operation consists of either bilateral ligation of the femoral veins or ligation of the inferior vena cava.

Anticoagulant Therapy

It would be out of place in an article of this nature to discuss anticoagulant therapy in detail, but a few practical points in relation to its use in venous thrombosis can be given. For prophylactic use heparin is unnecessary: one of the oral anticoagulant drugs, preferably warfarin, should be used. An initial dose of 30 to 50 mg. of warfarin should be given whenever the decision to start treatment is made, and subsequent dosage determined by the results of whichever laboratory test is used for control. In established deep-vein thrombosis heparin should be given in an initial intravenous dose of 15,000 units, followed by 10,000 units at intervals of four to six hours. Whether to continue with heparin alone or to change to an oral anticoagulant is largely a matter of personal preference. Many surgeons believe that heparin is the better anticoagulant in these patients and continue with it for 10 to 14 days, which is often as long as is thought necessary. There is good evidence that treatment with heparin is followed by rapid improvement in the local clinical signs,[16] but the risks of bleeding with prolonged heparin treatment are undoubtedly greater than with oral anticoagulants.

If the policy is to use heparin only for its immediate effect, and to maintain therapy with an oral drug, then the loading dose of the latter should be given at the same time as the initial dose of heparin. In these circumstances heparin can be stopped when the results of laboratory tests show that the depression of the coagulation factors has reached the so-called "therapeutic level." As far as laboratory tests are concerned there is little to choose between them, and the decision whether to use the "Thrombotest" or Quick's one-stage "prothrombin time" is a matter of personal preference. If the former is used the therapeutic level to be aimed at is 5 to 10%; if the latter, two to three times the normal.[17]

Special Types of Venous Thrombosis

Thrombophlebitis Migrans

In this condition there are recurrent episodes of thrombosis affecting short lengths of superficial veins, usually in the extremities, but also sometimes on the trunk. Deep-vein thrombosis is uncommon and pulmonary embolism is rare. In some of these cases arterial lesions are also present, and then the diagnosis is thromboangiitis obliterans; others are associated with carcinoma, but many of the patients continue to have intermittent attacks of superficial thrombophlebitis for years without other manifestations. There is no good evidence that anticoagulants modify the course of this condition, and apart from the use of phenylbutazone as an anti-inflammatory agent in severe attacks no special treatment is necessary in most cases.

Axillary Vein Thrombosis

Spontaneous thrombosis of the axillary or subclavian vein, often associated with effort (Paget-Schroetter Syndrome), occasionally occurs in fit young persons. The symptoms are swelling and a feeling of tightness in the arm with cyanosis of the hand. Early treatment with elevation of the limb and anticoagulants is often effective, but sometimes the diagnosis is missed, and by the time the patient is seen there is chronic oedema of the hand and forearm, which is difficult to relieve. Sympathetic block has been suggested, but I have never seen any benefit follow this procedure in such a case.

Phlegmasia cerulea dolens

This is the syndrome of sudden massive thrombosis of the veins draining the lower limb, which becomes swollen, blue, and painful, and gangrene of venous origin is not uncommon. Anticoagulants seem to have little effect on this condition, and it may even develop in a patient who is on anticoagulants. Conservative management with elevation of the limb and analgesics is usually recommended, but there is probably a case for considering surgical treatment with thrombectomy, as recommended by Haller.[18]

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Drugs and Placental Barrier

Q.—*Is it possible to say in general which drugs cross the placental barrier and which do not?*

A.—In recent years there has been much interest in the passage of drugs and other substances across the placental barrier, and there are a number of excellent reviews dealing with this subject.[1-4] In general terms it can be said that almost any substance can penetrate the placental barrier to some extent, although some drugs are so rapidly destroyed that they do not reach an effective concentration in the maternal blood. When the degree of permeability is low the amount which reaches the foetus is neither pharmacologically active nor physiologically detectable.

It is possible to recognize the passage of drugs through the placenta either by detecting their presence in the foetal blood after administration to the mother or by observing their known pharmacological effects on the foetus. For example, it can be inferred that antithyroid drugs cross the placental barrier because babies born to mothers receiving these drugs have enlarged thyroids. Similarly, oral anticoagulant drugs administered during pregnancy can cause a haemorrhagic state in the foetus. Naturally, most information is available about drugs which are used in obstetrics.

