THE "EFFECTIVE" PULMONARY COLLATERAL BLOOD FLOW IN MAN[1]

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Anatomists have long been aware that an extensive pulmonary collateral circulation is a common feature of various types of heart and lung disease (1–5). In recent years, as the result of refinements in methods for the anatomic display of pulmonary vessels, they have been able to gain further insight into the nature and extent of the collateral circulation and to establish that many of the systemic arterial branches join the pulmonary vascular tree proximal to the pulmonary capillary bed (6–11).

Angiocardiography and observations during thoracotomy (12) suggest that these communications may transmit appreciable quantities of blood. Efforts have been made to measure the volume rate of flow through such vessels (13–17). These physiologic studies have been predominantly oriented toward the assessment of the hemodynamic burden which is imposed upon the left heart by the systemic contribution to pulmonary blood flow. In theory, a dye-dilution method could serve this purpose by providing a measure of *total* pulmonary collateral blood flow (18, 19); in practice it has been found more feasible to use the Fick principle, recognizing that this method measures only the "effective" collateral blood flow, *i.e.*, the component of the total collateral blood flow which reaches the alveolar-capillary surface of the lung to participate in gas exchange.

Only few measurements of pulmonary collateral blood flow have been attempted in either animal or man. This paucity stems from: *1*) a lack of suitable animal preparations or human subjects to whom available techniques may be applied; *2*) the inaccessibility of the collateral circulation for direct blood sampling; and *3*) the complexity of the experimental protocols and procedures which are entailed in such studies.

The largest body of data (13) is based on ingenious, but exceedingly indirect, applications of the Fick principle. During recent years, considerable insight has been gained into potential errors which attend the application of the Fick principle to the measurement of blood flow even under *ideal* experimental circumstances (20–22). The indirect applications have exaggerated these sources of error in several major respects: *1*) the use of serial rather than simultaneous sampling of the inter-related blood and gas phases; *2*) the existence of fluctuating levels of anesthesia; and *3*) the administration of 100 per cent oxygen to fix the oxygen content of pulmonary venous blood in a situation where the quantity of dissolved oxygen cannot be accurately predicted (13).

The experiments described in the present report were designed to measure "effective" rather than total collateral blood flow in man. They extend the earlier observations in several directions: *1*) the use of a more direct Fick method; *2*) the avoidance of general anesthesia; and *3*) the application of these methods to a variety of clinical states in which the existence of a pulmonary collateral circulation has been inferred or anatomically demonstrated.

METHODS AND MATERIALS

SUBJECTS

The present report is concerned with 12 subjects who had some anatomic basis for a pulmonary collateral circulation. Their anatomic abnormalities were such as to lend themselves to classification into three groups: *1*) prolonged obstruction of a major pulmonary artery, so that one lung is perfused solely by systemic arterial blood;

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TABLE I

Vital statistics and clinical description of all subjects

Subject	Sex	Age	Surface area $M.^2$	Clubbed digits	Clinical description
			Perfusion of one lung solely by systemic arterial blood		
O. B.	F	34	1.60	0	Status 11 years post ligation of left pulmonary artery
A. B.	M	71	1.65	++	Status 6 months post occlusion of left pulmonary artery by bronchogenic carcinoma
			Perfusion of one lung by both mixed venous and systemic arterial blood		
J. S.	M	42	1.69	++	Bronchogenic carcinoma of right upper lobe
J. Mc.	M	55	1.95	++	Bronchogenic carcinoma of left upper lobe
P. C.	M	54	2.13	0	Bronchogenic carcinoma of right lower lobe
J. C.	M	54	1.71	0	Bronchiectatic and cystic changes in right middle and lower lobes, 10 years after Friedlander's pneumonia
T. C.	M	53	1.93	++	Bronchiectasis of right lower lobe
J. G.	M	27	1.57	++++	Idiopathic clubbing of digits recognized in early childhood
			Perfusion of both lungs solely by systemic arterial blood		
J. W.	F	24	1.55	++++	Tetralogy of Fallot; atresia of pulmonary artery
W. Y.	M	30	1.77	++++	Tetralogy of Fallot; atresia of pulmonary artery
A. K.	F	5	0.50	++++	Tetralogy of Fallot; atresia of pulmonary artery
B. C.	M	13	1.10	+++	Tetralogy of Fallot; atresia of pulmonary artery

2) unilateral intrinsic pulmonary disease, so that one lung is perfused both by mixed venous blood through the pulmonary artery and by systemic arterial blood through the collateral vessels; and *3*) congenital absence of a normal pulmonary artery associated with either atresia of the main pulmonary artery or a truncus communis, so that both lungs are perfused solely by systemic arterial blood.

