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Drugs used in Cardiological Practice

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It is manifestly impossible to deal with all the drugs used in cardiological practice. There are some 400 medical journals in the English language published annually, and these contain some 800 articles on cardiology, so that it is merely possible to touch on the fringe of the subject.¹

The table (Table 1) shows the commoner drugs used in cardiology, and from this one can appreciate the enormous range.

TABLE 1
DRUGS USED IN CARDIOLOGICAL PRACTICE

- A. CARDIAC FAILURE
1. Digitalis and similar cardiotonic drugs.
 2. Diuretics: (a) Mercurials.
(b) Cation exchange resins.
(c) Diamox.
(d) Theophyllene ethylene diamine.
(f) Ammonium chloride.
- B. ARRHYTHMIAS
1. Digitalis and glycosides.
 2. Ouabain (Strophanthin).
 3. Quinidine.
 4. Procaine amide.
 5. Procaine.
 6. Potassium.
 7. Mecholyl.
 8. Prostigmine.
- C. VASODILATORS IN CORONARY INSUFFICIENCY
1. Nitrates: Glyceril trinitrin.
Metamine and praeinitron.
 2. Papaverine and paveril phosphate.
- D. PERIPHERAL CIRCULATORY FAILURE (SHOCK)
- (a) L. Nor-adrenaline (Levophed).
 - (b) Mephentermine (Wyamine).
- E. HYPERTENSION
- Rauwolfia serpentina.
Hydralazine (Apresoline).
Methonium compounds (Vegolysen).
Pentapyrollidum (Ansolysen).
Veratrine derivatives.
- F. ANTI-BIOTICS
- Rheumatic fever.
Subacute bacterial endocarditis.

G. ANTIHYROID AGENTS TO LOWER METABOLIC NEEDS

- (a) Thiouracil.
- (b) Mercaptozole.
- (c) Radio-active iodine.

H. ANTI-COAGULANTS

- (a) Heparin.
- (b) Dicoumarol.
- (c) Phenylindanedione (Dindevan, Hedulin).
- (d) Tromexan.

Attention will be drawn to some of the newer drugs and to new facts concerning the older drugs such as digitalis, quinidine and the mercurial diuretics, which are still used very casually and without due respect by most practitioners.

DIGITALIS

Digitalis is undoubtedly the most valuable drug used in cardiology. When, in 1775, Withering made use of what he thought was the diuretic property of the leaves of the foxglove, he could have had no idea of the impact of this drug on the future of medicine.

Digitalis is available in a variety of forms, and it is important for the practitioner to become familiar with the use of two or three varieties at most, and to restrict himself to these particular drugs. The introduction of the purer glycosides led to the belief that these substances were less toxic and more efficacious. However, it must be stressed that digitalis substances devoid of toxic properties are also therapeutically inert.^{2a} It is necessary to have an idea of the equivalent doses of the various preparations. Table 2 is arranged to show the approximate

EQUIVALENT STRENGTHS (BY MOUTH)	
POWDERED DIGITALIS LEAF (B.P.)	1 grain (65 mg.)
TINCTURE OF DIGITALIS (B.P.)	10 minims (0.6 ml.)
⊙ DIGOXIN	0.25 mg.
⊙ LANATOSIDE C (CEDILANID)	0.5 mg.
⊙ DIGILANID	0.25 mg.
⊙ NATIVELLES DIGITALINE	0.1 mg. (1/600 grain)
⊙ DIGITOXIN (e.g. PURODIGIN, CRISTODIGIN)	0.1 mg.
⊙ GLYCOSIDES of DIGITALIS LANATA	
⊙ GLYCOSIDES of DIGITALIS PURPUREA	

TABLE 2

equivalent in regard to tablet size rather than to give the exactly equivalent dosages.

The action of digitalis has been the subject of considerable study in recent years. The digitalis drugs are the only known substances which have a direct myocardial action and actually improve the vital function of the heart in propelling blood. They increase the force of systolic contraction of the heart with a consequent rise in cardiac output. By shortening the duration of systole they allow more time for ventricular filling and heart rest, with reduction of oxygen expenditure by the heart, and a digitalised heart can thus do the same or more work with less energy utilisation.

The second major cardiac action is on the heart rate. Two mechanisms slow the heart. Firstly, small doses of digitalis act on the sino-auricular and auriculo-ventricular nodes by vagal stimulation, and this effect can be abolished by atropine or exercise. Thus the patient with auricular fibrillation who has a satisfactory rate at rest but excessive tachycardia on exertion requires more digitalis. By increasing the dose the second mechanism arises. This is an increase in the refractory period of muscle throughout the heart, especially in the auriculo-ventricular node and bundle of His. The resulting conduction defect accounts for the great value of digitalis in auricular fibrillation with rapid ventricular rate.

In the presence of failure with sinus rhythm, digitalis may improve the clinical state before there is a material reduction in heart rate, and subsequent slowing is often the result of restored compensation rather than the other way round.^{2a} It is well known that in tachycardia without heart failure, as in thyrotoxicosis or fever, digitalis is ineffective in slowing the rate.

