EDEMA III. TREATMENT

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The treatment of edema is at first directed toward correction of the causal mechanisms. These were reviewed in the first paper of this series, the clinical states in which they act discussed in the second. Since in many diseases more than one mechanism operates in causing edema, the treatment of different types overlaps. Some of the abnormal mechanisms are not wholly reversible. In such cases treatment is aimed toward symptomatic relief rather than radical cure.

GENERALIZING EDEMAS

Cardiac Edema

Cardiac edema, the most important, is also the most common and easily treated form; it is that which occurs in chronic congestive cardiac failure. The principles underlying its treatment are: (1) rest, (2) digitalization, (3) restriction of sodium salts, (4) diuresis by drugs, and (5) diuresis by water. These principles apply to forms other than cardiac edema. Their application is, therefore, discussed in detail under the present heading only.

Rest

By complete bed rest is usually meant that the patient at all times must lie quietly in bed. While bed rest is essential, in cardiac failure the rule is relaxed to greater or less degree. Adherence to complete bed rest may be quite as dangerous as the effort it seeks to avoid.

Thus the patient with congestive cardiac failure is nearly always more comfortable in the sitting or semi-sitting position than in the supine posture and will naturally assume this position. Imposition of a recumbent posture in the presence of massive cardiac edema may increase discomfort by translocating fluid from the limbs, where it may be harmless, to the body cavities, where it is dangerous. The ideal bed for the patient with cardiac failure is the so-called "cardiac" bed. This can

be adjusted from the recumbent position to one in which the patient sits upright. When this is not available, the customary hospital bed with Gatch frame can be adjusted so that the back and knees may be raised. If the patient is not comfortable in such a bed, an arm chair large enough to permit the use of bedclothes is a practical alternative. In the home an ordinary bed may be improvised to accommodate the orthopneic position by placing pillows at the back, sometimes supported by a kitchen chair and pillows under the knees. It is important to secure these improvised supports so that they do not slip and leave the patient in a position of strain.

Whatever the choice of bed and posture, it is desirable that the patient change his position, with assistance if necessary, several times a day. In general the patient is allowed to sit in a chair for one or two hours daily. Bathroom privileges are usually better permitted than forbidden, at least when such visits do not require much walking. When they do, a simple substitute is the commode, the convenience of which contrasts with mental and physical stresses imposed by the bedpan.

These relaxations of the rule of rest do not apply to the patient whose condition is the result of acute myocardial disease such as that which follows myocardial infarction, although even in this state some relaxations from total rest are desirable, e.g., passive movements of the legs and arms.

Digitalization

Digitalization of patients with chronic congestive failure is best accomplished orally. It is doubtful whether the risks of intravenous therapy, however slight, are worth-while in this condition.

The preparations used are tablets of digitalis leaf and tablets of purified digitalis glucoside. The tincture has fallen into disuse because its potency is always uncertain and the dosage subject to vast errors of measurement.

Digitalization depends on attaining within a reasonable time an adequate concentration of digitalis glucoside in cardiac muscle. Until this concentration has been attained, the full therapeutic action of the drug is not exerted. The exact dosage which will have this effect on any patient is not easily predicted. In the past it has been estimated from body weight. For an adult of average body size the present general rule is that 18 to 21 gr. of digitalis leaf should be given in divided doses during forty-eight to seventy-two hours. It may be given more rapidly if the situation demands, although in such a case the purified glucoside is probably preferable. The dosage of digitalis leaf necessary to maintain

the desired concentration of glucoside in the myocardium is about 1½ gr. per day. Larger doses are often temporarily desirable at the beginning of treatment. The final dosage level is determined by persistence of a full clinical effect without toxic manifestations. The clinical effect is gauged from symptomatic relief and a resting ventricular rate of between 60 and 80 beats per minute.

Among the various purified glucosides with digitalis action, the most generally useful is the glucoside of Digitalis purpurea, digitoxin, therapeutically just as effective as the leaf. It is sometimes preferred because it is less nauseating. It is also more useful when digitalization must be rapidly obtained. The digitalizing dose in adults is 1.2 to 1.5 mg. This amount may be given orally in divided doses over a period of twenty-four hours or, if desired, the whole may be given at one time. Oral administration of the full dose yields a therapeutic effect in about six hours, so that intravenous digitalization is rarely necessary. When an instant effect is desired, the full digitalizing dose may be given intravenously. The maintenance dose of digitoxin is 0.1 to 0.3 mg. daily and, as with the leaf, varies somewhat with the individual.

Regardless of the preparation used, it is essential that no glucoside having digitalis action be given in full dosage for a week or ten days after the last use of digitalis or other cardiac glucoside with prolonged activity.

