A SIMPLE TEST FOR INTERATRIAL COMMUNICATION

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Atrial septal defect is one of the commoner congenital heart lesions. Wood (1956) found it in 18% of 900 cases of congenital heart disease that he studied. A large proportion of patients with this defect remain symptom-free for many years, but the average age of those seen by Wood was 23 years, and 84.5% were under 40, which suggests that these individuals tend to die young. Therefore it is not surprising that methods for surgical closure of the defect have now been developed, and, although the operative risks are being reduced, the physician is faced with the problem of weighing the prognosis of the natural course of the disease against the hazards of surgical correction at the present time. However, the risks and inconveniences to the patient suspected of having an atrial septal defect often begin long before surgery is even contemplated; for clinical diagnosis from physical signs, electrocardiography, and chest x-ray examination are not absolutely reliable, and more or less elaborate and potentially hazardous investigations involving cardiac catheterization and angiography are required before an accurate anatomical diagnosis can be made. These procedures are justified in patients with symptoms, but it would be a great convenience if a simple test were available that enabled the clinician to arrive at a firm diagnosis in the symptomless patient with atrial septal defect.

The present paper describes such a test, which depends upon being able to alter the pressures within each atrium separately. This produces changes in pressure differential between the two chambers, which consequently result in alterations of blood flow across any defect that may exist in the septum. As a result, alterations occur in oxygen saturation of the blood leaving the left atrium, and these can be detected by an oxymeter placed on the patient's ear.

Methods

Thirty-two patients have been studied. An oxymeter earpiece (Wood, 1950) was placed on the right ear and connected to a chopper amplifier similar to that described by Stott (1953), enabling percentage arterial oxygen saturation to be recorded continuously. The intrathoracic pressure was measured via a water-filled catheter placed in the oesophagus, connected to a Hansen capacitance manometer (Dornhorst and Leathart, 1952), while the brachial artery pressure was recorded by a second Hansen manometer (Hansen, 1949) connected via a "polythene" catheter to a fine needle inserted in the brachial artery after the overlying skin had been anaesthetized with 2% lignocaine hydrochloride.

The patient usually sat in a chair, or sat propped up on a couch or bed. A period of 10 minutes was allowed for him to become used to his surroundings; continuous recordings of arterial oxygen saturation, intra-oesophageal (intrathoracic) pressure, and brachial artery pressure were obtained. The patient was then asked to perform Valsalva's manoeuvre; this consisted in blowing a mercury column to a height of 50 mm. for 10–15 seconds. The mercury column

consisted of a standard blood-pressure machine, with a mouthpiece provided in place of the arm cuff and bellows. Following this procedure, the patient repeated the manoeuvre after exercising against two car foot-pumps. Patients who showed negative responses to the Valsalva tests were then asked to perform the reversed procedure, or Müller's manoeuvre. This consisted in inspiring against a fixed resistance to produce a negative intrathoracic pressure of 40–50 mm. Hg for 10–15 seconds. Most individuals found this a much more difficult task to perform. Lastly, the patient's legs were lifted whilst a continuous oxymeter recording was made. In three patients the test was also performed during diagnostic cardiac catheterization and the oxymeter record obtained simultaneously with the oesophageal and net intracardiac pressures, using a differential manometer system (Lee, Matthews, and Sharpey-Schafer, 1954).

Results and Discussion

A previous study of the pressures within the right atrium and "pulmonary capillary" (Lee *et al.*, 1954) has been used as the basis for the design of the present test. Right atrial and "pulmonary capillary" pressures minus the intrathoracic pressure were obtained, using a differential manometer system, and are referred to as net pressures. At rest, the net right atrial pressure was found to be 2–4 mm. Hg below the net pulmonary capillary pressure in the normal individual. Epps and Adler (1953) have shown that the pulmonary capillary pressure is almost identical with the left atrial pressure in man, so that this slight difference in pressure level is also representative of the pressure difference between the right and left atrium. Recently, Dexter (1956) has confirmed that the same pressure differences exist between the two atria in those individuals who have small atrial septal defects, but that in patients with larger atrial septal defects pressures tend to become uniform throughout both atria.

