TREATMENT IN GENERAL PRACTICE

This article is one of a series on the management of some diseases of the blood and blood-forming organs met with in general practice.

TREATMENT OF HAEMORRHAGIC DISEASES

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PART II

Anaphylactoid Purpura

This type of purpura lies between urticaria and purpura haemorrhagica, and includes both Henoch's purpura and purpura rheumatica. There is an escape from the vessels of much plasma and little blood, but as a small number of blood cells can stain a large area of tissue impregnated with plasma this leads to the formation of extensive ecchymoses, which suggest the escape of much blood. The escaping plasma manifests itself in urticarial forms such as abdominal pain, diarrhoea, colic, and pain and swelling of joints. The patient is more sick than purpuric. As might be expected the signs and symptoms of purpura haemorrhagica are less marked in this group. Thus the degree of anaemia is less. The platelet count is diminished in the severer cases often to the neighbourhood of 100,000 or 150,000 per c.mm. The statement that the platelets are not reduced in this group is incorrect, but even when the constitutional symptoms are severe and there are considerable ecchymoses the number of escaping blood cells may be small and the degree of anaemia and reduction of platelets will be slight. The bleeding time and the capillary-resistance test may or may not be abnormal.

Anaphylactoid purpura usually appears first in childhood; it may continue into or cease in later life. It is, however, erroneous to suppose that it is confined to childhood, as its first manifestations may not be shown until the middle decade. There is a definite predisposing factor in some cases, and before further treatment is undertaken it is essential to ascertain whether there is any focal sepsis or any sensitivity to items of food or foreign protein. In its pathogenesis this group has no inherent difference from purpura haemorrhagica, and the questions of splenectomy and blood transfusion should be considered on the grounds which have already been discussed.

Certain special points apply to this group. Constitutional disturbances during attacks may be so severe as to interfere with education or occupation, but they should not be regarded as a decisive factor, for they tend to diminish with the passing of time. In the absence of anaemia and with a normal platelet count operation is contraindicated. Intussusception due to an area of swollen gut is a not infrequent complication, and should be remembered when diarrhoea is marked and the motions contain blood. The urine of some patients contains a large amount of albumin during acute attacks. This is due to protein sensitivity rather than nephritis, and in such cases special search should be made for some causal agent. The risk of the development of nephritis has been exaggerated in the past.

Treatment.—Intramuscular injections of horse serum, 10 c.cm., or of whole blood, 10 to 20 c.cm., have temporary beneficial effects in some patients although in others, apparently similar, they may fail entirely. The

other methods of treatment described for purpura haemorrhagica also apply in these cases.

Symptomatic Haemorrhagic States or Secondary Purpura

This group differs essentially from those which have already been discussed in that there is a primary causal factor, the influence of which varies greatly, since it may be still continuing in some cases whereas in others it has ceased and is non-recurrent. For example, in the case of a streptococcal septicaemia the recovery from the causal factor is practically hopeless, and the haemorrhages can only be regarded as a terminal incident; in purpura due to drugs the causal factor, if discovered, may be regarded as non-recurrent. It is not always easy to find out from a sick patient that such a drug has been taken recently. With regard to the infectious fevers it must be borne in mind that the haemorrhagic tendency may develop at different periods. Thus it may appear at the time of the eruption, but sometimes it arises considerably later, when convalescence would seem to have begun. When associated with infectious fevers or drugs the haemorrhagic tendency is transient, lasting only until the effects of the drug or the infection have worn off; there will be no future tendency to haemorrhages unless the same or a similar factor reappears. Obviously the object of treatment is to tide the patient over the dangerous period.

In the presence of definite septic foci, such as otitis media, the position is more difficult as the cause is still operative. The focus of infection must be dealt with, but as little operating as possible should be done. In the symptomatic group the haemorrhagic tendency is sometimes of such extreme severity as to come under the heading of purpura fulminans, the mortality of which is very high.

The general indication is to make every effort to tide over the immediate haemorrhagic period. It can properly be said that blood transfusion should always be performed, but splenectomy is absolutely contraindicated. Blood transfusion should be carried out according to the principles already described. It should be repeated at short intervals if constitutional disturbances are severe, if the bleeding time remains prolonged, and if the anaemia is increasing. The introduction of injections of vitamin C as cevitamic acid is so recent that at present there is no record of its use in this group, but its trial would be fully justified. Protein shock is clearly contraindicated in an acute condition in which sensitivity may be an important factor. Severe bleeding from a single mucous membrane will call for the usual methods of treatment or the special methods referred to under haemophilia.