The rapid shrinkage of plasma and interstitial fluid volume which may result from diuresis in a patient with congestive failure sometimes proceeds more rapidly than the excretion of the digitalis glucoside. The result is accumulation of the glucoside to toxic levels with the consequent manifestations of toxic action, e.g., coupling of the pulse, nausea, and diarrhea. Should this supervene, the dosage of digitalis is temporarily interrupted.

Sodium Restriction

Sodium restriction has as its aim the reduction of sodium intake below the level of average sodium loss. The principal mode of sodium intake is in the form of sodium chloride. The least stringent form of sodium restriction, therefore, consists in forbidding the addition of extra salt to that ordinarily used in cooking and in omitting salt meat, fish, or breads from the diet. This has the effect of reducing salt intake from 5 or 10 to about 3 Gm. daily. Further restriction is accomplished by forbidding the use of salt in cooking meats and vegetables. The intake is thereby reduced to between 1 and 2 Gm. Salt intake may be further reduced to less than 1 Gm. by the use of salt-free bread and butter.

A salt-poor diet is often distasteful and the cause of much complaint. However, the patient should be made to realize that such a diet is an essential part of the treatment of edema and that adherence to it will be well worth-while. Salt substitutes so far in use have been unsatisfactory. Some of them actually contain sodium and thus defeat their purpose. Others are distasteful. A few patients find that the use of a shaker containing potassium chloride adds some flavor to their food, while others find it nauseating. For those who use it, it has the advantage of stimulating water loss.

Diuretics

The most important diuretics in the treatment of congestive heart failure are the mercurials. These act on the kidney by inhibiting reabsorption of sodium chloride, thus initiating water loss from interstitial fluid. Their action is one of controlled and highly selective intoxication of tubular cells. The fears once felt that such an action might in the long run impair renal function have not been realized. Many patients have been kept in fair comfort by the frequent use of mercurials over periods of months and years.

The toxicity of mercurial diuretics is more often cardiac than renal. In spite of the millions of doses given, there is no more than a scattering of reports of severe reactions. These reactions are usually immediate and take the form of ventricular fibrillation. When distress is or has been experienced during injection of the drug, the injection should be stopped. Any later similar medication should be given intramuscularly or rectally rather than intravenously. It has been suggested[1] that magnesium sulfate administered intravenously will prevent the toxic myocardial action of the mercurials if given just before the injection of the diuretic.

The most satisfactory and least irritating mercurials in present use are those which combine an organic mercurial compound with one of the xanthines. These are usually made up so that the therapeutic dose is about 2 cc. The smallest effective dose (0.25 to 2 cc.) is given intramuscularly or intravenously. When given intravenously it is preceded by a test dose of 0.25 cc. The injection is always made slowly, taking about three minutes. It is repeated every three to five days according to need. The drugs may be safely given over long periods if necessary.

Ammonium chloride and ammonium nitrate in doses of 30 to 90 gr. (2 to 6 Gm.) daily are given either alone or in conjunction with mercurials. These salts acidify the urine, thus causing sodium and water loss. They thereby add to and potentiate the effect of the mercurial. They are most palatably given as enterically coated tablets. However,

the contents of the tablets are sometimes not absorbed, and the expected effect is not obtained. In such cases the salts may be given as elixirs. The use of the acidifying diuretic salts may be continued over long periods.

The xanthine compounds, although possessed of some diuretic action, have little significant effect in the treatment of edema as such. They are used in the treatment of congestive failure for their other activities.

Water

The dictum that water is the best diuretic has been revised in recent years and supplemented by convincing clinical study.[2] This represents a reversal from the view that edema should be treated by water restriction. It is a correlation of clinical treatment with physiologic principles.

At the least, provision of water *ad lib.* increases the patient's comfort and, as long as sodium is restricted in the diet, cannot increase edema. Schemm[2] goes far beyond this and utilizes the chloride loss caused by water diuresis. His regime for the treatment of edema, which applies principally to cardiac edema, has as its basis the administration of from 6 to 8 liters of water daily. The exact amount given and the manner of its administration depends on the condition of the patient. It is difficult to give all of it orally, although as much as possible (2 to 5 liters) may be given hourly as glasses of water acidulated by addition of a few drops of dilute hydrochloric acid. The deficit is made up in an intravenous injection of 5 per cent glucose in water.

This regime is accompanied by severe sodium restriction, the degree of which is gradually relaxed as edema lessens. It is supplemented by routine use of one of the acidifying diuretic salts.

It should be noted that water diuresis permits the kidney to excrete substances which might otherwise be retained, so that such treatment not only washes out salt and water but also tends to relieve nitrogen retention due primarily to cardiac failure.