All the commonly used hypnotics, analgesics, narcotics, and anaesthetics cross the placental barrier readily and rapidly. The notable exceptions are the muscle relaxant drugs such as tubocurarine, gallamine, decamethonium, and suxamethonium, which, when administered in the usual doses, apparently do not cross the placenta. In animals, however, it is found that when these drugs are given in large doses they do affect the foetus, so that the placenta is a relative rather than an absolute barrier to their passage. Of other

drugs, the sulphonamides, most antibiotics, the cardiac glycosides, adrenal corticosteroids, and hypotensive drugs are all known to cross the placenta readily.

The evidence suggests that drugs cross the placenta by a process of simple diffusion, and that the main factor which determines the rate of passage is the fat solubility of the non-ionized drug. Substances such as insulin, dextran, and quaternary ammonium compounds, which are relatively insoluble in lipids, reach the foetus slowly and in relatively low amounts. Other factors such as the concentration gradient and the molecular weight of the drug are probably of secondary importance.

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Beans and Favism

Q.—*Are phaseolus beans, commonly sold in England as "baked beans in tomato sauce," capable of causing haemolysis and haemoglobinuria in subjects deficient in glucose - 6 - phosphate dehydrogenase (G-6-P.D.), or is the broad bean, Vicia fava, the only bean capable of doing this?*

A.—The exact nature of the substance in the pollen and bean of *Vicia fava* that causes haemolysis in people deficient in glucose-6-phosphate dehydrogenase (G-6-P.D.) is not known. There is some evidence, moreover, that there is an additional inherited factor involved.

No other food substance has been proved to produce haemolysis in persons deficient in G-6-P.D., but Motulsky[1] gives a list of foods, including the garden pea and the whortleberry, that have been implicated in haemolytic reactions, although the mechanism is not certainly the same as that producing favism. There has been no evidence to associate the ingestion of baked beans (Phaseolus family) with haemolysis.

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Hazards of Abortion

Q.—*Now that medical control of disease before operative treatment is more possible, does it still hold that induction of abortion is extremely hazardous for women who have a serious medical indication?*

A.—Medical conditions that might be considered an indication for the termination of pregnancy and that are themselves serious hazards to life include advanced pulmonary tuberculosis, bronchiectasis, bronchial asthma, blood disorders, chronic nephritis, disseminated lupus erythematosus, malignant disease, diabetes, thyrotoxicosis, Addison's disease, Cushing's disease, poliomyelitis, ulcerative colitis, and heart disease.

I would agree with the point of view which seems to prompt the question that we are now able to control most of these diseases sufficiently well to allow pregnancy to be terminated as safely as possible. However, the patient with cardiac disease who is severely decompensated or the patient with chronic pulmonary disease who has a diminished vital capacity cannot be rendered always as fit as she should be to withstand termination of pregnancy, which exposes her to infection, the risks of anaesthesia, sudden changes in blood volume, and to an increased risk of thrombosis and embolism. In these two conditions termination of pregnancy must still be regarded as hazardous, and at least possibly as dangerous as allowing the pregnancy to continue.

The final decision, however, could not be made without considering all the circumstances in the individual patient. Moreover, it should also be remembered that the recent advances in medical knowledge that have made therapeutic abortion so much safer have also made it possible for a wanted child to be carried and borne more safely.

Paraesthesia after Herpes Zoster

Q.—*Is there any effective treatment for residual distressing paraesthesia after an attack of herpes zoster in an elderly person?*

A.—Pain and paraesthesia after herpes zoster are not uncommon in the elderly. Treatment can be very successful if it is optimistic and enthusiastic, but is difficult when the symptoms have been present for five years or more.[1] Mild symptoms often respond to simple analgesics and encouragement to use rather than to protect the affected part. Rubbing the skin or applying firm pressure to it are helpful. A mechanical vibrator is particularly useful on hyperaesthetic skin.

More severe cases may need admission to hospital for such measures as infiltration of local anaesthetic or nerve block. Specific treatment for accompanying anxiety and depression is sometimes needed, but these symptoms will often improve when the local disorder is relieved.

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Endocervical Ectopia

Q.—*What is the current view on the causation of so-called "virginal" cervical erosion? Does it do any harm and is there a need to treat it, and, if so, what is the treatment?*

A.—So-called "virginal" or "congenital" cervical erosions are merely an anatomical variant in which the columnar-celled epithelium of the endocervical canal extends on to the portio vaginalis of the cervix.[1] They appear as velvet-like red patches surrounding the external cervical os. Kaufmann and Ober[2] have shown that the level of the lowest cervical glands advances from the endocervix during childhood and adolescence and then recedes again. The recession is, however, only apparent. The columnar epithelium on the ectocervix disappears because it is overgrown by squamous epithelium as age advances.