Haemorrhagic Deficiency Disorders

SCURVY

The specific treatment of scurvy has now been reduced to a simple form by the preparation of L-ascorbic acid or cevitamic acid in a pure form. This is rapidly effective in scurvy when given by the mouth, but can also be safely injected intravenously. The dose by either method varies from 50 mg. in an infant to 150 mg. in an adult for a daily injection. This should be continued until improvement is obvious, usually from four to eight days.

Subsequently orange juice, 50 to 100 c.cm., should be given by the mouth. Recovery is rapid and the anaemia scarcely needs treatment even by iron. The dietetic deficiency which has led to the onset of scurvy must necessarily be corrected for the future.

MELAENA NEONATORUM

This curious condition in newborn infants between the third and tenth days is not hereditary, has no relation to the haemorrhagic diathesis, and is apparently distinct from haemophilia. The pathogenesis is unknown, but it is probably due to some deficiency. The bleeding is usually from the bowel, but may be from any mucous membrane. The specific treatment is the intramuscular injection of 10 c.cm. of whole blood. The blood can be drawn direct into a syringe from the vein of the mother or any healthy person and injected immediately, grouping being unnecessary. A single injection is often sufficient, but it should be repeated once or twice a day if the haemorrhages continue. Blood transfusion is only indicated if the amount of blood lost has been excessive. There is no subsequent tendency to recurrence.

Hereditary Haemorrhagic Disorders

There are several groups of hereditary haemorrhagic disorders which have no direct connexion with each other, although there are intermediate forms which are difficult to classify.

HAEMOPHILIA

The haemorrhage in haemophilia consists of a steady ooze at the site of trauma as distinct from the purpuric spots and petechiae of the haemorrhagic diathesis. It is now recognized that the females of a haemophilic family may have an abnormal tendency to bruising and bleeding and the coagulation time may be somewhat increased, but rarely do females exhibit the full manifestations of haemophilia. If a haemophilic male marries a female of a haemophilic family one child in four should be a female haemophiliac, but even this possibility is made very remote by the fact that few males live to have children. There is no known cure, and all treatment is transient and directed towards stopping the immediate haemorrhage. The haemophilic tendency is intermittent and the coagulation time may be temporarily normal, but it must not be considered that the patient is safe from haemorrhage in such circumstances, since there is reason to believe that with any stimulus, such as trauma and slight haemorrhage, the condition rapidly returns.

GENERAL TREATMENT OF HAEMORRHAGE

Haemophiliacs at an early age are always aware of their disability and become greatly perturbed at the continuation of bleeding. The patient should be put to bed at once, kept quiet, and given morphine without hesitation if necessary. Blood transfusion has the effect of reducing the coagulation time, and may even bring it close to normal limits, but this only lasts for about five days. A haemophiliac does not bleed from the puncture made by a sharp needle, and blood transfusion can safely be performed; the amount injected should be from 300 to 500 c.cm. Transfusion should always be undertaken immediately before any operative procedure.

The injection of whole blood intramuscularly may reduce the coagulation time. This is less definite than the effect of blood transfusion, but has the advantage that the blood need not be of the same group as the recipient's. Injections of normal horse serum, from 20 to 30 c.cm., may also be employed intramuscularly. It has been suggested that such injections should be given at frequent intervals with the idea of maintaining a normal coagulation time, but the duration of the response

is so short that the practical difficulties are insuperable, apart from the risk of producing haematomata.

The administration of calcium has proved of no value; it is striking that the blood calcium in haemophilia is abnormally high, usually 13 to 14 mg. per 100 c.cm. Liver extract also is ineffective. Oestrogenic hormones have been tried on the theory that some female sexual characteristic protects females, but no good results have been observed. Protein shock and injections of adrenaline are useless. There are no records of the intravenous injection of cevitic acid, but anti-scorbutic methods by the mouth have no effect.

The most efficient treatment at present of a haemophilic subject involves the most careful avoidance of trauma and the treatment of haemorrhage, when it occurs, by blood transfusion, repeated when necessary and locally by the application of a diluted solution of Russell's viper venom.