Nephritic Edema

To the extent that the edema of acute hemorrhagic nephritis is inflammatory and due to local vascular or renal glomerular injury, it is not amenable to specific treatment.

The edema of acute nephritis of insidious onset may be considered the same as that of the nephrotic stage of chronic glomerulonephritis into which it insensibly merges.

The principles of treatment of nephritic edema are: (1) sodium restriction, (2) administration of adequate dietary protein, and (3) diuresis by acidifying salts and plasma proteins.

The method of sodium restriction in nephritic edema is the same as that described for cardiac edema.

Protein is given to the patient with nephritic edema in an amount sufficient to establish a normal intake (1 to 1.5 Gm. per kg. daily). This amount of protein is supplemented by an amount which compensates for that lost in the urine and by a further supplement which makes up for any protein deficiency established previously by protein deprivation. The total dosage given adults should not exceed 2 Gm. per kg., and it is usually desirable to give rather less than this. While a high protein diet may compensate for urinary loss and previous protein starvation, it cannot be expected to correct that part of the hypoproteinemia which reflects the underlying renal lesion.

Some of the protein intake may be made up with amino acids given orally or intravenously, although in most patients suitable dietary protein is both cheaper and more palatable. The amino acids have their principal but rare application in the treatment of the hypoaminoacidemic crises of nephrosis. Here they specifically restore the temporary deficit of blood amino acid. It should be recognized that the amino acids have no specific effect on the course of protein metabolism.

Among the drug diuretics only the acidifying salts have proved useful in nephritic edema. Their application lies largely in their promotion of sodium loss, thus supplementing the dietary regulation of sodium intake.

Intravenous injection of a sufficient amount of osmotically active colloid causes temporary diuresis in patients with nephritic edema. Thus acacia has been widely used but more recently discarded in favor of plasma and serum albumin. Intravenous injection of plasma or of the much more expensive serum albumin results in temporary diuresis and is therefore useful when edema has advanced to a dangerous or crippling degree. It does not correct the underlying disability, which is hypoproteinemia.

When proteinuria is severe and the number of urinary casts great, it is probably desirable to substitute potassium citrate for the acidifying diuretic salts. This chemical, in doses of 60 to 90 gr. daily, tends to maintain the urine at a neutral or slightly alkaline reaction, thus inhibiting the precipitation of casts within the renal tubule, while it also tends to wash out salt and water.

A few cases of seemingly intractable nephritic edema have been relieved by renal denervation. The mechanism of the effect is unknown, and this means of treatment is still experimental.

Hepatic Edema

Edema in hepatic disease is either generalizing and due to hypoproteinemia or localized, as ascites, the result of portal hypertension. In either case the provision of a high protein, high caloric diet such as that recommended by Hoagland[3] may be dramatically effective in arresting or even reversing the course of the disease.

The patient is encouraged to take at least 3600 calories daily consisting of 150 Gm. each of animal protein and fat supplemented by carbohydrate. The fat is given chiefly as milk, cream, and butter, but not as fat that has been brought to a high temperature, such as bacon. It is believed that the aldehydes and ketones formed in fat at high temperatures are injurious. The patient is given as much carbohydrate as he will take. In general, patients should double their caloric intake within a week.

Crude liver extract is given in large doses. Extracts intended for this use are now commercially prepared. The appetite often improves markedly after liver administration.

Fifty to 100 Gm. of human albumin is given intravenously. This often causes an immediate positive nitrogen balance which lasts for several weeks. This may be augmented by administering 500 to 750 cc. of plasma per week for four weeks.

Nutritional Edema

Nutritional edema responds to a diet which corrects the varied deficiencies of protein, iron, and vitamins.

Endocrine Edema

Premenstrual edema and tension states may respond to the use of acidifying diuretic salts during the ten days before the menstrual period. When this treatment is not wholly effective, injection of progesterone (5 to 10 mg. daily for three days before the period) or oral use of anhydro-hydroxyprogesterone may prevent the disturbance.

Localizing Edemas

Most of the localizing edemas result from local causes which require surgical correction. Their treatment does not enter into this discussion.

The most frequent among them are the edemas of venous origin. Thrombophlebitis is best treated during its onset by anticoagulants such as heparin or dicoumarol, which prevent its spread. At the onset, and

even in the later stages, lumbar sympathetic block may result in dramatic relief of pain and edema.

Phlebothrombosis is most commonly a complication of bed rest incidental to surgical operation. It is prevented by routine active and passive movements and massage of the limbs and early mobilization of the patient. Once it has developed, anticoagulants should be used. Ligation of the deep veins, especially of the femoral vein, is still a controversial procedure, although certainly justifiable in patients who have shown evidence of pulmonary embolization.

References

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