threshold and showed a 40% incidence of fetomaternal haemorrhage with a significant difference according to the site of the placenta.

Administration of anti-D immunoglobulin is routine after invasive procedures in Rh negative patients but is not appropriate for those already sensitised, in whom it would be ineffective.¹⁵ In patients undergoing intrauterine transfusions, however, fetomaternal haemorrhage may enhance maternal sensitisation. Not only might the disease be worsened in a subsequent pregnancy but also in the present pregnancy the rate of fall in fetal packed cell volume might be accelerated by an increase in maternal antibody titre, particularly after the first transfusion, when fetal erythropoiesis is generally not yet suppressed.

Precisely estimating the volume of fetomaternal haemorrhage is difficult. In patients undergoing intrauterine transfusions the Kleihauer-Betke test cannot be used because donor red cells cannot be identified in the maternal circulation. The increase in maternal α fetoprotein concentration can give a reliable estimate if fetal α fetoprotein concentration is also assayed. Possible sources of error are the estimated maternal blood volume, which cannot practically be assessed in each patient, and passage of α fetoprotein into the maternal circulation from fluids other than fetal blood, such as the amniotic fluid. This second possibility is unlikely as fetomaternal haemorrhage occurred most commonly when the site of sampling and transfusion was the placental cord insertion with an anterior placenta—that is, when the needle entered directly into the cord without any communication with the amniotic cavity. Moreover, any contribution of α fetoprotein from the amniotic fluid to the rise in maternal α fetoprotein concentration should be irrelevant as the concentration in fetal blood is more than 100 times that in amniotic fluid.¹⁶

De Silva *et al* reported that 0.28 ml of red cells produced a secondary Rh immune response in all of their 14 volunteers¹⁷; in our study the increase in maternal Rh (D) antibody concentration was clinically important when the volume of haemorrhage was greater than 1 ml. As the mean fetal packed cell volume at the first transfusion was 0.20 (range 0.08–0.31) the results were comparable. In some instances the rise in antibody titre was dramatic, and although the consequences were not important as far as the rate of fall in fetal packed cell volume was concerned, the course of the disease in a subsequent pregnancy will probably be affected.

These results also suggest that sampling of fetal

blood in patients with Rh isoimmunisation should not be routinely done for blood grouping early in pregnancy. It would be without consequence in Rh negative fetuses but might convert a mild case into a severe one if a considerable increase in maternal antibody titres was provoked by the procedure. Because fetomaternal haemorrhage can also occur in patients with posterior placentas, albeit less commonly, the risk of further sensitisation is present in all patients. The optimal time for intrauterine transfusion is the latest possible gestational age before fetal anaemia becomes severe. Other sites of sampling and transfusion can be chosen instead of the placental cord insertion, especially at the first transfusion, when fetomaternal haemorrhage would transfer only fetal cells. This policy would considerably reduce the risk of haemorrhage.

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Sensitivity and specificity of Rinne tuning fork test

G G Browning, I R C Swan

The Rinne tuning fork test is used regularly by specialists and non-specialists in patients with hearing impairments to indicate whether there is a conductive (external or middle ear) component to their deafness. Its ability to do this can be judged only by its sensitivity and specificity in detecting conductive hearing defects of various magnitudes as determined by pure tone audiometry. To our knowledge these have not been previously reported.

Methods and results

The Rinne test was done in a standard manner¹ with 256 Hz and 512 Hz tuning forks in 132 patients with

otological symptoms, before reading the referral letter, taking the history, examining the patient, or carrying out pure tone audiometry. All patients were tested by both loudness and threshold comparison methods. To compare loudness the forks were presented alternately as air and bone conduction, and the patient was asked to report which was louder. In the comparison threshold method patients reported when they no longer heard the sound by bone conduction and were then asked whether they heard it again when it was presented by air. The responses were classified as Rinne positive if the sound by air conduction was louder than that by bone conduction, Rinne negative if bone conduction was louder than air conduction, and equivocal if the bone conduction and air conduction were equally loud. Subsequently, pure tone audiometric thresholds were assessed by standard methods.²

We analysed the results from the better hearing ear (defined as better bone conduction at the frequency of the tuning fork used) to eliminate any potential need to

Department of
Otolaryngology, University
of Glasgow, Royal
Infirmary, Glasgow G4 0SF
G G Browning, MD, reader
I R C Swan, MD, senior
lecturer

Correspondence to:
Mr Browning.