The extracardiac actions of digitalis are unimportant. While digoxin has been shown to have a moderate but definite diuretic action, even in non-cardiac oedema,^{2a} diuresis in congestive failure is mainly secondary to improved cardiac function. Clinical improvement with digitalis often precedes any significant diuresis. McMichael^{4, 5} at one time considered that digitalis acted by producing venoconstriction and lowered venous pressure with reduction of venous return and work load on the heart, but this has not been confirmed.^{4, 5}

It is well to remember that digitalis has no effect on the contractile power of a normal myocardium and does not increase the cardiac output in normal persons.^{2a, 5} Why digitalis acts on the failing myocardium is not known for certain,

but suffice it to say that its action is dependent on cellular potassium, and that therapeutic doses increase while toxic doses decrease cellular potassium.^{2a}

There are four main indications for the use of digitalis. Firstly, nearly every case of congestive failure requires digitalis. Some can be maintained on salt restriction and diuretics, but unless there is some special reason, digitalis should be used as a routine and may prove sufficient by itself. It is of value in all phases of congestive failure from the incipient phase where the only symptom is effort dyspnoea, to advanced failure with raised venous pressure and dependent oedema, irrespective of whether the rhythm is regular or irregular. Secondly, the drug is indicated in auricular fibrillation or flutter with rapid ventricular rates even in the absence of failure. Thirdly, it is the agent of choice in cases of paroxysmal supraventricular tachycardia, when simpler measures of vagal stimulation such as carotid sinus pressure have proved unavailing. Finally, digitalis may be indicated as a therapeutic test when it is uncertain whether dyspnoea is due to congestive failure or some respiratory disease such as emphysema.

Congestive failure does not always respond to digitalis. In thyrotoxicosis, emphysema, anaemia and other "high output" failures there may be little or no improvement, and failure due to mechanical causes such as constrictive pericarditis or pericardial effusion may not respond unless in addition the myocardium is itself diseased. Digitalis is often said to be of little value in failure due to acute rheumatic carditis, but this is probably untrue.¹²

There are practically no contraindications to the use of digitalis, but it should be used with care in certain conditions. In heart block, digitalisation should be slow and the onset of a Stokes-Adam attack would indicate the need to stop the drug. In the first few days after a myocardial infarction it is possible that digitalis may precipitate ventricular fibrillation,⁶ and if it is necessary to use it for failure, quinidine should be used simultaneously. Digitalis is best avoided in paroxysmal ventricular tachycardia in order to avoid the danger of ventricular fibrillation.

Digitalis intoxication is common and is due to the very narrow margin between the toxic dose and digitalising dose.⁷ With most preparations about 60 per cent. of the toxic dose is necessary to produce a therapeutic effect, but this margin may be greater with one of the

newer glycosides called Gitalin.^{2a} This fact makes it essential to be familiar with the signs of toxicity.

Allergic idiosyncrasy or hypersensitivity rarely if ever occurs and may be discounted.

It is important to realise that the extent of failure, serum electrolyte levels and the use of other drugs such as diuretics all have some bearing on the onset of toxicity. As a rule too the more severe the myocardial disease and the older the patient, the less is the margin between the toxic and therapeutic effects.⁷

The earliest toxic effects are related to the gastro-intestinal tract. Anorexia, and later nausea, vomiting and diarrhoea, are the most frequent symptoms of overdosage.^{2a, 7} They occur whether the drug is administered orally or parenterally, and are mainly of central origin. Nausea after the first dose or two is due to gastric irritation, and is less likely to occur with the purer glycosides, especially digitoxin, but

after initial digitalisation anorexia or nausea indicate overdosage.

Central nervous system symptoms are usually early and should be enquired after in cases of nausea where the question of toxicity is in doubt. A change in personality in a cheerful individual to a morose, melancholy person is common. Headache is frequent and may be the sole subjective symptom of toxicity, while in elderly patients nocturnal restlessness, lassitude, apathy, delirium and confusion may occur. Vertigo is unusual, but may be severe enough to make an ambulatory patient bedridden. Direct questioning reveals that blurred or yellow vision or "dots before the eyes" occur in 25 per cent. of patients.^{2a}

As most of these effects may also be caused by cardiac failure or anoxia, they may be overlooked as signs of toxicity and increased doses of digitalis may actually be given!

