approximately equal weight, using the bacterial emulsion alone. Two methods of dosage were employed. By the first method, small doses of flavine were repeatedly injected at comparatively short intervals, beginning a few minutes after the injection of the infecting organism. By the second method, an interval of 12 hours was allowed to elapse before commencing the injections of flavine which were given thereafter at longer intervals. All the injections were into the auricular vein. Cultures were made from the heart blood after death of any animal, and occasionally during life. Smears and cultures were also made, in some instances from the liver, spleen, and kidneys, immediately after death. Yellow staining of the externally visible mucous membranes was frequently noticed after one or more injections of flavine. The flavine was freshly dissolved in normal saline before each experiment. [The results were here tabulated.]

Conclusion.

The injections of flavine appeared in some of the Series III. experiments to have some *delaying* effect upon the early death of rabbits from staphylococcal septicæmia. (Experiments II., III., IV., V.) It would appear, however, that the dose required to produce this effect may later contribute to the death of the animal. (Experiments VI. and VIII.) The net result is that no definite curative influence can be demonstrated either with proflavine or acriflavine in the treatment of bacillæmia due to the organisms injected in these experiments. This result is only what might be expected in view of the rapidity with which the flavine compounds are eliminated from the circulation, as shown in the experiments of Series II.

It is possible by the use of a method which ensures the gradual dilution of the flavine solution by the blood to guard against the immediate effects of its agglutinating action on the red blood corpuscles.

In vitro, flavine proved highly efficient as a disinfectant for blood, if allowed time to exert its full action.

INFECTIVE SCAR TISSUE AND ITS RELATION TO PAINS,

PARTICULARLY PAINFUL AMPUTATION STUMPS.¹

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ALL the structures which have been divided, as in the operation of amputation, take part in the healing of the wound. Thus normally and naturally there is a reparative osteo-myelitis, osteitis, periostitis, myositis, neuritis, arteritis, phlebitis, lymphangitis, &c., and their attendant external and surrounding inflammations like perineuritis. The perineuritis is really a lymphangitis, and, clinically, there is a most important practical observation to be made; the peri-inflammation—e.g., perineuritis—extends outside higher up the structure, a nerve trunk, than the concurrent internal endoneuritis. This enables the surgeon to see that a nerve is divided above its internal inflammation.

Painful Nerves.

Beneath the sawn end of the divided bone there is an empty space, a dead space, which becomes filled up with scar tissue, which takes its character from that of the healing of the wound. At times it is filled with non-infective scar tissue, as when the wound heals well; and at others the scar tissue is irritative and infective from the micro-organisms imprisoned in its meshes. Professor Marinesco and I² have shown at the Royal Society of Medicine some organisms grown from the nerve-endings in a wound which had been healed for three years. Hence the local cause for painful nerves is to be found in a terminal infective neuritis and not in any "bulbosity." A bulbous nerve results from every division of a nerve trunk. But if the ends of the nerves are inflamed the bigger and the more tender the nerve bulb.

The healing of the wound apparently by first intention does not exclude the possible presence of harmful organisms in the tissues of the deeper part. A sharp line is to be drawn between the external scar in the skin and the internal scar under the bone. The condition of the former is an uncertain guide to the condition of the latter. It would appear that the changes in the behaviour

of the phantom limb are a better guide. Previous to this inflammatory theory of the origin of the pains of wounds and amputation stumps, the pains were always regarded as due to nerve adhesions and strangulation by cicatrices. From an examination of painless stumps it is plain that such conditions are frequent in them and that they themselves produce little or no pain provided the nerve-end is not inflamed. Hence it is possible for the pathologist to decide by the presence or the absence of signs of inflammation if any given specimen shows evidences of the peripheral or central (neurotic) origin of the pain. At least nine out of ten complaints are purely central.

Reparative Processes.

Silk and other unabsorbable material, such as iron, is slowly fragmentated and removed when situated in infective scar tissue. They are not isolated by encapsulation as in ordinary non-infective scar tissue. Thus all foreign bodies are best removed and their tracks drained. The body only slowly sterilises infective scar tissue. Silk ligatures are apt to become, if infected, centres of irritation. Specimens were shown to illustrate these points, and new bone formations, actual increases in the length and breadth of the divided bone, bony bridges, non-infective sequestra being built into the scar like a brick into a wall, the mushroom flattening of the sawn end of a bone, &c. The osseous problems are many and various.