The members of the three groups are briefly described in Table I. For the sake of convenience, the patient with idiopathic clubbing of the digits is included in Group II.

GROUP I. PERFUSION OF ONE LUNG SOLELY BY SYSTEMIC ARTERIAL BLOOD

This group consists of two subjects in whom blood flow through the left pulmonary artery had been arrested; however, the cause of the obstruction, and its duration, was strikingly different in the two cases.

Subject O. B. has been described in a previous publication from this laboratory (23). In brief, she had undergone surgical ligation of the left pulmonary artery in 1947, during the course of an operation designed to close an infected patent ductus arteriosus. Her clinical course and laboratory studies were reviewed in 1949 to demonstrate the effects on ventilatory and circulatory performance of depriving a lung of its normal perfusion by mixed venous blood. These earlier observations are compared with the pulmonary function studies of 1956 in Table II, and the corresponding bronchospirometry records are reproduced in Figure 1. This table and figure are interpreted as showing that ligation of a major pulmonary artery has only slightly impaired total respiratory function and,

TABLE II

Pulmonary function studies in Subject O. B., measured two and eleven years after ligation of the left pulmonary artery

	Normal	1947	1956
Lung volumes			
Vital capacity*	100	91	99
$\frac{\text{Residual volume}}{\text{Total lung capacity}} \times 100$	25–30	27	28
Maximum breathing capacity*	100	76	100
Alveolar N_2†	<2.5	1.4	2.0
Arterial HbO_2‡			
Rest	96 ± 2	96	96
Exercise	96 ± 2	93	98
Arterial P_{CO_2}§	39 ± 2	39	39
D_{CO}‖			
Rest	14		11
Mild exercise	20		15

* The vital capacity and the maximum breathing capacity are expressed as per cent of predicted, based on previous data from this laboratory.

† Alveolar N_2 = fraction of nitrogen in the lungs after breathing pure oxygen for seven minutes.

‡ Arterial HbO_2 = saturation of hemoglobin in arterial blood, in per cent.

§ Arterial P_{CO_2} = partial pressure of carbon dioxide in arterial blood, in mm. Hg.

‖ D_{CO} = diffusing capacity of the lung for carbon monoxide determined by a steady state method (39) in ml. per minute per mm. Hg.

