seem to appear rather late in the development of this disorder, for these antibodies were not detected in parietal cell antibody-positive individuals with hydrochloric acid in their gastric juice and in only 13 out of 50 parietal cell antibody-positive subjects with achlorhydria. Because we think that parietal cell antibodies are an earlier and more frequent symptom pointing to the possible development of pernicious anaemia than intrinsic factor antibodies we consider the detection of the latter antibodies of little value as an early diagnostic procedure.

Some years ago we stated that the method for the detection of parietal cell antibodies is a valuable test for selecting those relatives of patients with pernicious anaemia who run the risk of developing this disease.[3] Dr. J. H. Dagg and colleagues (10 September, p. 619) have shown that this method also can be used for the detection of latent pernicious anaemia in patients with iron-deficiency anaemia. On the basis of the evidence available at present we like to think that the method for the detection of parietal cell antibodies should be employed as a routine procedure in all conditions frequently associated with the occurrence of these antibodies. Parietal cell antibody-positive individuals should be investigated for the presence of hydrochloric acid in their gastric juice, and when they are found to be achlorhydric the intrinsic factor secretory capacity of their gastric mucosa should be examined. If they lack intrinsic factor they should receive prophylactic treatment with vitamin B_{12} before a deficiency of this vitamin may lead to irreversible neurological complications.—We are, etc.,

K. TE VELDE.
PH. J. HOEDEMAEKER.
G. J. P. A. ANDERS.
A. ARENDS.
H. O. NIEWEG.

Departments of Medicine,
Pathology, and Human Genetics,
State University,
Groningen, The Netherlands.

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SIR,—It is fascinating to watch the unfolding of clinical phenomena which have been recognized for many years. The absorbing study of immunology has provided much material for thought and some of the solutions.

Forty years ago in general practice one attempted to treat iron-deficiency anaemia accompanied by histamine-fast achlorhydria with hydrochloric acid. One also tried the effect of hydrochloric acid in persistent cases of simple anaemia. The results in both cases were mixed, but some responded in each. Later stomach extract and then cyanocobalamin became available, and an effective treatment for pernicious anaemia was in our hands. The temptation was to use it in cases of persistent simple anaemia to observe the clinical effect. This was wrong, not only in making subsequent diagnosis more difficult but because it evaded tests which were available for diagnosis—for example, blood examination, Rehfuss's meal, and sternal puncture.

The article of Dr. J. H. Dagg and others (10 September, p. 619) interested me deeply, and I wonder how far it is necessary in general practice to submit one's patient to such particular examination as they have done to theirs in the detection of a latent pernicious anaemia. For example, I have made it a practice when a patient with a family history of pernicious anaemia develops iron-deficiency anaemia to arrange a blood examination, and if necessary a test for histamine-fast achlorhydria. If both tests are normal I still give cyanocobalamin and find a good clinical response in an improvement in the anaemia.

Now that autoantibody to gastric mucosa, probably genetically determined, has been discovered and can be measured, does it affect treatment to know whether it is present or not?

One has recognized that some cases of apparently simple anaemia, which have given normal results to tests for pernicious anaemia, have responded to cyanocobalamin. Dagg *et al.* state that "patients with iron-deficiency anaemia have an increased liability to Addisonian pernicious anaemia, and it is important to detect such iron-deficient patients at risk." As a preventive measure how far should we go? To be certain of a diagnosis one must test for histamine-fast achlorhydria, radioactive vitamin-B_{12} absorption, and serum vitamin-B_{12} levels, autoantibodies to gastric mucosa, and in spite of a normal Schilling test perhaps a search for intrinsic-factor activity in the gastric juice, as in their Case 3.