Sensitivity and specificity of 256 Hz (●) and 512 Hz (○) tuning forks in detecting differences in air and bone conduction of various magnitudes

mask the other ear. The figure compares the sensitivity and specificity of a 256 Hz fork with those of a 512 Hz fork in detecting differences in air and bone conduction (air-bone gaps) by the occurrence of a Rinne negative response with the loudness comparison method. The sensitivity of the 256 Hz fork was significantly superior ($p < 0.05$). Neither the sensitivity nor specificity of either fork was increased by excluding equivocal responses. The sensitivity and specificity were not improved by combining the results of the 256 Hz and 512 Hz forks. The threshold method was inferior to the loudness comparison method in all aspects.

Comment

We concluded that the Rinne test should be carried out with a 256 Hz fork using the loudness comparison method. The figure can be of guidance as once the required magnitude of air-bone gap is decided, the

doctor can work out what percentage of patients will give a false negative or a false positive response. Few doctors would consider detecting an air-bone gap of less than 15 decibels necessary, but gaps of 20 decibels or more would be considered important as patients with such conductive impairments may benefit from an operation. Unfortunately a 256 Hz fork will detect only 69% of such gaps. If a criterion of a 25 decibel gap is set, however, 87% will give a Rinne negative (true conductive deafness) response with the 256 Hz fork. The most encouraging aspect is the test's high specificity. The chance of getting a Rinne negative response in patients without a conductive component to their impairment is less than 10%.

The Rinne test is unnecessary when there is otoscopic evidence of middle ear disease as a conductive impairment can then be assumed and pure tone audiometry will be needed to quantify it. If a patient with impaired hearing and an otoscopically normal tympanic membrane shows a Rinne negative response there is an extremely high possibility that there will be a conduction component to the impairment because of the test's high specificity. If the pure tone audiogram does not indicate a conductive defect then the position should be reviewed. On the other hand, because of the test's fairly low sensitivity in detecting surgically important defects in conduction, a Rinne positive response in these patients should be interpreted with caution.

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Chronic urticaria with angio-oedema controlled by warfarin

J Berth-Jones, P E Hutchinson, A C B Wicks, V E Mitchell

We report a case of severe recurrent angio-oedema that responded to warfarin. This was a chance observation and may have implications for the pathogenesis and treatment of chronic urticaria.

Case report

The patient, a 42 year old man, presented in March 1977 with weekly episodes of severe angio-oedema, which were unresponsive to chlorpheniramine and trimeprazine prescribed by his general practitioner. He also had essential hypertension, familial combined hyperlipidaemia, and ischaemic heart disease, having suffered his first myocardial infarction in 1975.

Treatment with H_1 receptor blocking antihistamines was continued for 18 months, during which time he suffered episodes of urticaria and angio-oedema virtually daily, at times with severe facial swelling necessitating admission to hospital. He was subsequently treated with the H_2 antagonist cimetidine combined with H_1 antagonists, subcutaneous adrenaline, danazol, and systemic steroids. Only the steroids had any effect, and the urticaria eventually became stable when he took prednisolone 12.5 mg on alternate days. Numerous attempts to reduce this dose failed.

In February 1981 he had a further myocardial

infarction, which was complicated by multiple pulmonary emboli. He was treated with intravenous heparin, prednisolone 40 mg to control his angio-oedema, and subsequently oral warfarin. He remained completely free from urticaria throughout this admission and was discharged taking warfarin, prednisolone 12.5 mg on alternate days, cimetidine, and brompheniramine.

The dose of steroid was gradually reduced to 2 mg on alternate days, and the antihistamines were withdrawn with no deterioration. In May that year warfarin was stopped and his angio-oedema returned. The warfarin was restarted and his angio-oedema again came under control. He subsequently reported that he had repeated this procedure with the same result. He continued to take warfarin alone for his urticaria until July 1983, when he was admitted to hospital for further investigation and, without being informed or his consent being obtained, was given placebo warfarin tablets. One week later he developed severe generalised angio-oedema. Warfarin was restarted, and he subsequently had only occasional mild episodes of urticaria without angio-oedema. These episodes affected small areas of the arms, legs, and trunk; were transient, lasting less than two hours; and were usually associated with a fall in the international normalised ratio to below 2.5 (full anticoagulation (international normalised ratio ≥ 2.5) was required for optimal benefit). He had two further small myocardial infarctions.

The following measurements were normal: routine haematological and biochemical variables; concentrations of Clq esterase inhibitor, factor XII, antinuclear factor, antithrombin III (by functional and immunological assay), and protein C (corrected for the effect of warfarin); fibrinolysis induced by factor XII; and results of challenges with oral aspirin, tartrazine, benzoic acid, and yeast.

Leicester Royal Infirmary,
Leicester LE1 5WW
J Berth-Jones, MRCP,
registrar in dermatology
P E Hutchinson, FRCP,
consultant in dermatology
A C B Wicks, FRCP,
consultant physician
V E Mitchell, MRCPATH,
consultant in haematology

Correspondence to: Dr
Berth-Jones.