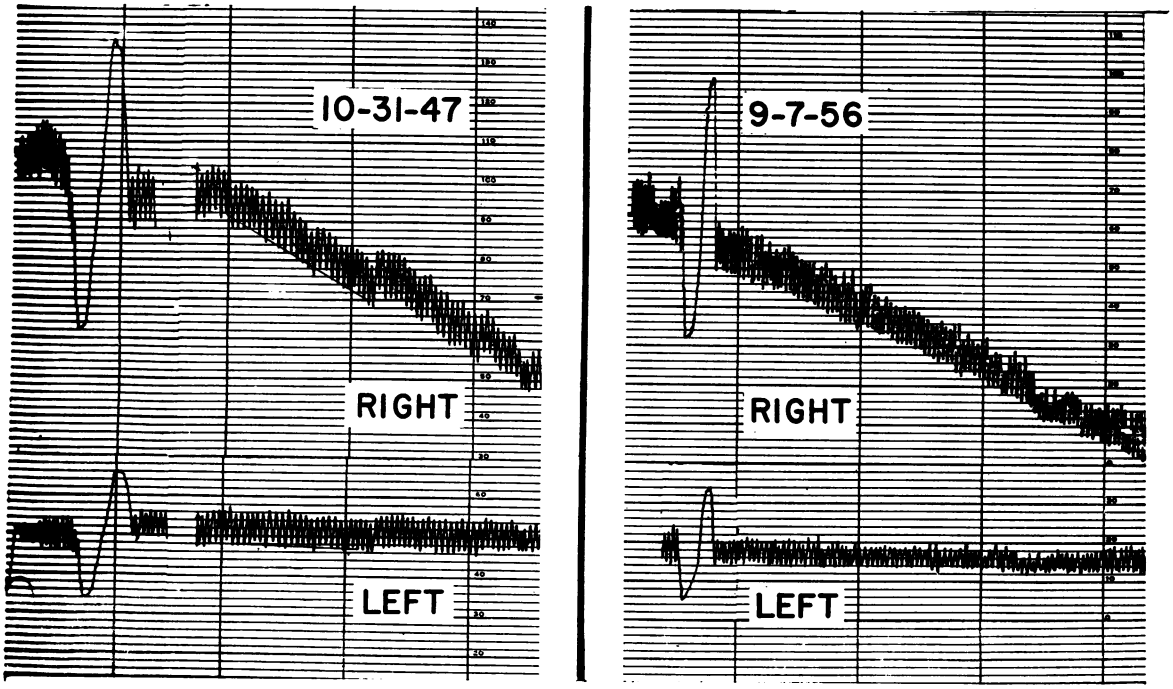

FIG. 1. BRONCHOSPIROMETRIC RECORDS OBTAINED FROM SUBJECT O. B. ON TWO SEPARATE OCCASIONS

Despite an interval of ten years between records, they are strikingly similar. In each instance, oxygen uptake by the left lung is barely perceptible.

moreover, that a stable state has persisted during the intervening 10 years.

In Subject A. B., with a circumscribed mass in the region of the left hilum, contrast substance failed to enter the left pulmonary artery during two separate trials of angiocardiography (Figure 2). At thoracotomy, the left pulmonary artery was found to be occluded by a carcinomatous mass. The duration of the obstruction was estimated to have lasted for no longer than six months.

GROUP II. PERFUSION OF A LUNG BY BOTH MIXED VENOUS AND SYSTEMIC ARTERIAL BLOOD

Each of the six subjects in this group had a clinical state generally associated with a collateral circulation to the lung. As may be seen in Table I, five of the subjects had unilateral pulmonary disease, *i.e.*, bronchiectasis, or bronchogenic carcinoma, and the other had idiopathic clubbing of the fingers and toes. Each of the three patients with bronchogenic carcinoma had a solitary circumscribed lesion, ranging from lemon (J. S.) to orange (P. C.) in size, and affecting only a single lobe; the diagnosis, in each instance, was established by histologic examination of excised lung tissue or lymph node. In the two patients with bronchiectasis, the diagnosis was established by bronchograms; in Patient J. C., an extensive collateral circulation to the affected lung was subsequently visualized at the time of right lower and middle lobectomy.

GROUP III. BOTH LUNGS PERFUSED BY SYSTEMIC ARTERIAL BLOOD

This group consists of four subjects. Their common denominator is a lack of perfusion of the lungs by mixed venous blood, and, perforce, perfusion only by systemic arterial blood.

In Subject J. W. the clinical diagnosis of Tetralogy of Fallot, with atresia of the pulmonary valve, was confirmed at autopsy. In addition, an extensive pulmonary collateral circulation, arising from the internal mammary, pericardiophrenic and intercostal arteries, as well as from the aorta was displayed by injection of plastic material into the thoracic aorta.

In the other three subjects, identical diagnoses were suggested by the clinical picture, and the data obtained during cardiac catheterization and angiocardiography; an alternative diagnosis which could not be excluded, particularly in Subject B. C., was truncus arteriosus. However, from the point of view of the present study, this distinction is unimportant since the method for estimation of collateral blood flow in such subjects is independent of the nature of the congenital malformation as long as both lungs are perfused solely by mixed systemic arterial blood.

PRINCIPLES

The Fick principle was applied to the measurement of collateral blood flow in all three groups; special protocols