LOCAL TREATMENT

The local application of the diluted venom of certain vipers has been found highly effective in controlling the haemorrhage. The credit for the practical application of this method is due to R. G. Macfarlane and B. Barnett, whose writings are here followed. The most powerful coagulant venom is that of Russell's viper. This is now prepared by Messrs. Burroughs Wellcome and Co. under the name of stypven, and is issued in the form of dried venom, together with ampoules of sterile water for solution. The venom is sterilized by passage through a Berkefeld filter and used in a dilution of 1 in 10,000, at which strength it has no toxic effects; it keeps well when dried in ampoules, but is not stable in solution. It is also effective in checking the local haemorrhages in the haemorrhagic diathesis.

The bleeding site should be carefully cleaned and useless clots removed. A dressing of gauze is then applied soaked in equal parts of diluted venom solution and adrenaline 1 in 1,000. Pressure should only be sufficient to keep the dressing in position; in the mouth a carefully fitted plate may be necessary. The results have been extremely satisfactory, and the venom can be applied on numerous occasions without affecting the patient and without losing its powers. If viper venom is not obtainable, the wound should be carefully cleaned and fresh normal blood applied on gauze. This undoubtedly has some power to coagulate haemophilic blood. The application of adrenaline 1 in 1,000 temporarily checks the haemorrhage, but is not of permanent value. Pressure should only be applied for the purpose of retaining a dressing in contact with the bleeding site. The cautery is worse than useless. Hot water and hot air have no appreciable effect. When haemorrhage has occurred into a joint the blood should be aspirated and the joint elevated and lightly bandaged with cold applications. Haematomata should also be aspirated.

Hereditary Haemorrhagic Diathesis

This group is much rarer than the non-hereditary form. The diathesis may be transmitted and exhibited by both sexes. In many of the cases the manifestations are identical in every way with those in the non-hereditary group, and it is difficult to know whether they should be regarded as possessing a different pathogenesis. It has been said that splenectomy is contraindicated in hereditary cases, but there is on record a family of which the father was operated upon with complete success many years ago, but the child died after splenectomy without any rise of the blood platelets. On the whole it is best to neglect the hereditary factor and consider the treatment of the hereditary group on exactly the same lines as the non-hereditary form. There are a number of patients whose

symptoms and signs do not conform exactly with those of a haemorrhagic diathesis, and many of these appear to be intermediate between the haemorrhagic diathesis and haemophilia. Thus the diathesis may be transmitted through males and exhibited by both sexes, the coagulation time may be considerably prolonged, while the blood platelets may be normal and the bleeding time variable. In such a case the normal number of platelets would contraindicate splenectomy. Many variations of the manifestations exist, and each case must be judged on the principles already enunciated. During an acute attack it can never be wrong to give a blood transfusion. Cases of a similar character occur without a hereditary factor and have to be dealt with on the same lines.

In a very rare group of cases, the so-called fibropenia, the tendency to haemorrhage is due to a deficiency of fibrinogen in the blood. No treatment is known which will remedy this deficiency.

Hereditary Capillary Telangiectasia

In this condition fragile naevi of various shapes and kinds develop in the skin and mucous membrane, probably owing to congenital weakness of the capillary endothelium. The naevi tend to rupture and bleed, and thus produce anaemia. A local bleeding naevus if accessible can be treated either by the cautery or by pressure, but neither method is very successful, and probably snake venom would be better. Many of these patients finally die from a slowly advancing anaemia.

THE NEW POISONS RULES

THEIR EFFECT UPON THE POSITION OF THE MEDICAL PRACTITIONER

The provisions of the new Poisons-Rules which come into effect as and from May 1st are of importance to the medical practitioner. The general effect of these Rules, so far as they concern members of the profession, is as follows.

Poisons to which Special Restrictions Apply

The list of substances to which special restrictions apply is given at the end of this article. A reference to the list will show that it is largely based upon the present schedule of poisons, but that it has been elaborated in greater detail.

A medical practitioner may "for the purpose of his profession," purchase poisons from any "authorized seller of poisons"—that is, a chemist, or from a wholesale or manufacturing firm. Those poisons which are the subject of special restrictions will be supplied only upon a written order signed by the practitioner. In an emergency the written order is unnecessary if the practitioner gives an undertaking that such an order will be furnished to the supplier within the next twenty-four hours and actually supplies it within that time. If he does not do so he will be deemed to have contravened the provisions of the Rule, and will be liable to a penalty. The practitioner may, however, attend at the premises of the seller and obtain such a substance by signing the Poisons Register.

