antigen-induced D.N.A. synthesis in in-vitro cell cultures. This is indeed suggested by the experiments of Dutton and Eady (1964), who showed in-vitro antigenic stimulation of spleen cells of rabbits immunized intravenously to heterologous serum proteins and therefore likely to have produced an antibody response but little or no delayed hypersensitivity. Stimulation of mesenteric node lymphocytes by G.F. III in adult coeliac patients could then reflect merely the presence of precursors of antibody-forming cells; moreover, the presence of such cells might be expected because antibodies to G.F. III are known to be present in some patients (Taylor *et al.*, 1964).

On the other hand, the weight of evidence is that stimulation of lymphocytes by antigens in vitro correlates much more closely with the cell-mediated immune response than with the antibody response (Oppenheim, 1968), and our results could alternatively be interpreted as showing localized delayed hypersensitivity in the intestine.

So far as is known, the cell-mediated immune response in man is always generalized (as was shown for purified protein derivative in our experiments when peripheral blood, axillary node, and mesenteric node lymphocytes all responded to antigen in vitro). But some degree of localization may be found in experimentally sensitized guinea-pigs (Oppenheim, Wolstencroft, and Gell, 1967; Dineen, Ronai, and Wagland, 1968; Oppenheim, 1968), and it is possible that this also may occur in man.

If adult coeliac patients do have delayed hypersensitivity to gluten, manifested only or predominantly in the intestine, it still seems unlikely that this could be the primary aetiological factor. It is difficult to believe that such a response in the gut could initiate the disease in childhood and yet remain localized during adult life. Furthermore, the evidence that relapse may be induced by autoclaved G.F. II (Frazer *et al.*, 1959) and by ultrafiltrates of gluten digests (Krainick and Mohn, 1959), which are unlikely to be antigenic, suggests that the primary mechanism of the toxicity of gluten is probably not immunological. Delayed hypersensitivity to gluten is more likely to be a secondary phenomenon, arising as a consequence of a primary mucosal lesion allowing abnormal access of antigenic gluten fragments to immunologically competent cells in the gut

wall; a suggestion that could also explain the production of antibodies. Nevertheless, a chronic delayed hypersensitivity reaction thus established could perhaps aggravate the primary mucosal lesion.

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Medical Memoranda

Termination of a Tachyarrhythmia by Paired Pacing

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The technique of using paired impulse stimulation of the heart was initially reported by Lopez, Edelist, and Katz (1963). They showed that the leading and trailing edges of a long-duration impulse caused electrical depolarization of the heart of dogs. When the duration of the electrical impulse was of critical length, the second depolarization occurred when the heart was incapable of mechanically responding, though it could still respond electrically. As a result of this it was found that the refractory period of the heart could be prolonged and therefore the ventricular rate decreased.

Later it was found that this long-duration impulse could equally well be replaced by a pair of very short-duration impulses separated by a critical interval (Pickers, 1969). The critical interval between the first and second impulses varies according to the ventricular rate of the heart to be paced and is best found by experiment. An ideal method of finding this

critical time interval is to monitor the right ventricular pressure via a hollow electrode catheter. This is not always possible, however, but very close observation of the electrocardiogram on an oscilloscope provides a reasonable compromise.

If the time interval between the first and second impulse is too short, the second impulse will arrive during the absolute refractory period and so will have no effect. If the time interval is too long, both impulses will cause ventricular contractions and serve only to increase the tachycardia.

The technique of paired pacing need not only be confined to pacing the ventricles. In the presence of normal A-V conduction paired pacing can be used to stimulate the atria and so reduce the ventricular rate. Nevertheless, as the A-V node is still refractory from the first impulse, the second of each pair of atrial depolarizations fails to pass through it. Because of this, the decrease in ventricular rate is unaccompanied by electroaugmentation. This situation is in effect an electrical 2:1 A-V block. The advantage of this technique is that during paired pacing of the atria the atrial contribution to ventricular filling is maintained.

A disadvantage to the technique of this kind is that the second of each pair must be delivered at about the time of the

most vulnerable period of the cardiac cycle. It has, however, been found that the lowest threshold producing ventricular fibrillation was 30 times the pacing threshold (Frommer, 1965). This provides a reasonable margin of safety.

The theoretical advantages of paired pacing to terminate a tachycardia are that most tachyarrhythmias of any origin can be controlled, even those induced by toxic doses of drugs (Braunwald, Gay, Morrow, and Braunwald, 1964). Paired pacing also increases myocardial contractility, resulting in an increase in intraventricular pressure. It has also been shown that during paired pacing there is an increase in coronary blood flow (Katz, 1965).