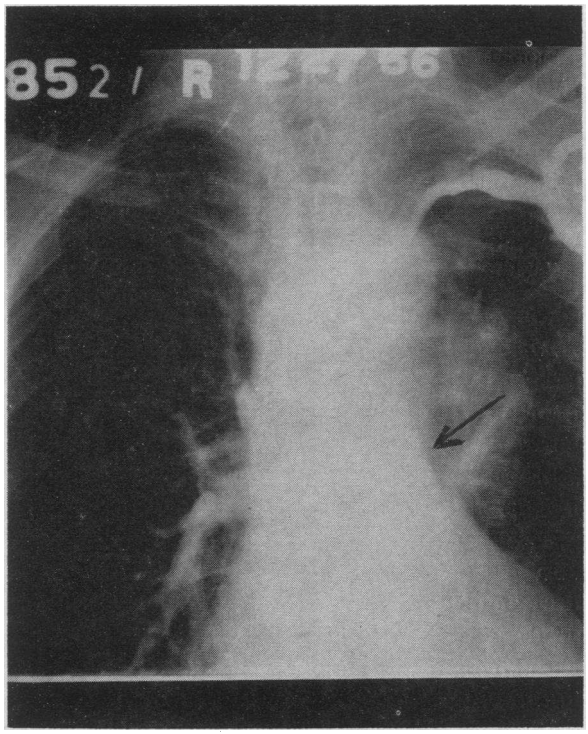

FIG. 2. ANGIOCARDIOGRAM OF PATIENT A. B.

The arrow points to main pulmonary artery, the border of which is sharply outlined by contrast substance. The left pulmonary artery is not opacified.

were required to adapt this concept to the peculiar anatomic circumstances of each group.

GROUP I. PERFUSION OF ONE LUNG SOLELY BY SYSTEMIC ARTERIAL BLOOD

Two inter-related measurements were made: *a*) the volume rate of "effective" collateral blood flow, and *b*) the fraction of total pulmonary blood flow contributed by the "effective" collateral blood flow.

a) The rate of "effective" collateral blood flow through the lung with the occluded pulmonary artery

The method used here is essentially a straightforward application of the Fick principle, entailing: *1*) the use of bronchospirometry to procure gas samples for the calculation of the oxygen uptake and respiratory exchange ratio for each lung separately; *2*) the sampling of peripheral arterial blood for the estimation of the oxygen content of the blood entering the pulmonary capillaries of the affected lung; and *3*) the fixation of the oxygen content of the blood leaving the capillaries of the involved lung by the administration of an appropriate inspired-oxygen mixture. In these broad aspects, the concepts resemble those previously applied to the measurement of unilateral pulmonary blood flow during acute hypoxia (24).

Unfortunately, this application of the Fick principle to a collateral blood flow arising from the systemic circulation is complicated, under the usual circumstances of ambient-air breathing, by the high oxygen content of the afferent blood. The consequences of this situation are illustrated for Patient O. B. in Figure 3 and the actual slopes of oxygen uptake obtained from this patient during ambient-air breathing, on two separate occasions, are illustrated in Figure 1.

The experimental approach used to circumvent this difficulty is illustrated in Figure 4. According to this figure, the lung with the ligated pulmonary artery breathes a slightly enriched oxygen mixture whereas the intact right lung breathes a low-oxygen mixture to induce systemic hypoxemia. By this device, the lung with a systemic arterial blood supply is perfused by hypoxemic blood while being ventilated by an enriched oxygen mixture. The consequences of this arrangement are: *1*) the alveolar-pulmonary capillary diffusion gradient for oxygen is increased, thereby augmenting oxygen uptake; *2*) the pulmonary arteriovenous difference in oxygen content is widened, thereby minimizing the effects of analytic error; and *3*) the hemoglobin in the blood leaving the pulmonary capillaries is fully saturated with oxygen, without unduly increasing the concentration of dissolved oxygen.

In a previous report concerned with *changes* in blood flow, the oxygen content of pulmonary venous blood was equated to the oxygen capacity of systemic arterial blood

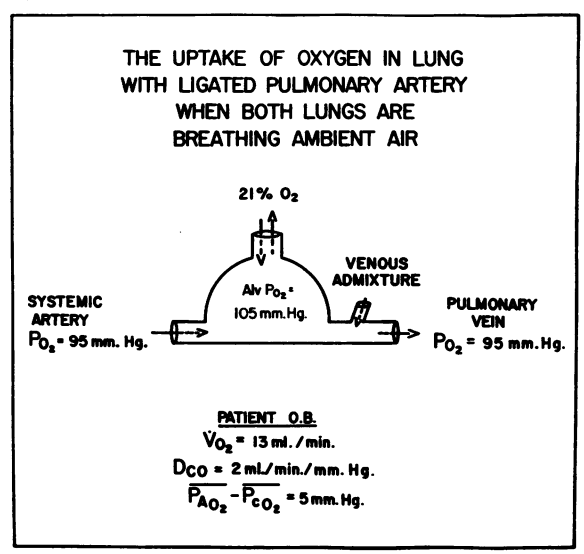

FIG. 3. SCHEMATIC REPRESENTATION OF GAS EXCHANGE IN A LUNG PERFUSED SOLELY BY SYSTEMIC ARTERIAL BLOOD WHILE BREATHING AMBIENT AIR