By reparative myositis the muscles attach themselves to the internal scar which in its turn is attached to the end of the bone. This is the normal reattachment of muscles to the end of the stump.

Spread of Infection: Regeneration of Nerves.

Among channels for disseminating the irritation of infection the vascular lymphatics come first. They carry the infection furthest and widest. The lecturer showed a triangular plug of scar tissue in the popliteal space causing an intractably flexed knee. In this irritant scar tissue is to be found the key to the flexion of joints.

The irritation of this inflammation ascends along the vessels like smoke up a chimney. Particular reference may be made to those situations in the body where the "smoke" meets a nerve, as the internal saphenous nerve in Hunter's canal,³ the sciatic nerve in the upper part of the popliteal space, the posterior tibial nerve in the calf, and the neurovascular bundle on the inner side of the arm. If the irritation gets into a place like the chest, whence the scar tissue cannot be removed completely by operation, time and drugs alone cure, and we can understand the intractable nature of brachial neuralgia.

All these considerations may be called those of an early and often immediate sequence. Usually nerves regenerate more slowly. The regeneration of a nerve is like to the flow

¹ Brief abstract of Arris and Gale lecture delivered before the Royal College of Surgeons of England, Feb. 19th, 1919. The lecture was freely illustrated with the epidiascope.

² Proceedings of the Royal Society of Medicine, April, 1918, xi., 4-24.

³ Brit. Med. Jour., June 15th, 1918.

of a great river: if it meets an obstruction it banks up, forming a lake until it gets round the obstruction. In regeneration of nerves an enlargement corresponding to a lake is formed; it may be termed a *regeneration neuroma*. They may be multiple, for it is as difficult to stop the regeneration of nerve as to stay the flow of a large river. As they grow the new-formed regeneration fibres, tender and destitute of a medullary sheath, branch, and if they grow into yet irritative infective scar tissue pain is bound to result. If the scar tissue has been rendered non-irritative by the body chemicals in the interval, when regeneration occurs it is not accompanied by pain. Thus we can understand pains coming on again and dying out. In conclusion, drawings of specimens illustrating the presence of foci of inflammation in new nerve-clusters and fibres themselves were shown.

QUININE AS AN ABORTIFACIENT.

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Glaister¹ states that all drugs having an abortifacient effect act in one of three ways: (1) by a toxic action on the system; (2) by acting locally or directly on the muscular structures of the uterus; (3) or by acting locally or indirectly on the uterus through the gastro-intestinal or genito-urinary tract. He cites quinine as one of those to be classified under the second heading. A herbalist was brought to trial before the Recorder at Bristol in July, 1918, on a charge of producing abortion by means of quinine.

Analysis of Pills.

One of us had occasion recently to examine a large number of pills brought by the police from the herbalist and apparently sold in large numbers to his female clients. The following analytical figures were obtained by the analysis of one batch of these pills.

Pills of a light brown colour mixed with dark pills in boxes (65 light and 15 dark) in each box.

Weight of light pill, 0.105 g. Moisture, 10 per cent.; organic matter, 87.8 per cent.; ash, 2.2 per cent. The organic matter gave characteristic reaction for quinine sulphate, which by the Stas process amounted to 70.4 per cent. of the pill mass, equal to 0.077 g. per pill, or 1.19 gr. of crystalline quinine sulphate.

Weight of black pill, 0.154 g. This pill was not entirely soluble in water. The following figures were obtained on analysis: moisture, 3.0 per cent.; organic matter, 53.9 per cent.; ash, 43.1 per cent. No sugar and no alkaloid were detected; no lead was present. A portion of pill was extracted by alcohol in a Soxhlet extractor. The following figures were obtained: alcohol, soluble portion, 19.3 per cent.; bicarbonate of soda (NaHCO_3), 63 per cent.; residue (maize starch), 12.2 per cent.

The light pill therefore appeared to be a quinine pill, and the dark one a bicarbonate of soda pill with starch and organic excipient.