Unfortunately too the more serious signs of

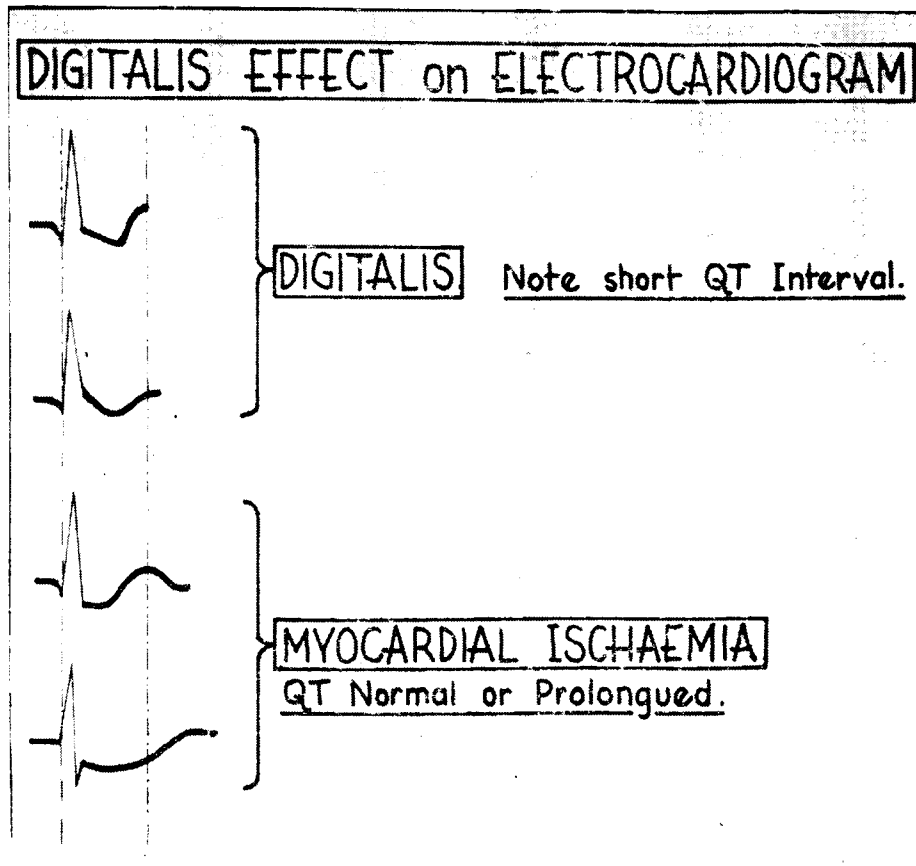


Fig. 1
(Modified from Goldberger (1953) Unipolar Lead Electrocardiography H. Kempton, London.)

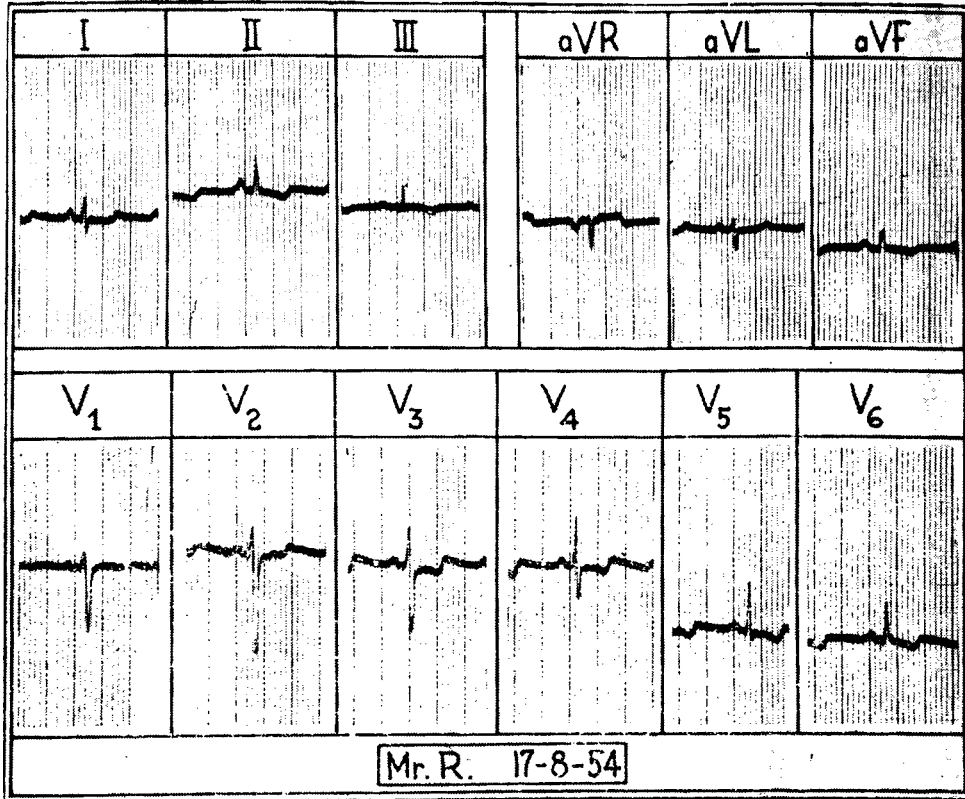


Fig. 2--E.C.G. in a 40-year-old man with a normal heart six days after digitalisation for paroxysmal auricular tachycardia.

toxicity such as arrhythmias may occur without any of the above subjective symptoms.