Since the oxygen tensions (P_{O_2}) in alveolar gas and arterial blood are quite similar, oxygen uptake ($\dot{V}_{O_2}$) is low. From a separate measure of the diffusing capacity of the lung for carbon monoxide (D_{CO}), it may be seen that the mean diffusion gradient for oxygen along the length of the capillary ($\overline{P_{A_{O_2}}} - \overline{P_{c_{O_2}}}$) is abnormally low.

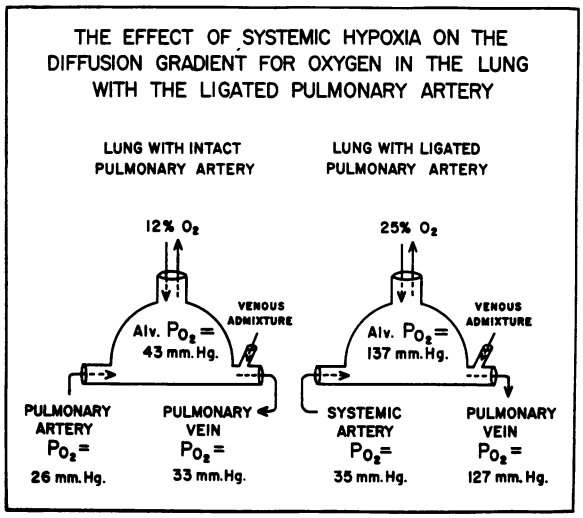

FIG. 4. SCHEMATIC REPRESENTATION OF THE EXPERIMENTAL DEVICE USED TO FACILITATE OXYGEN UPTAKE IN THE LUNG PERFUSED SOLELY BY SYSTEMIC ARTERIAL BLOOD

By ventilating the lung with an enriched oxygen mixture (25 per cent O_2) while it is perfused by hypoxemic blood (P_{O_2} equals 35 mm. Hg), suitable pressure gradients are established for the diffusion of oxygen from alveoli to pulmonary capillary blood.

(24); in the present experiments, concerned with *absolute* blood flow, the oxygen content of pulmonary venous blood was assumed to equal the oxygen capacity of arterial blood minus 0.6.[4]

b) The fraction of total pulmonary blood flow contributed by the "effective" collateral blood flow

For this calculation, a measure of the total pulmonary blood flow, *i.e.*, collateral plus pulmonary artery, is required. In this instance, total blood flow cannot be directly obtained by the Fick principle since the two lungs are perfused by blood of different oxygen contents.

Two devices were used to calculate blood flow through the intact pulmonary artery: *1*) a mixing formula, and *2*) a dye-dilution technique.

1) Mixing formula. According to the protocol outlined above for the measurement of "effective" collateral blood flow through one lung, the other *intact* lung is required to breathe a hypoxic mixture. In this circumstance, arteriovenous differences in oxygen content across the intact lung are narrowed and equilibrium between oxygen tensions in alveoli and in the pulmonary capillaries does not occur; consequently, the oxygen content of blood leaving the intact lung cannot be accurately predicted.

For these reasons, a simple mixing formula was applied to the calculation of blood flow through the intact lung; its basis is illustrated in Figure 5. In this calculation the complicating factor of venous admixture is ignored on two grounds: *a*) theoretical, since the effect of venous admixture on arterial blood oxygen content is minimal under the conditions of this experiment, and *b*) practical, since a trial correction of the calculation for venous admixture (26) in Patient O. B. failed to alter appreciably the value for the rate of blood flow through the intact lung.