Even if a patient is diagnosed as a potential sufferer from pernicious anaemia, no action would be taken unless iron-deficiency were present. Ideally a periodic check of the haemoglobin of the families of all pernicious anaemia sufferers would be made, but it seems simpler to wait till the patient arrives with symptoms of anaemia. It might be argued that some would put up with symptoms till nerve damage was present, but would such folk be the type to turn up for a periodic check? I shall be grateful for guidance.—I am, etc.,

R. A. MURRAY SCOTT.
Lymington, Hants.

Use of Vasodilator Drug in Shock

SIR,—Shock which does not respond to blood, fluids or plasma, is sometimes described as "irreversible." In the past vasoconstrictor agents like noradrenaline and Aramine (metaraminol) have been given to such cases without benefit. The following illustrates the usefulness of a vasodilator drug in prolonged and resistant shock.

A 6-year-old child had a ventricular septal defect repaired in May 1965. This was followed by some improvement for a few months, but in January 1966 he started getting attacks of bronchitis and became progressively more breathless on exertion. He was readmitted on 24 March 1966 with signs of severe congestive heart failure with engorged neck veins, peripheral oedema, and enlarged liver. His heart was enlarged and a pansystolic murmur was heard maximally in the third and fourth left intercostal space. The diagnosis of reopened ventricular septal defect with functional tricuspid incompetence was confirmed by cardiac catheterization and cineangiocardiography. In May the ventricular septal defect was repaired with a patch, and aortic incompetence, due to a torn aortic cusp, was corrected. Following operation the right ventricular pressure dropped from 55/6 to 25/0, and the mean centre venous pressure from 23 mm. to 12–14 mm. Hg.

Post-operatively blood was transfused slowly, but after 350 ml. had been given the haemoglobin was only 66% with a P.C.V. of 34. His systolic pressure had dropped to 60 mm. Hg, and the pulse was feeble and of low volume. The extremities were cold and cyanosed. The standard bicarbonate was 17 mEq with a *p*H of 7.25, and this was corrected later by sodium bicarbonate. Further blood transfusion, intravenous epinephrine, digoxin, sodium bicarbonate, and hydrocortisone failed to improve the clinical condition. His blood-pressure was unrecordable, there was intense peripheral vasoconstriction in the extremities, and he had severe metabolic acidosis.

At this stage 1.5 mg. of Priscol (tolazoline hydrochloride) was given slowly into a vein over a period of two minutes. This resulted in dramatic improvement in the skin colour, and after a minute or two the peripheral pulses were readily palpable. The blood-pressure was easily recorded—90/60 mm. Hg—the blood *p*H improved to 7.365, the standard bicarbonate rose to 23 mEq/l., and he made an uneventful recovery.

Lillehei[1] and his colleagues have suggested that prolonged vasoconstriction is the key factor in "irreversible" shock. In the early stages of shock regional vasoconstriction occurs owing to excessive catecholamine production, and this phenomenon protects the circulation in the coronary and cerebral arteries. At this stage the administration of fluids, plasma, or blood, or the treatment of the causal factor, will relieve hypotension, but if treatment is delayed further vasoconstriction occurs and in turn causes reduced tissue perfusion. These events lead to severe metabolic acidosis, which impairs cardiac function and may result in the low cardiac output syndrome, which is a further stimulus to arteriolar and venous constriction. The arterioles become less and less responsive to catecholamines, while the venular spasm increases. The gradient between these two vascular systems causes exudation of blood in the tissues and even lower cardiac output. At this stage fluids or blood transfusion or epinephrine produce no improvement because of the intense vasoconstriction. Progressive deterioration leads on to death.

Starting with the assumption that a potent vasodilator might be used to break this vicious circle we found that tolazoline hydrochloride, with only a transient vasodilator effect, gave a most satisfactory response. Ganglion-blocking agents and dibenamine have been recommended for the same purpose, but we have not yet had an opportunity to assess their value.

I wish to thank Dr. C. G. Parsons and Mr. K. D. Roberts for permission to publish this case and for their helpful criticism.

—I am, etc.,

S. P. SINGH.
Children's Hospital,
Birmingham 16.

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