The most important toxic effects are the cardiac disturbances, and virtually every form of arrhythmia and conduction disturbance has been attributed to digitalis. The earliest change is in the electrocardiogram. Figures 1 and 2 show the "scooped" ST segment with inversion of the first portion of the T wave and the shortened QT interval. These changes provide no index of the therapeutic activity of the drug, nor do they indicate the presence of toxicity, and severe digitalis poisoning may occur in their absence.^{2a}

Apart from gastro-intestinal symptoms, ventricular extra-systoles are the most common indication of overdosage and indicate that 50 to 80 per cent. of a lethal dose has been given. A bigeminal rhythm in which every alternate beat is due to a ventricular extra-systole is a further stage of toxicity and may be felt at the wrist. Unidirectional or bidirectional paroxysmal ventricular tachycardia as seen on the electrocardiogram may follow, and at this stage fatal

ventricular fibrillation is imminent. Various degrees of heart block may also occur. Unfortunately these arrhythmias may only occur sporadically on straining at stool, or with anoxia or exertion, and may remain unnoticed. It is of interest that in normal individuals these arrhythmias seldom result from an overdose of digitalis. Toxicity may persist for days and sometimes even months after the drug has been stopped, especially in the presence of electrolyte disturbances.

An often forgotten danger in the digitalised patient is the use of intravenous calcium which, because of its synergistic action with digitalis, may cause sudden death.

It is now known that a profound relationship exists between digitalis and the body potassium, and that toxic doses liberate potassium from heart muscle, while therapeutic doses restore the cellular potassium.^{2a} In congestive failure there is a loss of body potassium. This loss is aggravated by such factors as mercurial diuretics and low salt diets, which also accentuate an electrolyte shift between intracellular and extracellular

compartments so that cellular potassium is depleted while the serum potassium remains normal.^{2b} The potassium loss lowers the body's threshold to the toxic action of digitalis, and explains the well known phenomenon of "post-mercurial redigitalisation." It is well recognised that for 24 to 48 hours after an injection of a mercurial diuretic, a digitalised patient may experience nausea and other signs of digitalis overdosage. This is now thought to be due to the production of a negative potassium balance despite a normal serum potassium, and can be prevented by oral administration of potassium.

A curious side effect of long continued digitalis is the production of gynecomastia in men, due to its oestrogen-like structure. Digitalis has also been said to cause intravascular thrombosis, but this is open to considerable doubt and is only a very academic objection to its use.^{8,9}

The treatment of digitalis intoxication consists of withdrawing digitalis when in doubt, restricting the patient's activities and withholding mercurial diuretics, doca or cortisone which cause potassium loss. Potassium chloride in doses of 3-5 gm. per day in divided doses should be administered. For severe intoxication 5 gm. can be given in one dose in iced orange juice.^{2b}

Procaine amide (Pronestyl) can also be used in the treatment of digitalis-produced arrhythmias and will be discussed later.

With any preparation of digitalis, digitalisation should if possible be achieved gradually, starting with a large dose, and giving progressively smaller doses, so that the possible appearance of toxic signs is not aggravated by further large doses. The oral route is suitable for at least 95 per cent. of cases and is always to be preferred to the intravenous route. With digitoxin, "single dose digitalisation" is possible, as this substance is not irritant to the gastric mucosa and is completely absorbed.¹⁰ While 1.2 mg. of digitoxin is sufficient for most patients, it is toxic for a few and inadequate for others and this method is not to be recommended. Gastric irritation prohibits the use of such large single doses with digitalis leaf or digoxin, and a digitalising dose can be spread over 24 hours or more with the avoidance of toxicity. The table (Table 3) shows the usual oral digitalising doses of the common preparations.

Intravenous digitalisation should be reserved for the few patients unable to take oral medication because of coma or vomiting due to other causes, or for cases of pulmonary oedema and some cases of supraventricular tachycardia or

PREPARATION	ORAL DIGITALIZING DOSE	DAILY MAINTENANCE DOSE
DIGITALIS LEAF	9gr. 6gr. 3gr. at 6-hourly intervals to total of ± 22 grains	1-3 grains
DIGOXIN	1½ mg. followed by 1mg. and 0.5mg. 6-hourly to total of 2-5 mg.	0.25-0.75 mg.
DIGITOXIN	1.2-2 mg. in single or divided doses	0.1-0.3 mg.

TABLE 3

auricular fibrillation. If possible this route should be avoided in patients who have had digitalis within the preceding six weeks, and if used the drug should be injected in very small doses with intervals of an hour or more to see the effect before repeating the dose. Once the patient can take the drug by mouth, intravenous administration should cease. Table 4 shows the usual intravenous digitalising doses and their times of action.

Once a digitalising dose has been given, a maintenance dose is prescribed. In the presence of auricular fibrillation an adequate dose is one which keeps the apical and pulse rates at approximately 70 per minute and which does not produce toxicity or allow too much acceleration on effort. In the presence of regular rhythm,

INTRAVENOUS DIGITALIZATION				
PREPARATION	DOSE	ONSET of ACTION	PEAK of ACTION	DURATION
CEDILANID	0.8 - 1.2 mg. (4 - 6 cc.)	20-30 minutes	2-4 hours	24-48 hours
DIGOXIN (Dilute with 9 vols. of Saline)	1.0 - 1.5 mg.	20-30 mins.	2-4 hours	24-48 hours
FOUABAIN LSTROPHANTHIN	0.25 - 0.75 mg.	5-20 mins.	1-2 hours	12-24 hours

TABLE 4

if clinical benefit is not apparent, it may be necessary to push the dose to toxic levels producing mild gastro-intestinal symptoms, and then withholding the drug for 48-72 hours, in order to know that the initial dose has been adequate.¹¹ If using digitoxin it must be borne in mind that the excretion is very slow and, particularly in elderly people, is liable to produce cumulative effects with severe intoxication. The use of digitoxin is partially responsible for the increasing incidence of digitalis intoxication.²⁰ Table 3 shows the usual maintenance doses, but each patient is an individual problem.