2) Dye dilution. This method entailed the measurement of blood flow through the intact lung by the Stewart-Hamilton principle (19), following injection of the blue

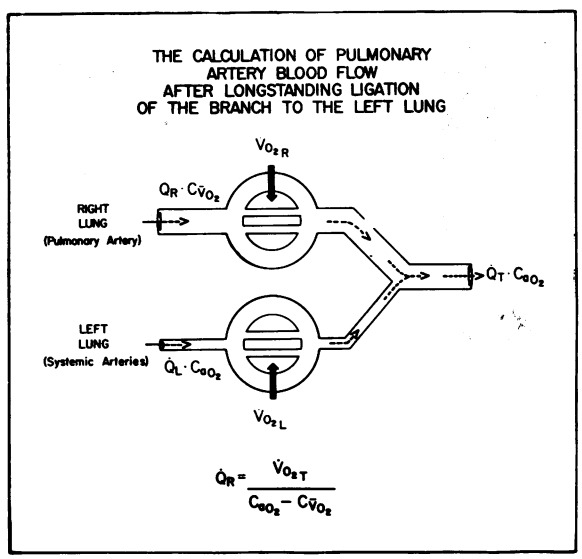

FIG. 5. SCHEMATIC REPRESENTATION OF THE BASIS FOR CALCULATING BLOOD FLOW THROUGH THE UNOCCLUDED PULMONARY ARTERY ($\dot{Q}_R$) WHILE THE IPSELATERAL LUNG BREATHES A HYPOXIC MIXTURE

Symbols are discussed in text. The final formulation for $\dot{Q}_R$ is based on the premise that the total rate of oxygen flow from both lungs ($\dot{Q}_T \cdot Ca_{O_2}$) equals ($\dot{Q}_R \cdot C\bar{v}_{O_2} + \dot{V}_{O_{2R}} + \dot{Q}_L \cdot Ca_{O_2} + \dot{V}_{O_{2L}}$). By substituting $\dot{Q}_R + \dot{Q}_L$ equals $\dot{Q}_T$, and $\dot{V}_{O_{2R}} + \dot{V}_{O_{2L}}$ equals $\dot{V}_{O_{2T}}$, the final form of the equation for $\dot{Q}_R$ is easily derived.

[4] The equation of the oxygen content of pulmonary venous blood (Pv_{O_2}) to the oxygen capacity of arterial blood minus 0.6 was empirically derived in the following way. In nine normal subjects, the Fick principle was applied to the measurement of blood flow through a lung breathing a mixture of 25 per cent oxygen and nitrogen (24) by: *1*) measuring ipselateral oxygen uptake, *2*) analyzing mixed venous blood for oxygen content, and *3*) assuming a value for Pv_{O_2} which would yield a normal ratio of right-to-left pulmonary artery blood flow, *i.e.*, 55/45. The average value for Pv_{O_2} obtained under such conditions equaled the oxygen capacity of arterial blood minus 0.6. A similar value was obtained by applying the more elaborate formulation of Cournand, Fritts, Harris and Himmelstein (25) to the same data. It is to be noted that an error in the estimation of Pv_{O_2} has little effect on the calculated collateral blood flows because of the wide pulmonary venous-arterial oxygen differences which characterize these experiments.

dye T-1824 into the main pulmonary artery. On theoretical grounds, this value will exceed that obtained by the mixing formula if: *1*) an appreciable quantity of venous blood entering the intact lung escapes oxygenation by by-passing the alveolar-capillary interface, and *2*) a collateral circulation also perfuses the unoccluded lung. The latter consideration is pertinent only to the subjects of Group II and was circumvented by selection of patients with bronchogenic carcinoma or bronchiectasis affecting only one lung.

GROUP II. PERFUSION OF A LUNG BY BOTH MIXED VENOUS AND SYSTEMIC ARTERIAL BLOOD

In order to apply a similar type of protocol to the measurement of pulmonary collateral blood flow in subjects with intact pulmonary arteries, temporary arrest of blood flow through one major pulmonary artery was effected by inflating a balloon affixed to the tip of an appropriately placed cardiac catheter (27–30). The occlusion of the right pulmonary artery by this device is illustrated in Figure 6. For the sake of visualization during fluoroscopic examination, the balloon was filled with diodrast. Also visible in this figure is the location of the bronchospirometry tube within the tracheobronchial tree.

