals and their geographical distribution. The book is absolutely first rate, and every naturalist will find much in it to interest him.

After a very full discussion of geographical variation, the author concludes that some geographical races may develop into species, though he cannot agree with Darwin that "varieties are incipient species," since very few are likely to reach specific rank. The essential step in species formation is the prevention of crossing between two races. Dr. Mayr believes that, in animals at least, this almost always occurs in the first instance through geographical isolation. This may cause such differences of behaviour that the new species will not mate when they get the chance, and simultaneously or later, physiological differences which render the hybrids inviable or sterile. Here he will not convince all readers, though he makes a strong case.

Medical readers will be interested to see that he divides the malaria mosquito *Anopheles maculipennis* without hesitation into six species, which are reproductively isolated from one another, and does not regard them as mere "biological races," even though the adult forms cannot as yet always be distinguished. The student of *Homo sapiens* in his and her infinite diversity will find Mayr's discussion of other "polytypic species," all of whose geographical races can breed together, of great interest. It would have been a wholesome discipline if Hitler on the one hand and some of the more extreme exponents of human equality on the other had been compelled to study the geographical races of some of the birds of New Guinea in order to obtain a biological background for their theories.

While Dr. Mayr's book is not for general consumption, it should be within reach of every student and practitioner of medicine who wishes to keep up with the present position of evolutionary theory on the one hand and zoological classification on the other, as well as every ornithologist. To the student of genetics it presents a vast array of problems, of which the simplest is to determine, for every geographical race described, how far its characters are due to heredity, and how far to environment. I for one am going to re-read it several times.

J. B. S. HALDANE.

VASCULAR LESIONS AND TUMOURS OF THE SPINAL CORD

Vascular Abnormalities and Tumours of the Spinal Cord and its Membranes. By Roger Wyburn-Mason, M.D., B.Chir., M.R.C.P. (Pp. 196, 18s.) London: Henry Kimpton, 1943.

The relative rarity of the pathological lesions with which this volume is concerned must be largely responsible for their comparative neglect. Dr. Wyburn-Mason has been fortunate in having access both to the collection at the National Hospital and to cases coming under the care of neurosurgeons at several other centres. He has given a full, careful, and interesting presentation of his gleanings, which comprise 67 well-illustrated cases. This series represents a substantial addition to the literature, which so far contains little more than twice that number of cases. It will be profitably studied by those who are interested in these lesions, whether from the clinical or from the pathological aspect. The classification follows much the same lines as those previously outlined by Bailey and Cushing, and by Bergstrand. From the last-named, however, he differs in requiring a separate class for arterial anomalies and in including the cavernous angiomas with the telangiectases,