Valsalva's manoeuvre produces characteristic pressure changes in both the right atrium and pulmonary capillary (Fig. 1). Prior to the manoeuvre, the patient usually breathes in deeply. This lowers the intrathoracic pressure, which has the effect of sucking blood from the systemic venous system into the thorax, so that the net right atrial pressure rises (Fig. 1, A). During Valsalva's manoeuvre the intrathoracic pressure is raised, which impairs venous return to the heart, and the net right atrial pressure falls towards zero (Fig. 1, B).

FIG. 1.—Comparison of effect of Valsalva's manoeuvre on net right atrial pressure (above) and net pulmonary capillary pressure (below). Time in seconds. BA=brachial artery pressure. dRA=net right atrial pressure. dPC=net pulmonary capillary pressure. OES=intra-oesophageal pressure. A, B, and C=before, during, and after Valsalva's manoeuvre, respectively.

The deflection below zero seen on the atrial pressure record is due to an artifact produced by a contraction wave passing down the oesophagus affecting the differential manometer system. After Valsalva's manoeuvre the intrathoracic pressure returns to normal, and the previously impaired venous return from the now engorged systemic veins is suddenly resumed. The net right atrial pressure therefore

FIG. 2.—Effect of Valsalva's manoeuvre on arterial oxygen saturation in atrial septal defect. Abbreviations as Fig. 1. Middle line = arterial oxygen saturation (oxymeter).

FIG. 3.—Effect of Valsalva's manoeuvre on arterial oxygen saturation in patient with small atrial septal defect. Abbreviations as Fig. 1. A, at rest. B, calibration of oxymeter for ear thickness change. C, after exercise.

FIG. 4.—Effect of Valsalva's manoeuvre on the brachial artery blood pressure. Abbreviations as Fig. 1. A, Normal subject. B, Patient with congestive cardiac failure.

risers well above its resting level, and this becomes particularly marked during each phase of inspiration (Fig. 1, C). A similar series of events occurs in the pulmonary capillary, but some three to five seconds after events in the right atrium because of the circulation time through the right ventricle and lung vessels. There is not the same degree of modification by respiration as in the right atrium.

If an atrial septal defect exists, then a right-to-left shunt of desaturated blood should occur across the defect during the first few seconds after the end of the Valsalva manoeuvre, because the sudden rise in net right atrial pressure will cause a right-to-left pressure gradient across the defect. This has been found to be the case.

Fig. 2 shows a typical tracing obtained from a 24-year-old man with an atrial septal defect and moderate pulmonary hypertension. His resting arterial oxygen saturation was 89% (Fig. 2, A). Swan and his colleagues (1954) have shown by dye-injection studies in patients with atrial septal defect that, although the predominant shunt is from left to right, small right-to-left shunts also take place at the same time, due to streaming effects from the two venae cavae across the right atrium. We found that minor degrees of systemic arterial oxygen desaturation were common, and the oxymeter test confirmed that they were due to small right-to-left shunts at the atrial level. This was shown by the oxymeter response during the Valsalva manoeuvre (Fig. 2, B). At this time, when the intrathoracic pressure was raised and the net right atrial pressure was falling because of the decreased venous return to the heart, the systemic arterial oxygen saturation rose towards normal (97%). This was due to the disappearance of the small right-to-left shunt previously present. When Valsalva's manoeuvre was concluded and right atrial filling suddenly resumed (Fig. 2, C), the net right atrial pressure rose rapidly and a temporary pressure gradient was created from right to left across the atrial defect, with the result that desaturated blood entered the left atrium and the oxymeter record showed a fall in oxygen saturation below the initial resting level (81%). It will be noted that events in the oxymeter record occurred two to three seconds after the changes in intrathoracic pressure. This lag was accounted for by the circulation time from the atrial defect to the ear.