The adjectives "virginal" and "congenital" and the term "erosion" are inappropriate, since these lesions are not confined to unmarried women, they are not always present at birth, and the epithelium is intact. No one has bettered Hinselmann,[3] who described the lesion as endocervical ectopia.

Endocervical ectopia is not a pathological condition and does not therefore require treatment. It does not usually cause symptoms. In a few women it may be associated with a somewhat excessive mucoid discharge. If this causes them annoyance an astringent douche of alum containing 1.5 g. in 500 ml. of water used once or twice weekly may keep them more comfortable. In exceptional cases the ectopic columnar epithelium may be destroyed with cautery or diathermy so that it can be replaced by squamous epithelium that covers any mucous-secreting glands.

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Infection after Splenectomy

Q.—*Is a child's future health likely to be affected in any way as a result of a splenectomy for traumatic rupture of the spleen?*

A.—King and Shumacker[1] suggested that after splenectomy there was an increased risk of severe infection. Huntley[2] believed that this risk was highest when the spleen was removed in infancy. In a recent review Lowdon *et al.*[3] found that half the splenectomies in childhood were done for injury, but in none of them was there an infective complication. Three severe and two doubtful infections occurred in other patients under the age of 14 after splenectomy for haemolytic or other anaemias or thrombocytopenic purpura, and three of these patients were aged less than 3 years.

It seems unlikely that the incidence of infection is any greater than normal after splenectomy for accidental rupture in a normal child or that any other particular complications should arise.

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Emergency Transfusion for Hypovolaemic Shock

Q.—*What should be used for transfusion in the emergency treatment of hypovolaemic shock while waiting for cross-matched blood? Is polyvinylpyrrolidone satisfactory?*

A.—The principal aim in the emergency treatment of hypovolaemic shock is to restore the blood volume to near normal levels. Plasma is the most effective transfusion alternative while waiting for blood to be cross-matched.[1 2] When plasma is not available a suitable plasma substitute, such as 6% dextran, is a safe plasma-volume expander and its effect is comparatively long lasting.[3]

Not more than 1 litre should be given.[1] Rheomacrodex, a low molecular weight dextran, may be used, but, because of its low molecular size, its effect is of only short duration and it should be infused fairly quickly.[4]

Polyvinylpyrrolidone has been widely used as a plasma-volume expander in Europe, but has gained little acceptance in Britain or America. On account of its relatively low molecular size (range 30,000 to 60,000, depending upon product) it is rapidly excreted and less than 50% remains in the circulation after 24 hours.[5] In addition it is taken up by the reticulo-endothelial system, and there have been reports that it is carcinogenic. However, it may be used in an emergency and on the rare occasion where none of the above alternatives are available.

It is well to remember that occasionally in severe hypovolaemic shock resulting primarily from marked loss of blood it may be expedient to give O Rh-negative blood, or wait for an emergency cross-match, when replacement of red cells must not be delayed lest there is irreversible damage caused to tissues by prolonged anoxia. There is little place for normal saline transfusion, though occasionally it is useful when a large component of the hypovolaemic shock is due to actual fluid loss.

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Hirsuties in Women

Q.—*What treatment is there for a heavy growth of dark hair in the beard area in a female member of each of three generations of a family? The onset in each case was at puberty. One of the patients has attacks of the hyperadrenaline type, with severe headache, sweating, flushing, and palpitations. Would x-ray depilation be suitable?*

A.—The principal factors influencing hair patterns are genetic and endocrine. The predominant influence is genetic, and male and female patterns of facial and body hair differ only in degree.[1 2]

A heavy growth of facial hair after puberty in females of three generations of a family strongly indicates that genetic constitution of the hair follicles rather than an endocrine abnormality is at fault. Attacks of headaches, sweating, flushing, and palpitations may be associated with a tumour or hypertrophy of the suprarenal medulla, which, unlike the suprarenal cortex, does not produce androgens. The presence of a virilizing tumour like an arrhenoblastoma may have to be excluded. Unfortunately hirsuties in women due to a virilizing tumour is rarely reversed by its removal.

However, the symptoms mentioned need not be due to a tumour. If underlying organic disease can be excluded symptomatic treatment of facial hirsuties in women is usually satisfactory. Sometimes bleaching of dark hair with hydrogen peroxide will suffice. The most satisfactory and permanent treatment is epilation by electrolysis. This requires considerable expertise. *X*-ray depilation can be achieved only by radiation causing conspicuous and irreversible damage in the exposed skin, with the long-term risk of neoplasia.

