more sourly since he ended his song. By the late 1950s its lower reaches had become so lifeless as to differ from the moon (the subject of a neighbouring exhibit) only in being wetter. But in the last ten years the measures taken to control its pollution have had their effect. Fish have reappeared, and a few of those that did not get away—probably owing to their small size—were shown for all to see. If not altogether "sweet," that noble river does at least show signs of life again.

Oral Contraceptives and Hypertension

How many women will become hypertensive when given oral contraceptives is not known, nor are the mechanisms by which the blood pressure is raised fully understood. In 1967 J. W. Woods[1] reported that in six women patients with hypertension the blood pressure rose further when they were given oral contraceptives which contained a high dose (greater than 0·05 mg.) of oestrogen with a progestogen. J. H. Laragh and his colleagues[2] enlarged on these findings. They studied 11 women with hypertension, all taking oral contraceptives with high oestrogen content. Five were known to have been hypertensive before contraceptive therapy was given, the other six were known to have had a normal blood pressure. When the agent was withdrawn from eight patients, the blood pressure fell to normal levels and remained normal in three; in another three it was markedly lower. Two women whose pressure had returned to normal were given the contraceptive agent for a second time, and the blood pressure rose again. A recent report by M. H. Weinberger and his colleagues from Palo Alto[3] shows essentially the same. They investigated 16 hypertensive patients who were taking combined oral contraceptives. Some of these agents contained what is now thought to be a small dose of oestrogen (0·05 mg. or less). Eleven women were known to have had a normal blood pressure before contraceptive treatment was started. The increase in blood pressure was noted between 3 and 36 months after the first prescription of the combination. Five patients became normotensive when the contraceptive was withdrawn, and six had a significant reduction in pressure between two and six months later.

In an attempt to find how many women will become hypertensive when given oral contraceptives, J. E. A. Tyson[4] investigated 45 given oestrogen–progestogen preparations and found that seven (15·5%) had a significant rise in blood pressure, mostly after the second cycle of drug usage. Treatment was stopped one or two months after the pressure rose, and in all cases the blood pressure returned to normal within 30 days. These findings have been contested. R. C. Goodlin and V. Waechter[5] measured the blood pressure in 120 patients given eight brands of oral contraceptives and matched these patients for age with 100 control subjects. They were unable to show any significant rise in blood pressure in the treated subjects.

If the occurrence of hypertension in patients taking oral contraceptives is disputed, so is the mechanism. It has been shown that this form of contraceptive produces a number of abnormalities in the renin–angiotension–aldosterone system. Firstly, aldosterone excretion (which rises in pregnancy[6]) rises in patients given oral contraceptives, even when they are placed on a high sodium intake, which will suppress aldosterone excretion in normal subjects.[3] Not all patients, however, who become hypertensive on oral contraceptives have an increased aldosterone excretion. Secondly, the renin–substrate concentration in the plasma of patients receiving oral contraceptives may rise to between two to five times the control concentration.[2] Thirdly, the plasma renin level may be increased in these patients too.[2 3] Plasma renin also rises in pregnancy,[6] and under experimental conditions the administration of both oestrogen[7] and progestogens[8] will also cause an increase. But while all these biochemical changes may provide a reason for a rise in blood pressure, their relevance is obscured by the fact that the same changes can be found in patients given oral contraceptives whose blood pressure is unaffected. On present evidence it is difficult to see why only some women show a sensitivity to oral contraceptives manifested by a rise in blood pressure.

Ideally, all patients should have their blood pressure measured before these agents are prescribed. Before stating categorically that no women with raised blood pressure should be denied oral contraceptives, we need to know much more about the risk of precipitating severe hypertension in these patients. Fortunately, the levels of pressure associated with the administration of oral contraceptives are not usually very high, though one patient is alleged to have developed the changes of malignant hypertension.[9] In our present state of knowledge it is reasonable to suggest that a woman who is found to be hypertensive and who is taking an oral contraceptive should stop taking the agent. Her blood pressure should be measured over a period of a month or two before considering the need for hypotensive therapy. What is needed, however, is a detailed clinical appraisal of the size of the risk of normotensive women developing hypertension and of hypertensive women having an exacerbation of their blood pressure when given oral contraceptives.

Buruli Ulcer

Buruli ulcer or infection with *Mycobacterium ulcerans* must still be counted a newly recognized disease. Certainly most physicians are unfamiliar with it, partly because even in regions where it is most common it causes relatively few cases. But increasing knowledge indicates that when looked for it is commoner than had been thought, and its distribution is wide. Until recently its earliest lesions were ill-recognized for what they are. Now the paper at page 390 of the *B.M.J.* this week, by Dr. D. J. Bradley and his colleagues, helps to fill this gap in our knowledge.

Most of the patients are between the ages of 5 and 15 years, but some are 50 or more. The initial lesion usually consists

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[3] Weinberger, M. H., Collins, R. D., Dowdy, A. J., Nokes, G. W., and Luetscher, J. A., *Annals of Internal Medicine*, 1969, **71**, 891.
[4] Tyson, J. E. A., *American Journal of Obstetrics and Gynecology*, 1968, **100**, 875.
[5] Goodlin, R. C., and Waechter, V., *Lancet*, 1969, **1**, 1262.
[6] Brown, J. J., Davies, D. L., Doak, P. B., Lever, A. F., and Robertson, J.I.S., *Lancet*, 1963, **2**, 900.
[7] Crane, M. G., Heitsch, J., Harris, J. J., and Johns, V. J., jun., *Journal of Clinical Endocrinology and Metabolism*, 1966, **26**, 1403.
[8] Winer, B. M., *Journal of Clinical Investigation*, 1965, **44**, 1112. Harris, P. W. R., *Lancet*, 1969, **2**, 466.