The Valsalva test was positive in all 12 patients where the diagnosis of atrial septal defect had already been proved, either by an exploring cardiac catheter entering the left atrium or by subsequent thoracotomy to close the defect. In one of these patients the test was negative at rest but positive following exercise. For this reason we made it a rule to exercise all patients in whom a negative response was obtained at rest. The patient mentioned was a boy of 7, who was referred to Dr. Raymond Daley for a cardiological opinion because of a soft systolic murmur at the base of the heart and complete heart-block. He did not complain of symptoms. Cardiac catheterization revealed a small atrial septal defect with an insignificant left-to-right shunt. The catheter tip entered the left atrium. It would seem, therefore, that if the defect is small the build-up of pressure gradient from right to left atrium is not great enough to produce a detectable right-to-left shunt following Valsalva's manoeuvre at rest. This is shown in Fig. 3, A.

The oxymeter record showed no characteristic dip in saturation following Valsalva's manoeuvre, and the record was indistinguishable from that of a normal subject. The slight dip in the tracing is thickness artifact due to congestion of the ear as the patient strains during Valsalva's manoeuvre. This was shown by an equal and opposite deflection when the oxymeter was switched to record changes in haemoglobin content only (Fig. 3, B). It is important to calibrate each record for thickness artifact in this way to avoid errors in interpretation. However, when the cardiac output is increased by exercising, then right atrial filling becomes much more rapid and a sufficient pressure gradient is created to produce a small right-to-left shunt following Valsalva's manoeuvre, with a consequent transient dip in the oxymeter tracing (Fig. 3, C).

A further 14 patients with evidence of a left-to-right shunt at the atrial level, but in whom the cardiac catheter could

not be manoeuvred into the left atrium, gave positive Valsalva tests, indicating the presence of an atrial septal defect. In three of these patients, anomalous pulmonary veins were entered by the exploring catheter. Two children with systolic heart murmurs and x-ray evidence of prominent pulmonary vessels have also shown positive Valsalva's tests after exercise. They are symptom-free and we have felt confident enough in the test to avoid submitting them to cardiac catheterization.

The Valsalva test was negative in only two cases of atrial septal defect. Both these patients had large atrial septal defects, and both had congestive cardiac failure at the time of the test. The explanation for the test's failure is shown in Fig. 4. Fig. 4, A shows the brachial artery pressure and oesophageal pressure obtained from a normal subject during Valsalva's manoeuvre. At the beginning of the strain period the brachial artery pressure is raised by approximately the same amount as the rise in intrathoracic pressure. This is due to the increased intrathoracic pressure squeezing the thoracic aorta. However, as already shown (Fig. 1), right atrial filling is impaired at the same time, so that the stroke volume soon falls, with the result that the brachial artery mean and pulse pressures also fall. By inference, therefore, a fall in brachial artery pulse pressure during Valsalva's manoeuvre indicates that right atrial filling has been impaired effectively, and that when the Valsalva is concluded it will

be followed by a sharp rise in right atrial filling pressure, so that the necessary gradient across an atrial defect will be produced.

However, in very large atrial septal defects, and also in heart failure, no fall in brachial artery pulse pressure occurs during Valsalva's manoeuvre (Fig. 4, B), and the imposed squeeze on the thoracic aorta by the rise in intrathoracic pressure produces a sustained rise in brachial artery pressure, or square wave response. Under these circumstances, it appears that Valsalva's manoeuvre either produces insufficient change in right atrial filling pressure to alter the gradient across the atrial defect, so that no reversal of shunt occurs, or the defect is so large that the two atria behave as a common chamber (Dexter, 1956), and again no alteration of shunt is produced. However, if the right atrium is suddenly overfilled by elevating the patient's legs, then a reversal of shunt will occur across the defect and the systemic arterial oxygen saturation will fall. Fig. 5 shows this; it was obtained from a man aged 20 with congestive cardiac failure. The brachial artery pressure showed variations due to multiple extrasystoles. He died four days later with ventricular tachycardia, and at post-mortem examination a large fenestrated septum primum defect was found.