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Dapsone in Dermatology

Q.—*I found that pustular skin eruptions were uncommon in patients with leprosy treated with dapsone. Could dapsone be used in the treatment of pustular acne?*

A.—Dapsone was examined with other sulphones for bacteriostatic and bactericidal properties in 1937 when compounds related to sulphonamides were tested.[1] Bauer and Rosenthal demonstrated in 1938[2] that dapsone was 30 times more effective than sulphanilamide against experimental streptococcal infections and only 15 times as toxic. Rist *et al.*[3] found dapsone effective in suppressing avian tuberculosis. It has been used in the treatment of leprosy since 1943.[4]

Sulphones have been shown to be retained for long periods not only in the lesions of lepromatous leprosy but also in the skin, muscle, liver and kidneys.[5 6] Their use in skin disorders not related to leprosy has been extensively discussed by Lorincz and Pearson.[7] While dapsone is generally accepted as the treatment of choice for dermatitis herpetiformis, Lorincz and Pearson obtained good results with it also in acne conglobata and pyoderma gangrenosum, and suggested its trial in so-called allergic vasculitides representing abnormal tissue reactions to bacterial endotoxins. Dapsone has also been used by some dermatologists in the treatment of chronic pyoderma and infected eczema.

The clinical toxicity of dapsone is considerable. Haemolytic anaemia is the most serious risk, but it becomes demonstrable only with fairly high doses. However, there is much variation in individual susceptibility. Headache, nausea, insomnia, paraesthesia, haematuria, pruritus, and morbilliform rashes have been reported in isolated cases,[8] and suggest caution in using this drug in conditions where less toxic alternatives are available.

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Notes and Comments

Prickly Heat.—Dr. E. N. WARDLE (Manchester 20) writes: May I comment on the answer to this question? ("Any Questions?" 25 June, p. 1588). You have previously[1] kindly allowed me to point out that there is a strong association between the acquisition of prickly heat and the concern of people in the tropics to take extra salt. Horne and Mole[2] thought that prickly heat was made worse by a high salt intake, and Loewenthal[3] thinks that the rash may be caused by salt on the skin. Moreover, it is known that when subjects are acclimatized on a high salt intake there is no reduction of the sweat chloride.[4]

The salt conservation response of the sweat gland need not be an integral part of the process of acclimatization. Persons who have been three seasons in Aden still develop prickly heat in summer, and I myself, in examining Arabs on the Persian Gulf, who incidentally drink water of high saline content, found mild forms of prickly heat in 15% adult males and 45% children. Obviously, salt restriction is not to be advocated. On the other hand, the physiological requirement for salt is less than that needed to satisfy the taste.

In Aden I have found that air-conditioning reduces the prevalence of prickly heat from 95% to 75% in children, and from 80% in both adult sexes to 60% in men and 40% in women. However, I should add that, except in some children, the prickly heat of persons in air-conditioned quarters in much milder and the incidence of overt sepsis is reduced. Leithead and Lind[5] state that eight hours' relief from sweating each day is adequate.

It would be useful to categorize those who are at risk from prickly heat. Children up to the age of 7 are liable to develop a severe form covering the whole body. This is probably related to the fact that up to that age the density of sweat glands on the skin is three times that of the adult. Moreover, until puberty children sweat relatively more, and the sweat response is more readily activated. Predisposing factors in children are the childhood fevers and fretfulness, and in adults alcoholism, tea-drinking, obesity, and work with grease and oil, or in a hot kitchen. The localizing factors are well known.

As for the inefficacy of the various treatments, of which I personally have collected at least 50, I think certain principles could be elaborated. These are to counteract the sweat-sodden fatty-acid depleted skin of alkaline pH, to reduce the local deposition of salt, to produce mild desquamation of the skin surface, and to add a bacteriostatic agent. For example, the following lotion can be adapted by the addition of mercuric chloride or hexachlorophene: arachis oil, 5.0%; adeps lanae, 2.2%; lanette wax, 6.7%; salicylic acid, 2.0%; glycerin, 6.7%; tragacanth mucilage, 25.0%; water to 100%.

Alkaline soaps must be avoided, and also sunbathing, once a fatty cream has been applied to the skin. Furthermore, oral phenergan is invaluable to relieve itching and pricking, and proper bacteriological control and the use of Naseptin cream is useful in those families where there is superimposed sepsis.

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