The practitioner who dispenses a medicine containing a substance to which the special restrictions apply must also (1) distinctly label the bottle with his name and address, (2) enter in his daybook the date of supply of the medicine, or on the next following day the ingredients of the medicine, the quantity of it, together with the name of the person to whom it was supplied.

Labelling of Poisons

Where the practitioner supplies an embrocation, liniment, lotion, liquid antiseptic, or other liquid medicine for external application, the container must be labelled with the name of the article and the words "For external use only."

Poisons in the Fourth Schedule

Under the new rules the following substances *and any preparation containing them* may be sold retail only upon a prescription given by a registered medical practitioner, a registered dentist, or a registered veterinary surgeon:

Amidopyrine; its salts.
Barbituric acid; its salts; derivatives of barbituric acid; their salts; compounds of barbituric acid; its salts, its derivatives, their salts, with any other substance.
Dinitrocresols; dinitronaphthols; dinitrophenols; dinitrothymols.
Phenylcinchoninic acid; salicyl-cinchoninic acid; their salts; their esters.
Sulphonal; alkyl sulphonals.

Most of these substances are better known to practitioners under trade or other names different from those used to describe them in the Schedule, and consequently, before prescribing any article which by reason of its action and use is likely to be affected, the practitioner should satisfy himself whether it consists of or contains a substance in the Fourth Schedule. The following is a list of some of the substances coming within the Fourth Schedule in the forms in which they are usually prescribed.

Acitophosan	Diethylamonylurea	Pentobarbital
Agotan	Dinitrocresols;	Pernoclon
Alepsal	dinitronaphthols;	Phanodorm
Algodorm	dinitrophenols;	Phenobarbital
Allobarbitone	dinitrothymols	Phenobarbitone
Allonal	Diogenal	Phenoquin
Amidophen	Dismenol	Phenylcinchoninic acid
Amidopyrine	Disulphamin	Phenyl-ethyl-barbituric acid
Amytal	Ditonal	Prominal
Anegrine		Proponal
Angiolysin	Ephepyrin	Pyramidon
Anotal	Eupaco	Quadro-nox
Arcanol	Euvalerol elixir B	Quinophan
Asciatine	Evipan	Rutonal
Atocin		Salicylcinchoninic acid
Atophan	Gardan	Sandoptal
Atophanyl	Gardenal	Sciatego
Atoquinol	Gorun cachets	Sedal
Barbital	Hebaral sodium	Sinepan
Barbitone and soluble barbitone	Hemypnone	Somnacatin
Barbituric acid	Hypnogen	Somnifaine
Benzedo compound	Ipral	Somnifene
Cafinal	Leucotropin	Somnosol
Chineonal	Luminal	Sonalgin
Chloroxyl		Soneryl
Cibalgin	Malonal	Sulphonal; alkyl sulphonals
Cinchophen	Malonurea	
Cinchosal	Medinal	
Codeonal	Merbaphen	
Compral	Methylsulphonal	
Creslumin		Tetronal
Cyclobarbitol	Nembutal	Theogardenal
Dekrysil	Neocinchophen	Theominal
Dial	Neonal	Theotone
Dialacetin	Neophenoquin	Tolysin
Diallylbarbituric acid	Neoquinophan	Trigemin
Dibromin	Neurinase	Trional
Didial	Novasurol	Veramon
Diethylbarbituric acid	Novatophan	Veronal
	Optalidon	Veronigen
	Optinoktin	Veropyron

When writing a prescription for these poisons the practitioner must see that it contains the following particulars:

1. His signature.
2. The date, written by him.
3. His address (which is not required on National Health Insurance or local authorities' prescriptions).
4. The patient's name and address.
5. The total amount of the medicine.
6. The dose.

These prescriptions may be dispensed once only unless the practitioner states on them that they may be dispensed more than once; if he directs that they may be dispensed a certain number of times or at certain intervals they may be dispensed only in accordance with the direction. Practitioners are urged to exercise the greatest care in writing prescriptions for substances in the Fourth Schedule. If any of the particulars is omitted it will not be possible for the pharmacist to dispense the prescrip-