years later revealed a fall in the pulmonary vascular resistance to 55% of the preoperative level. This was associated with a further fall in the pulmonary artery pressure to 45 mm. of mercury.

The second patient demonstrates a slight reduction in pulmonary vascular resistance one year following operation at the time of a marked fall in the pulmonary artery pressure (to 45 mm. of mercury (Fig. 2). A study 3 years later revealed a further change in pulmonary vascular resistance to 55% of the preoperative level with no further reduction in pulmonary artery pressure. The cardiac output in this patient improved 50% in this interval.

Summary

Ten patients with pulmonary hypertension survived closure of artrial septal defects and were subjected to repeated clinical and hemodynamic assessment. Clinical improvement was noted in all as was a fall in pulmonary artery pressure. Electrocardiogram was moderately improved, x-ray varied from no change to moderate improvement and the pulmonary vascular resistance showed a late regression to approximately two-thirds of the preoperative value in three patients with severe pulmonary hypertension.

We conclude that pulmonary hypertension is not a contraindication to operation in atrial septal defect. There is long-term benefit to these patients and there is evidence from this small series to suggest a recession in pulmonary vascular resistance in the late follow-up period, even allowing for the possible errors in the measurement of this parameter.

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Discussion

Dr. Donald J. Ferguson (Chicago): Underlying the clinical phenomena which have been described by Dr. Coles are the remarkable reactions of the pulmonary arteries to the stress of hypertension. Dr. James Esterly and I have studied by electron microscopy serial lung biopsies from dogs in which pulmonary hypertension was produced by a left-to-right shunt.

(Slide) This is an electron micrograph of an endothelial cell from a normal small pulmonary artery in the dog. The particular character of this cell to which I wish to call your attention is the lack of very much visible organization in the cytoplasm. There are only a few mitochondria visible.

(Slide) The next slide shows a similar cell from a dog which has been subjected to pulmonary hypertension for a few weeks. This is a characteristic appearance of the endothelial cells, and the earliest change that we have been able to see in response to this stress. The changes here are the presence of numerous mitochondria, a rough endoplasmic reticulum, and small groups of ribosomes in the cytoplasm. There is now a characteristically enlarged Golgi apparatus present. Eventually these endothelial cells undergo degeneration, and then they all vanish, and the further process of arteriosclerosis goes on. So that to speak of the intimal lesion as intimal proliferation is incorrect.

(Slide) This shows another phenomenon which goes on after about 2 months of hypertension, and that is a migration of smooth muscle cells through the internal elastic lamina to fill up what was previously an intimal space, and eventually to occlude the lumen of some of the vessels. These cells are identifiable as smooth muscle by the presence in them of myofibrils, by numerous

pinocytotic vesicles along the surface, and by a basement membrane.

Now, if the hypertensive stress is removed, then a further change takes place. (Slide) This is a light microscopic picture of a small muscular artery from a dog which has had pulmonary hypertension for 3 months; developed partially occlusive lesions like the ones I have just shown; and then the normal connection of the pulmonary artery was reestablished, and the dog was followed for 5 years, after which this biopsy was taken. This shows a late stage of regression, or change in the intimal lesion. This material is partly collagen, partly elastin, and a few cells are left. This is probably the ultimate stage of regression. This corresponds, probably, to some of the vessels that would be seen in some of Dr. Coles' patients. (Applause)

DR. LYMAN A. BREWER, III (Los Angeles): Dr. Creech, Members and Guests: Dr. Coles has presented an excellent and timely review of atrial septal defect with pulmonary hypertension. Due to the pessimism on this subject I wish our medical colleagues could have been here to hear this excellent presentation. Pulmonary hypertension in 8% of cases of atrial septal defect is not a hopeless condition even though the mortality may be as high as 30%.

We have operated on 16 patients with pulmonary hypertension 5 of whom were under 10 years of age. Half the cases had cyanosis and heart failure and were prepared by digitalization and diuretics. Pulmonary insufficiency was treated by IPPV oxygen therapy and antibiotics, when indicated.

Although recently Viking Bjork and others have recommended hypothermia for surgery of atrial septal defects, we agree with those who believe that a more precise and permanent repair can be made with cardiopulmonary bypass. This is particularly important for large defects that need a patch for permanent closure. There has been no mortality which we attributed to the use of the heart lung machine. The bypass does not result in significant myocardial damage since our postoperative SGOT enzyme studies are similar to those for simple thoracotomy. Also there is no elevation of the SGOT levels in cases with pulmonary hypertension. The lateral intercostal approach is preferred, as it is simpler, more cosmetic and the left atrium is more dependent. If a ventricular septal defect is found, it can be repaired through the tricuspid valve. Additional exposure may be gained by a transverse section of the sternum.

Electrodes are left in the myocardium for evidence of delayed conduction or heart block and two of our patients had to have electropacing after the operation.

Postoperatively the pulmonary problem may be the most pressing. Although our experience in atrial septal defect with high pressure is limited, that with open mitral operations on patients with pulmonary hypertension is more extensive. Last year we reported the respiratory problems in 150 open mitral operations. Forty per cent of these had postoperative pulmonary problems. This was especially true if pulmonary hypertension was present. Tracheostomy and respirators have been used in the worst cases to afford adequate oxygenation, remove the secretions and relieve the patient of the work of respiration. The endotracheal tube is left in place for 12 to 36 hours while the necessity of tracheostomy is being decided. Monitoring the pH for acidosis is important for, contrary to what we heard yesterday, we believe that acidosis has an important bearing on myocardial function. The alveolar arterial oxygen gradients are helpful in determining early atelectasis while the arterial alveolar CO_2 gradients indicate embolism.

I would like to ask whether or not Dr. Coles' thesis that pulmonary hypertension is not a contraindication to surgery is always true, and whether or not there are any limitations that he would put on this operation? Thank you.

DR. J. C. COLES (Closing): I'd like to thank Dr. Ferguson for his comments.

We do not have any data to show that the organic changes in the pulmonary arterioles actually regress.

I'd like to thank Dr. Lyman Brewer for his very kind remarks. I think it extremely important that the pO_2 be kept at a reasonable level postoperatively, as Dr. Burchell and others showed a few years ago that hypoxia is one cause of an increase in the pulmonary vascular resistance that can usually be overcome.

There are contraindications to operation in pulmonary hypertensive atrial septal defect mainly in those with a cyanosis at rest, provided the cyanosis is not due to A-V shunts in the lung. By and large we are cautiously optimistic about operating on atrial septal defects with pulmonary hypertension and our referring cardiologists seem to hold a similar view. Thank you.