DIURETICS

The mercurial diuretics are so well known as to require little in the way of description. All known makes contain 40 mg. of mercury in various organic forms per millilitre, and all except Thiomerin are chemically linked with

theophylline.¹¹ They are very safe drugs when one considers the enormous number of mercurial diuretics given daily and the really insignificant number of toxic reactions and fatalities. It is probable that they act mainly by preventing renal tubular reabsorption of chlorides with resultant excretion of sodium and water. Mercurial diuretics are indicated in congestive failure not responding adequately to full digitalisation, acute pulmonary oedema and some cases of angina decubitus or nocturnal dyspnoea. In themselves they are not adequate treatment for cardiac failure,¹⁵ and are really supplementary to the use of digitalis. The only real contraindication to their use in heart failure is known severe impairment of renal function. Albuminuria and a moderately raised blood urea are almost invariable accompaniments of congestive failure and should be disregarded. A real contraindication to further mercurials is lack

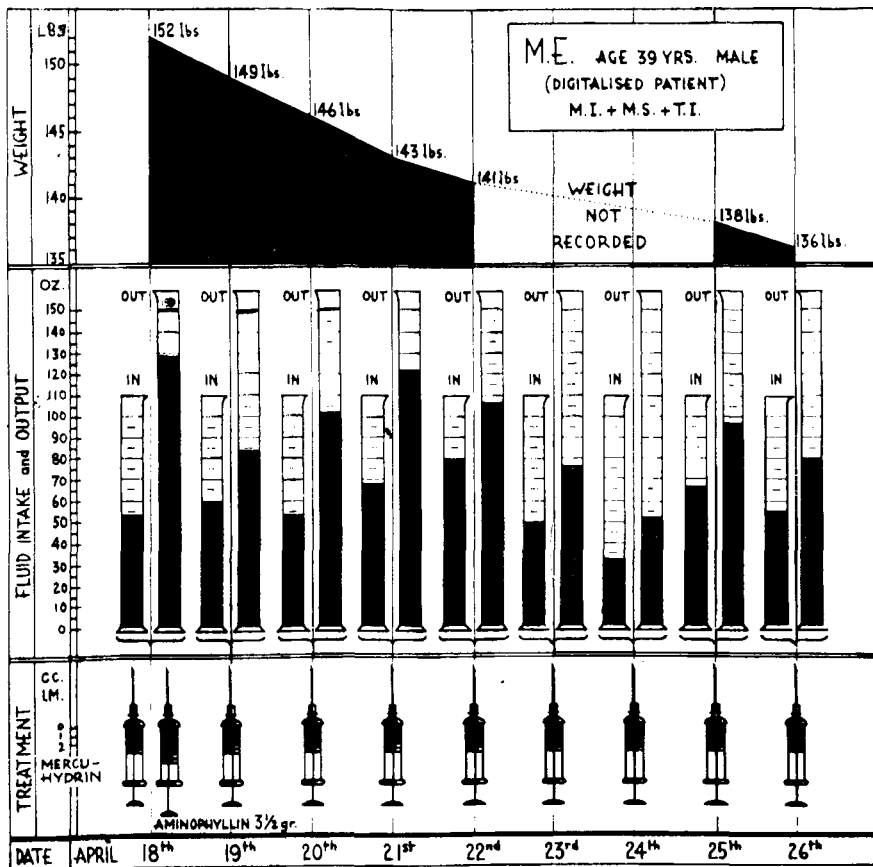


Fig. 3—This shows the weight loss and diuresis produced in congestive failure by a mercurial diuretic.

of response to two or three injections, as in these cases mercurialism may result. Intravenous administration, although more effective, is seldom advisable, as the intramuscular route is safer.^{11, 20} Mercurials should be administered in the morning so that the patient is not disturbed during the night by the diuretic effect.

An effective response is the loss of 3 lbs. body weight in 24 hours. Daily weighing provides a good indication of when the next injection is due, a gain of 3 lbs. or more suggesting the need for a further injection. The usual dose is 1-2 ml. on alternate days, but if necessary injections can be given daily or at weekly or fortnightly intervals, depending on the response. Figure 3 shows the amount of weight loss induced in congestive failure by a mercurial diuretic.

It is important to remember that frequent and prolonged use of mercurial diuretics cause a negative potassium balance, and potassium should be supplied in the form of a glass of fresh orange juice daily.