CASE REPORT

A 66-year-old widow was admitted to the cardiology unit of Groby Road Hospital, Leicester, on 5 July 1968 suffering from recurrent Stokes-Adams attacks, having been referred from a local general hospital.

In 1965 she developed recurrent bouts of syncope, and electrocardiograms taken at that time showed sinus rhythm and bouts of atrial tachycardia. She was treated with digoxin. After this she went into atrial fibrillation with complete heart block. Treatment with various drugs resulted in little improvement, and over the previous 18 months she had been incapacitated with recurrent Stokes-Adams attacks.

Her family history showed that a sister was said to have died of a myocardial infarction complicated by heart block and that her father died from a cardiac arrhythmia. Her brother also had a cardiomyopathy, which had been complicated by transient heart block.

On examination she was in a critical condition, having repeated Stokes-Adams attacks. The electrocardiogram showed complete heart block with multifocal ventricular extrasystoles, atrial fibrillation, long periods of cardiac standstill, and bouts of recurrent ventricular tachycardia. She was also in very severe cardiac failure. She was immediately taken to the cardiac catheterization room and a unipolar catheter electrode passed into the right ventricle. As soon as pacing started, ventricular fibrillation occurred, and this was abolished with a single D.C. shock. Her heart was extremely irritable, numerous multifocal ventricular ectopics competing with the paced beats, and she was therefore paced with a demand pacemaker.

Propranolol and quinidine were given to suppress the ectopics, but in the next two days she had eight separate episodes of ventricular fibrillation, all requiring D.C. shock. She subsequently required a lignocaine drip, quinidine, and propranolol to ensure stable pacing. Finally the ectopics were suppressed by propranolol 40 mg. q.d.s. and quinidine sulphate 200 mg. q.d.s.

Despite several repositionings of the pacing catheter the threshold was always rather high, and it was for this reason that she did not have a pacemaker implanted. She was finally discharged with an external pacemaker of our own design. Antiarrhythmic drugs were eventually withdrawn, and stable pacing appeared established.

On 25 August she was referred back to this hospital because of breathlessness and Stokes-Adams attacks, and it was noted that she was again having frequent ventricular ectopics. These were initially suppressed by a lignocaine drip, but only five days later she started to have bouts of repetitive ventricular tachycardia with a heart rate of 140 beats a minute. At this stage she was also having occasional bouts of ventricular fibrillation (Figs. 1 and 2), and these were terminated by external cardiac massage.

Lignocaine, procainamide, propranolol, and I.C.I. 50172 failed to control the ventricular tachycardia. She was taken to the catheter room and the position of the catheter electrode was found to be satisfactory.

Increasing her pacing rate up to 160 beats a minute failed to control the recurrent bouts of ventricular tachycardia, and at this

FIG. 1.—Showing ventricular fibrillation/tachycardia.

FIG. 2.—Showing results of fixed-rate pacing.

stage she was in a very low output state. A paired pacemaker was then attached to the catheter electrode and complete control of tachycardia was achieved with a heart rate of 120 beats a minute. Her condition immediately improved with a satisfactory increase in cardiac output.

After 48 hours it was possible to disconnect the paired pacemaker and revert to fixed-rate pacing, the ectopics having been eliminated by propranolol 50 mg. q.d.s. At this stage her fixed-rate pacemaker could be set to deliver 85 impulses a minute.

She was discharged two weeks later and since then has been pacing regularly without ectopic competition.

COMMENT

In view of this patient's family history it is likely that her heart block is secondary to a cardiomyopathy. Patients with heart block secondary to a cardiomyopathy are often difficult to pace because of cardiac irritability, and this proved to be the case with this patient. Stable pacing in some cases can be maintained only by the administration of large doses of propranolol.

Patients with complete heart block and slow ventricular rates not infrequently have Stokes-Adams attacks as the result of bouts of ventricular tachycardia, the heart rate rising sometimes to over 300 beats a minute. The bouts of ventricular tachycardia, however, are usually suppressed by pacing. In

FIG. 3.—Showing paired pacing. Paper speed 50 mm./sec.

this patient it was not possible to control the ventricular tachycardia by increasing the rate of pacing or by the use of antiarrhythmic drugs, even in large doses. D.C. countershock would not have been effective, as the ventricular tachycardia was repetitive.

Paired pacemaking was immediately effective and certainly life-saving in the present case.

Fig. 3 shows the effect of paired pacing. The pacing impulse has been intensified for clarity.

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