An alternative method of suddenly raising the right atrial pressure in such patients is by means of Muller's manoeuvre. Fig. 6 shows the oxymeter record from a 27-year-old man who had severe congestive cardiac failure, auricular fibrillation, coarctation of the aorta, and bacterial endocarditis. A systolic and diastolic murmur was audible in the pulmonary region. Valsalva's manoeuvre (Fig. 6, A) produced little alteration in brachial artery pressure, and the oxymeter recording showed no consistent change in arterial oxygen saturation. However, when the patient performed Muller's manoeuvre (Fig. 6, B) the systemic arterial oxygen saturation fell, indicating that a temporary right-to-left shunt had been produced. The patient died one month later, and post-mortem examination revealed an atrial septal defect 2 cm. in diameter, in addition to coarctation of the aorta, a bicuspid aortic valve, and bacterial endocarditis.

The oxymeter test has been negative in the small number of patients that we have studied with left-to-right shunts from causes other than interatrial communication. In these patients no significant alteration in arterial oxygen saturation occurred following Valsalva's manoeuvre, Muller's manoeuvre, or leg raising. One patient had a ventricular septal defect. The right ventricular pressure at rest was 63/3 mm. Hg, and at no time during the tests did the right ventricular pressure rise to systemic arterial levels. Two patients had evidence of a left-to-right shunt at the atrial level; both had moderately raised pulmonary artery pressures; in one, an exploring catheter passed into an anomalous right superior pulmonary vein entering the right atrium; in the other case, neither anomalous veins nor the left atrium were entered. From the negative oxymeter study, partial anomalous pulmonary venous drainage without an associated atrial septal defect was diagnosed. The diagnosis was confirmed in the first patient at post-mortem examination when she died from congestive cardiac failure a year later. Thoracotomy was performed in the second patient, as atrial septal defect was still suspect clinically and its repair was to be undertaken. Three anomalous pulmonary veins opening into the right atrium were found. No atrial septal defect was present. Mr. Charles Bailey, of Philadelphia, who undertook the operation, successfully corrected the anomaly surgically.

Occasionally data obtained from cardiac catheterization are still insufficient to allow an anatomical diagnosis to be made. Fig. 7 shows the oxymeter record and net right atrial pressure from such a patient in whom the Valsalva test was positive and aided the diagnosis. The patient was a 34-year-old woman who had a resting arterial oxygen saturation of 92% but who became deeply cyanosed on exertion. The cardiac catheter failed to enter the left atrium, to cross a ventricular septal defect, or to enter the aorta. Pulmonary hypertension was found. On the basis of the

FIG. 5.—Effect of leg-raising on arterial oxygen saturation of patient with atrial septal defect and congestive cardiac failure. Abbreviations as Fig. 1. Top line: arterial oxygen saturation (oxymeter).

FIG. 6.—Changes in systemic arterial oxygen saturation in patient with atrial septal defect, coarctation of aorta, and congestive cardiac failure. Top line: arterial oxygen saturation. Abbreviations as Fig. 1. A=During Valsalva's manoeuvre. B=During Muller's manoeuvre.

FIG. 7.—Effect of Valsalva's manoeuvre on systemic arterial oxygen saturation in patient with pulmonary hypertension and patent foramen ovale. Top line: arterial oxygen saturation. Abbreviations as Fig. 1.

positive Valsalva test, a patent foramen ovale was suspected. She died later from congestive cardiac failure, and post-mortem examination revealed a moderate-sized patent foramen ovale in addition to changes associated with pure pulmonary hypertension.

We have little experience in the use of the oxymeter tests in patients with cyanotic congenital heart disease, but preliminary work suggests that Fallot's tetralogy may be associated with a characteristic pattern of changing arterial oxygen saturation during Valsalva's manœuvre. One possible source of confusion in interpreting results from such patients may occur from individuals with cyanosis due to lung disease. We have found that patients with cor pulmonale and central cyanosis who perform Valsalva's manœuvre alter their arterial oxygen saturation considerably. During Valsalva's manœuvre the breath-holding that is entailed is associated with a fall in arterial oxygen saturation. Following the manœuvre the arterial oxygen saturation rises again, and often exceeds the resting value temporarily. This is probably due to hyperventilation that occurs as soon as the test is completed.