Thiomerin differs from other mercurial diuretics in that the organic mercury is combined with mercaptan. Mercaptan abolishes the toxic effects of mercury, and as the injection is relatively painless it can be given by subcutaneous injection. It is extremely effective by this route, and as it is so non-toxic can be safely administered by the patient himself without fear of mercurialism. Figure 4 shows how an intelligent patient can control his own weight and symptoms.

Another new preparation is an allylurea mercurial compound intended for oral use and

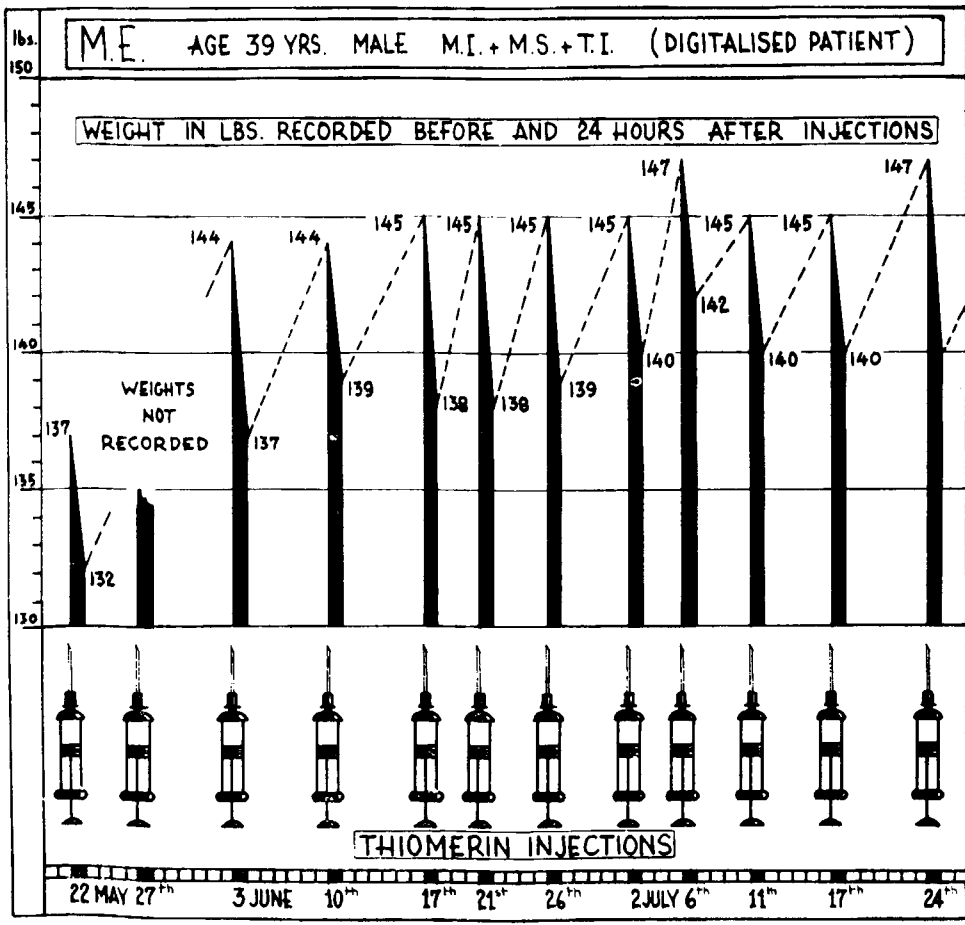


Fig. 4—The effect of self-administered Thiomerin injections on body weight in congestive cardiac failure.

known as chlormerodrin, which is available under the trade name of Neohydrin. This substance is unique among mercurial diuretics because its potency by mouth is actually as high as one-fourth of its potency by intramuscular injection, and a dose of 6-8 tablets daily achieves the same effect as 2 cc. of mercurhydrin by injection twice weekly. On this dosage at least 25 to 50 per cent. of patients develop nausea, vomiting, diarrhoea, abdominal cramps and melaena.^{17, 18} However, smaller doses such as 1 or 2 tablets daily may be effective in reducing the frequency of injections without producing these symptoms. The tablets are best administered after food and it is wise to increase the dose slowly over a period of days in order to prevent gastro-intestinal upsets. It is possible that if the total daily dose is given in a single dose after breakfast, it is more effective than in divided doses. In the patients who can tolerate it, it is a most effective agent.

Unfortunately mercurial diuretics are not free of danger. Rare cases of hypersensitivity with rigors, pyrexia, chest pain, skin rashes and even sudden death have been reported. Mercurialism may occur in patients with poor renal function and inadequate diuretic response. Rapid diuresis and dehydration may cause an increased clotting tendency and intravascular thrombosis.¹⁹

When the effect of a mercurial diuretic is inadequate, several substances may be used to enhance the effect. Of these, ammonium chloride in doses of 15 gr. three times daily for two to four days preceding injection is the most effective and prevents excessive chloride loss. The slow intravenous injection of 3½ gr. aminophylline two hours after a mercurial injection is an excellent potentiator because it increases the glomerular filtration rate.²⁰ Intravenous ascorbic acid, magnesium sulphate, dehydrocholin and pyridoxine are also said to act as potentiators.^{20, 21, 23}

When no response is obtained with a mercurial diuretic, there may be several causes. Firstly, physical exertion within 12 hours after administration may stop the diuretic effect.¹¹ Secondly, the concomitant administration of opiates, barbiturates or pethidine may diminish, delay or even prevent diuresis. The third and most important cause of mercurial resistance is disturbance in electrolyte balance.²² The importance of this cannot be over-emphasised. Chloride loss may cause hypochlorhaemic alkalosis as shown by a very low serum chloride value.