[1] Cook, A., *Mengo Hospital Notes*, 1897. Makerere Medical School Library, Kampala, Uganda.
[2] MacCallum, P., Tolhurst, J. C., Buckle, G., and Sissons, H. A., *Journal of Pathology and Bacteriology*, 1948, **60**, 93.

of a single, firm, painless, subcutaneous nodule. In about half the cases it is on the legs and in about a third on the arms, but in children it may be almost anywhere except the scalp, palms, or soles of the feet. It may extend slowly or rapidly. In the most fulminating case described in the present study an area of induration 5 cm. in diameter enlarged within three weeks to include much of the thigh and with an extent difficult to determine. Often the initial lesion quietly develops over months. In uncomplicated cases it is painless, free from tenderness, and not associated with fever, constitutional disturbance, or lymphadenopathy. It breaks down and causes an ulcer with undermined edges, and this may be of considerable extent. Only rarely are the lesions multiple. There is a natural tendency for the ulcer to heal, though it may take many months or years to do so, and the severe scarring resulting may cause lymphoedema.

Histologically there is a spreading necrosis, especially involving the subcutaneous fat. The cell nuclei disappear, but the outlines of the necrosed structures remain for weeks before sloughing renders them unrecognizable. In necrotic tissue from the base of the ulcer large numbers of acid-fast *Myco. ulcerans* will usually be seen, but these are scanty at the margins—a point of importance when diagnostic biopsy is being considered. The mode of transmission is uncertain, but the frequency with which the disease is found in riverine and similar regions has suggested that exposure to water containing the organisms plays a part. Swimming-pools may be sources of infection.

In treatment surgical excision of necrotic areas with skin grafting is the essential procedure, and with this the administration of B663 (Lamprene) or rifamycin (Rifadin) may be helpful. Until the mode of spread is ascertained, means of prevention will present difficulties, but there have been indications that B.C.G. vaccination may be protective and that in endemic areas the incidence is lower among persons who have positive tuberculin tests.

Among the first clinical descriptions of the disease was that of Sir Albert Cook[1] in Uganda in 1897, but P. MacCallum and his colleagues[2] in Australia were the first to describe the lesions in association with their causative *Myco. ulcerans*. Since then there have been reports from Uganda, both in the Buruli district from which the disease in that region takes its name and in the Madi district to the north near the Sudan. It has also been reported from the Congo (Kinshasha), Nigeria, Mexico, Malaya, and New Guinea. Doubtless descriptions from other places will follow, and it seems to be something which must be looked for throughout the tropics. Early recognition and treatment are necessary for the avoidance of crippling scars and deformities and in many cases for the preservation of affected limbs.

Paralysis in Herpes Zoster

Of all the complications of herpes zoster post-herpetic neuralgia is the most frequent and distressing. It particularly affects older patients. Dr. J. B. Foster recently discussed (13 December p. 667) the often unavailing treatment of this condition. Parts of the central nervous system other than the primary sensory neurone may also be damaged by the disease. Leptomeningitis, myelitis, and encephalitis have been described.[1-7] Lower motor neurone paralysis was first reported by W. H. Broadbent[8] in 1866 in a patient with a rash over the third and fourth cervical dermatomes and paralysis of the abductors of the shoulder. He believed the lesion to lie in the spinal cord. Post-mortem examinations of cases both with and without paralysis have since confirmed the frequency of inflammation in the anterior grey horns of the spinal cord.[2 3 9] Though herpes zoster occurs more often on the trunk than on the limbs,[10] paralysis is commoner in the latter,[11-13] probably because paralysis of one intercostal muscle or one segment of a lumbar muscle may easily escape notice.

S. K. Gupta and his colleagues[14] have recently reviewed 274 patients with herpes zoster referred to hospitals in the London area. They estimated that only about one case in 100 was referred to hospital. Of these 274 patients, 69 (25%) had cranial nerve palsies, 15 (5%) limb paralysis, 2 bladder and rectal paresis, and 1 trunk paralysis. Gupta and his coworkers restricted their attention to patients with paralysis affecting other than cranial nerves. Complete or nearly complete recovery of power occurred in 14 of 18 of their own cases and in 16 of 27 further cases collected from reports, a combined recovery rate of 67%. Most who were going to recover had done so by nine months. In only 18% was there no recovery.

The muscles innervated by the oculomotor, facial, and phrenic nerves are occasionally implicated in herpes zoster. The site of the lesion causing facial paralysis in herpes oticus still causes much debate. Ramsay Hunt believed it to be in the geniculate ganglion, though he unfortunately failed to obtain the ganglion in his dissection.[15] D. Denny-Brown and his colleagues[3] refuted this theory; in their case the geniculate ganglion was normal while the facial nerve nucleus itself was damaged. However, inflammatory changes in the geniculate ganglion have been described in one case.[16] In Gupta's study[14] the suggestion was made that the facial nerve becomes infected where the occipital muscles receive afferent fibres from the upper cervical nerves, and a similar explanation was proposed for the oculomotor lesions in ophthalmic herpes zoster. Facial palsy in ophthalmic zoster might be thought to have a similar basis.[3] Alternative mechanisms to be considered include a non-specific local spread, which probably explains the rare occurrence of optic neuritis in ophthalmic herpes zoster, and spread within the brain stem and spinal cord, a phenomenon which must underly paralysis of muscles innervated by different segments or the side of the spinal cord opposite to the sensory root affected.[3] Perhaps we are too obsessed with a single primary site of virus reactivation when the latent virus may be widely spread throughout nervous tissue.

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