The purchasers of these pills were directed to take a variable number (from 10 to 15), amounting to an average dose of 15 gr. of quinine. Although many analyses of this type of pill were undertaken the pill was practically always identical in composition, and the dosage in all cases amounted to about 15 gr. of crystalline quinine sulphate, taken together with a pill containing sodium bicarbonate and a vegetable substance, probably cascara sagrada extract.

Result of Trial of Accused.

What was the effect of the quinine and to what extent was its abortifacient effect in character and amount established? Several patients miscarried apparently as result.

Evidence (medical) showed—(1) that quinine is a protoplasmic poison and likely to affect growth of tissues of ovum; (2) that experiments on animals have shown that it produced rhythmical contraction of the uterus; (3) that it stimulates uterine contraction in labour; (4) that in malarial countries abortion is frequent, in some degree probably due to quinine but more largely due to malaria; (5) that quinine

in large doses produces toxic symptoms and had even caused death.

The Recorder asked the jury to decide: 1. Was quinine in ordinary doses a noxious drug? 2. Was quinine in large doses a noxious drug? 3. Was the drug administered by the accused with intent to produce abortion? The jury replied to (1) No; (2) Yes; (3) Yes. The accused was convicted and sentenced to 12 months' hard labour.

Action of Quinine.

The following points bear on the evidence and the learned Recorder's charge to the jury:—

1. Quinine in doses of 1:20,000 paralyses amœba and paramœcium, also destroys amœbic movements of white blood corpuscles (Binz). These observations have been confirmed.

2. Experiments on female animals have shown that it produces rhythmical uterine contraction (Cushing).

3. It is well known to stimulate uterine contractions in labour and is recommended by numerous British and American obstetricians for that purpose.

4. In malarial countries abortion is frequent. This may be due to the malaria, although it has been attributed to the large doses of quinine given.

5. Quinine in large doses is toxic. In 1885 two soldiers took 3 dr. each; one vomited and recovered, the other died. One of us had to treat a child, under a month, which had been accidentally given a 5 gr. dose intended for an adult; it was resuscitated with difficulty. A case was reported in THE LANCET of July 6th, 1918, in which a dose of 5 gr. caused œdema of eyelids, urticaria, vomiting, and headache. Doses of 1 gr. three times in 48 hours and 1 gr. in 48 hours produced the same result in this patient. Doses of 300 gr. and upwards have produced partial temporary blindness and loss, permanently, of colour vision.

There is no doubt that quinine in large doses produces toxic symptoms and, in some patients, even in small doses. Doses of over 10 gr. in the majority of non-malarial patients produce some toxic symptoms, and doses of 20 gr. and upwards, if repeated, may produce definite poisoning. Elimination, although rapid, is not so rapid as to allow of the repetition of doses of over 10 gr. in less than 12 hours.

In the case above the drug was held to be "noxious" in the doses given, and as to the intent there was no doubt. The learned Recorder's charge to the jury appears to cover the ground completely, and the jury had no hesitation in answering the questions put.

We are indebted to Mr. F. Beach, M.A., for his assistance with the analytical work.

A CASE OF ACUTE ASCENDING PARALYSIS.

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ACUTE ascending paralysis, first described by Landry in 1859, is produced by disease spreading rapidly upwards through the spino-muscular neurones from the lowest segments of the cord to the medulla oblongata, and is a pure motor palsy usually ending in death by paresis of the respiratory muscles.

Deaths from Landry's paralysis in the United Kingdom are recorded by the Registrars-General under Group 63 B of "The Manual of the International List of Causes of Death." This group, including other diseases of the nervous system, was analysed in 1913 for England and Wales, and I am indebted to the Registrar-General for the knowledge that there were 57 deaths, 28 of males and 29 of females, from acute ascending paralysis, equal to an annual death-rate of 1.6 per 1,000,000 living.

Account of Case.

Landry's paralysis is an uncommon disease, of uncertain cause, unknown ætiology, and of obscure morbid anatomy. The following case illustrates the course of the illness and has other points of interest.

Previous history.—Pte., aged 30, married, coal-miner, of temperate habits, smoked five cigarettes a day, drank an occasional glass of beer; no serious illness before joining the Army in 1915. Nothing unusual in family history. He contracted syphilis and gonorrhœa on Dec. 7th, 1915; three days later primary sore appeared on prepuce. When

¹ Medical Therapeutics and Toxicology.