This condition can be prevented by the administration of ammonium chloride, which should, however, only be given for two to four days at a time, as overdosage of this drug may in itself cause stupor or coma and mercurial resistance due to acidosis.²² The use of a low sodium diet with mercurials may result in the low salt syndrome, especially in warm weather. This syndrome is characterised by anorexia, weakness, muscle cramps and mercurial resistance. The serum sodium is low and the blood urea is raised. The ingestion of salt or intravenous infusion of small amounts of hypertonic solutions of sodium chloride may restore mercurial responsiveness. Finally, the fact that mercurials increase potassium loss and thus cause electrolyte "shifts" has already been mentioned.

Recently we have seen the introduction of a new oral diuretic named Diamox. This substance is a sulphonamide derivative and inhibits the action of the enzyme carbonic anhydrase. This enzyme is responsible for the formation of carbonic acid from carbon dioxide and water in the renal tubule as shown in Figure 5. The carbonic acid breaks down normally into a

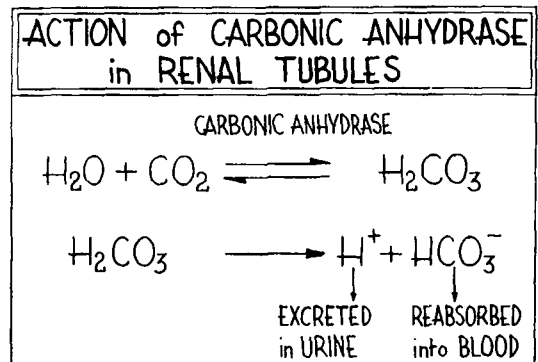


Fig. 5.

hydrogen ion which is excreted in the urine, causing urinary acidification, and bicarbonate which is reabsorbed into the blood. This reaction is prevented by Diamox, and as a result the bicarbonate is excreted, taking with it first potassium and later sodium ions and thus producing a diuresis.²¹ A mild hyperchloraemic acidosis occurs in the serum. In summary, the effect is on the serum bicarbonate, and when this has been lowered sufficiently to produce mild acidosis, the drug ceases to act. However, in cases of respiratory alkalosis with a high serum

bicarbonate such as *cor pulmonale*, a better theoretical response may be expected. Diamox is best administered in the early morning in a single dose of 5 mg. per kilogram of body weight. This usually means a dose of one to one and a half 250 mg. tablets daily. No side effects have been reported apart from drowsiness and paraesthesias of the fingers with daily doses of over 500 mg., but as a maximum response occurs with a smaller dose, such large dosage is unnecessary.²⁵ In my experience its diuretic properties are mild. Figure 6 shows a typical average response. In approximately 50 per cent. of cases the weight loss from the daily dose is under one pound.²⁵ Like ammonium chloride, however, it enhances the effects of mercurial diuretics, but cannot be used together with ammonium chloride, as they both tend to cause hyperchloraemic acidosis. It should only be given intermittently for three to five days at a time, as patients soon become unresponsive.

While it is not proposed to discuss the cation-exchange resins, their value in certain cases of chronic heart failure with no renal impairment should be remembered.^{26, 27}

ARRHYTHMIAS

Of the drugs used for arrhythmias, quinidine is the most important. It is a drug which is too often feared or incorrectly used. Its only value is to stop or prevent ectopic cardiac arrhythmias.

Among its important actions is the possibility of increasing the ventricular rate by vagal block. The auricular rate is, however, slowed and the excitability of heart muscle is depressed.²⁸

It is often said to be a myocardial poison and to reduce the contractile force of the heart, but in therapeutic doses this effect is negligible.²⁸ A significant fall in blood pressure is rare with oral therapy, but may occur with rapid intravenous injection.²⁸