Conclusion

The oxymeter tests described appear to be both simple and reliable for demonstrating the presence of an atrial septal defect or patent foramen ovale. Having established the conditions under which the tests can be relied upon, we feel that it is not strictly necessary to record either the oesophageal pressure or brachial artery pressure provided that one is careful to follow a routine to eliminate false-negative results. We therefore record the arterial oxygen saturation with the ear oxymeter during Valsalva's manœuvre at rest. If the test is negative it is repeated after exercise; if a negative response is still obtained, then the Müller procedure, followed by elevation of the patient's legs, is carried out. In this way what appears to be an extremely reliable test is available for use in the clinic, with symptom-free patients of any age suspected of having an interatrial communication. The youngest child we have studied was 3½ years old.

We have so far not encountered an incorrect response to the tests in any patient in whom the diagnosis was proved by alternative means. In addition, an atrial septal defect was demonstrated by the tests in three patients in whom catheter data were equivocal, and confirmed the absence of an atrial septal defect in two patients with anomalous pulmonary venous drainage, where atrial defects could not be definitely excluded from catheter data. Provided that balanced pressures between the right and left ventricles do not exist, the tests appear to be negative with ventricular septal defects; and the response pattern also appears to be different in the few cases of Fallot's tetralogy so far studied. We are also studying a group of normal subjects after exercise to discover whether it is possible to recognize those who have a persistent foramen ovale.

Finally, we would like to express our gratitude to Dr. Raymond Daley and Mr. Kent Harrison, who allowed us to study patients in whom they had established an anatomical diagnosis by cardiac catheterization or at subsequent thoracotomy. This information formed the main evidence that the oxymeter test was a reliable procedure for diagnosis of inter-atrial communication.

Summary

Thirty-two patients suspected clinically of having atrial septal defects have been studied by means of the ear oxymeter during the performance of Valsalva's manœuvre.

Twelve of these patients in whom the diagnosis was proved by cardiac catheterization or thoracotomy had characteristic and reproducible changes in arterial oxygen saturation during and following Valsalva's manœuvre.

If the defect was small, exercise prior to Valsalva's manœuvre was required in order to obtain a positive oxymeter response.

Fourteen further patients gave positive oxymeter responses to the Valsalva test. These patients had catheter evidence of a left-to-right shunt at the atrial level but definite anatomical proof of an atrial septal defect was lacking. One patient with pulmonary hypertension, who became cyanosed on exertion and in whom cardiac catheterization was unhelpful in locating the site of the shunt, gave a positive response to the Valsalva test. Subsequent post-mortem examination revealed a patent foramen ovale.

Five patients gave a negative response to the Valsalva test. Two of these were subsequently found to have partial anomalous pulmonary venous drainage but no atrial septal defect. One patient had a ventricular septal defect; and two patients had congestive cardiac failure associated with atrial septal defects.

In the patients with atrial septal defect and cardiac failure, Müller's manœuvre or elevation of the legs caused a fall in systemic arterial oxygen saturation, enabling the correct diagnosis to be made.

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GONADAL DYSGENESIS IN NORMAL-LOOKING FEMALES

A GENETIC THEORY TO EXPLAIN VARIABILITY OF THE SYNDROME

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Swyer (1955) described two cases with an unusual clinical picture under the heading of "Male Pseudohermaphroditism: A Hitherto Undescribed Form." Briefly, these patients showed normal height with eunuchoidal proportions, female appearance, and female genitalia. They did not develop secondary sexual characters nor did they menstruate. Their nuclear pattern was male. They had no congenital anomalies of the Bonnevie-Ullrich-Turner type. Attempts to place these two patients into one of the recognized categories of intersex appear to have failed. In the *Year Book of Endocrinology*, 1955-1956, a précis of Swyer's paper is followed by an editorial comment which confirms this dilemma.

It is our contention that these patients suffer from a variant of the syndrome of gonadal dysgenesis. We present the case report of a patient showing a similar clinical picture but with female "genetic sex" in whom the presence of dysgenetic gonads was demonstrated at laparotomy.