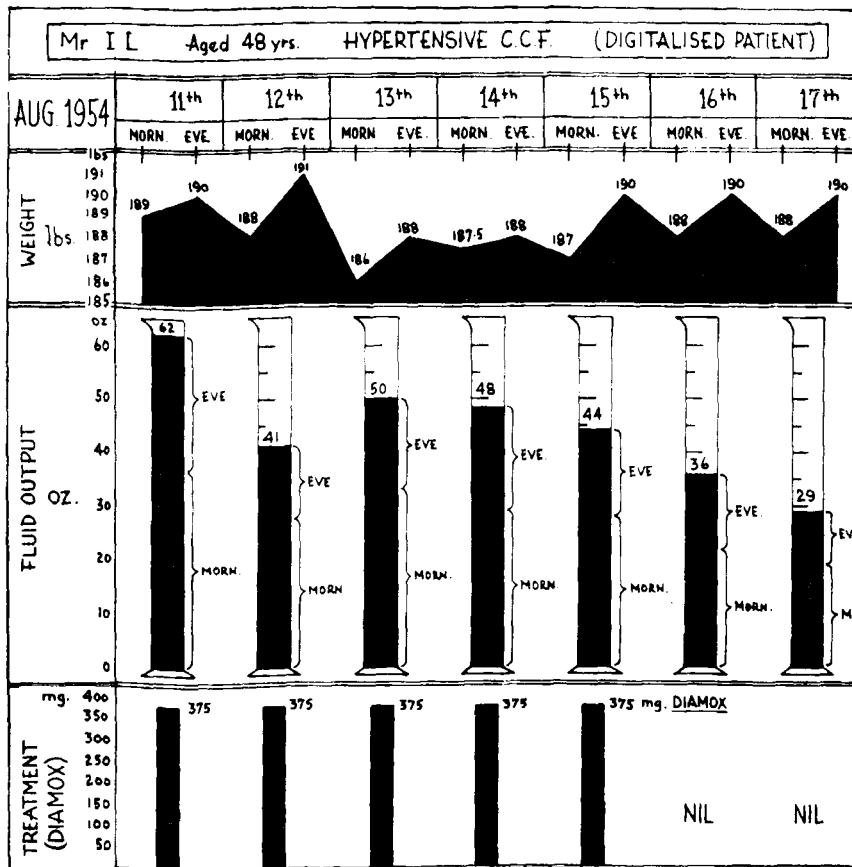


Fig. 6—This shows the typical diuretic response to Diamox.

Cinchonism in the form of tinnitus, blurred vision, urticaria and nausea may occur and should always be tested for with a preliminary dose of 3 gr. before proceeding to use therapeutic doses.

The danger of pulmonary embolism due to quinidine in reverting long standing cases of auricular fibrillation to sinus rhythm has probably been over-stressed in the past, and emboli are commoner in patients with established fibrillation than in cases of reversion.²⁹ However, in patients with a history of recurrent embolisation it is wiser to use anticoagulants for two weeks before using quinidine.³⁰ Sudden death due to ventricular standstill or ventricular fibrillation has been reported, but must be very rare.³¹ Even considering these dangers, quinidine is a reasonably safe drug if properly used. In auricular fibrillation or flutter it is advisable to digitalise the patient before using quinidine, which may cause a dangerous increase in ventricular rate if used alone; and when using doses in the neighbourhood of 45 gr. or more daily, frequent electrocardiograms are advisable. An increase of 50 per cent. in the width of the QRS interval over the pre-treatment measurement is an indication to stop quinidine therapy.^{28, 30, 31}

Quinidine therapy is of no value unless the arrhythmia is either stopped or prevented. A small maintenance dose of quinidine in cases of recurrent paroxysmal tachycardia is useless unless it is sufficient to prevent further attacks.

A common dosage schedule is to give 6 gr. of quinidine sulphate every two hours for five doses to stop an arrhythmia. If unsuccessful, 9 gr. every two hours for five doses can be given over the next two days. Bigger doses require electrocardiographic control. Phenobarbitone (1 grain) one hour before the first dose and amphotel with each dose help to prevent nausea.

For prophylaxis of arrhythmias or ectopic beats, 6 gr. four times daily are usually necessary and can be continued indefinitely without harm.³¹ Smaller or larger doses may be necessary in individual patients.

Should parenteral quinidine be necessary, it is probably better to use Pronestyl (procaine amide). This drug has essentially the same physiological effects and dangers as quinidine, but does not cause cinchonism and is much less effective than quinidine in the treatment of supraventricular tachycardia. Prolonged oral use has been known to cause agranulocytosis.³² Unlike procaine, it is stable in the body and in

therapeutic doses has no convulsant action. It is completely absorbed from the gastro-intestinal tract. By mouth the usual dose is 1 gm. (4 x 250 mg. tablets) followed by 0.5 to 1 gram every three to six hours, but in ventricular tachycardia or in a supraventricular tachycardia larger doses such as 1.25 grammes at once and 0.75 grammes two hourly till normal rhythm intervenes are necessary. The total daily dose is usually from one to five grammes.

For parenteral administration the safest route is probably the intramuscular injection of 1,000 mg. Intravenously, 50 mg. can be injected every two minutes, with blood pressure readings before each injection. If the pressure falls at all, the interval between injections should be lengthened to 5 or 10 minutes or the drug should be stopped. The total intravenous dose should not exceed 1,000 mg. The peak effect of an intravenous injection occurs in four minutes.^{2c}

Finally, it is worth mentioning briefly the subcutaneous injection of 1-2 mg. of Prostigmine or 5 to 20 mg. of mecholyl for the treatment of obstinate paroxysmal tachycardia. Intravenous use of 15 mg. of acetylcholine may also be of value.³³ All these agents require caution and the necessity of keeping a syringe charged with atropine ready in case of toxic effects.

Acknowledgments

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