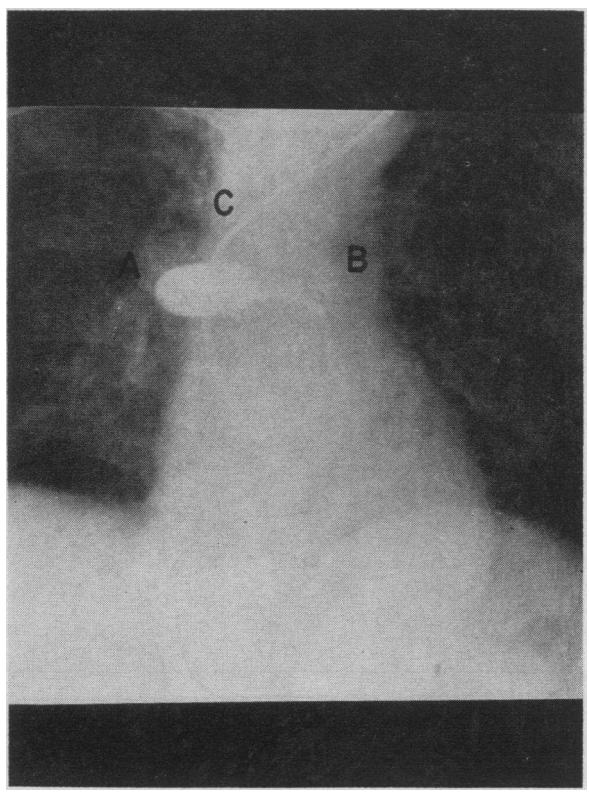

FIG. 6. A BALLOON SITUATED AT THE TIP OF THE CARDIAC CATHETER HAS BEEN INFLATED WITH DIODRAST (A) TO OBSTRUCT THE RIGHT PULMONARY ARTERY

The outline of the bronchospirometry tube is also visible with its tip (B) in the left main bronchus and its special side-arm (C) straddling the carina.

The following criteria were used as indices of complete occlusion of the artery by the inflated balloon: *1*) the cessation of oxygen uptake on the occluded side during ambient air breathing (Figure 7) and its return following deflation of the balloon at the end of the procedure; *2*) the replacement of a normal pulmonary artery pressure pulse, recorded from the lumen distal to the occluding balloon, by an undulating line (Figure 8); this line mirrored only the phasic respiratory variations, and oscillated around a pressure level of only a few mm. Hg greater than atmosphere; and *3*) the withdrawal of fully-oxygenated blood from the distal lumen.

The application of these criteria for complete occlusion of a pulmonary artery in conjunction with others previously proposed for identification of complete separation of the airways to each lung (24) led to the exclusion of six other subjects from this report.

GROUP III. PERFUSION OF BOTH LUNGS SOLELY BY SYSTEMIC ARTERIAL BLOOD

In the case of Tetralogy of Fallot with atresia of the main pulmonary artery, and in truncus communis, both lungs are perfused by systemic arterial blood. In these anomalies, anatomic observations suggest that the collateral vessels probably transport fully-*mixed* arterial blood since the systemic branches generally originate from either the descending aorta or large systemic arteries, or, in the case of truncus communis, from an unusually large vessel. In the face of such anatomic arrangements, a sample of brachial arterial blood may be considered to be identical in oxygen content and capacity to the blood *entering* the pulmonary capillary bed.

On the other hand, the hemoglobin of blood *leaving* the pulmonary capillary bed may be assumed to be fully saturated with oxygen, particularly if a slightly enriched oxygen mixture (25 per cent) is breathed. On grounds discussed in Principles for the calculation of "effective" collateral blood flow through a lung with an occluded pulmonary artery, the oxygen content of blood leaving both lungs is accepted as equal to the oxygen capacity of arterial blood minus 0.6. Also, as in the previous calculations, small errors in $P_{V_{O_2}}$ are relatively insignificant because of the wide arteriovenous differences in oxygen content across the pulmonary vascular bed.

CALCULATIONS

GROUP I. PERFUSION OF ONE LUNG SOLELY BY SYSTEMIC ARTERIAL BLOOD

a) The absolute value for "effective" collateral blood flow through the lung with the occluded pulmonary artery (Lung O)

The rate of systemic arterial blood flow through this lung ($\dot{Q}_O$) is equal to the oxygen uptake by this lung per minute ($\dot{V}_{O_{2O}}$) divided by the corresponding difference in oxygen content between pulmonary venous and systemic

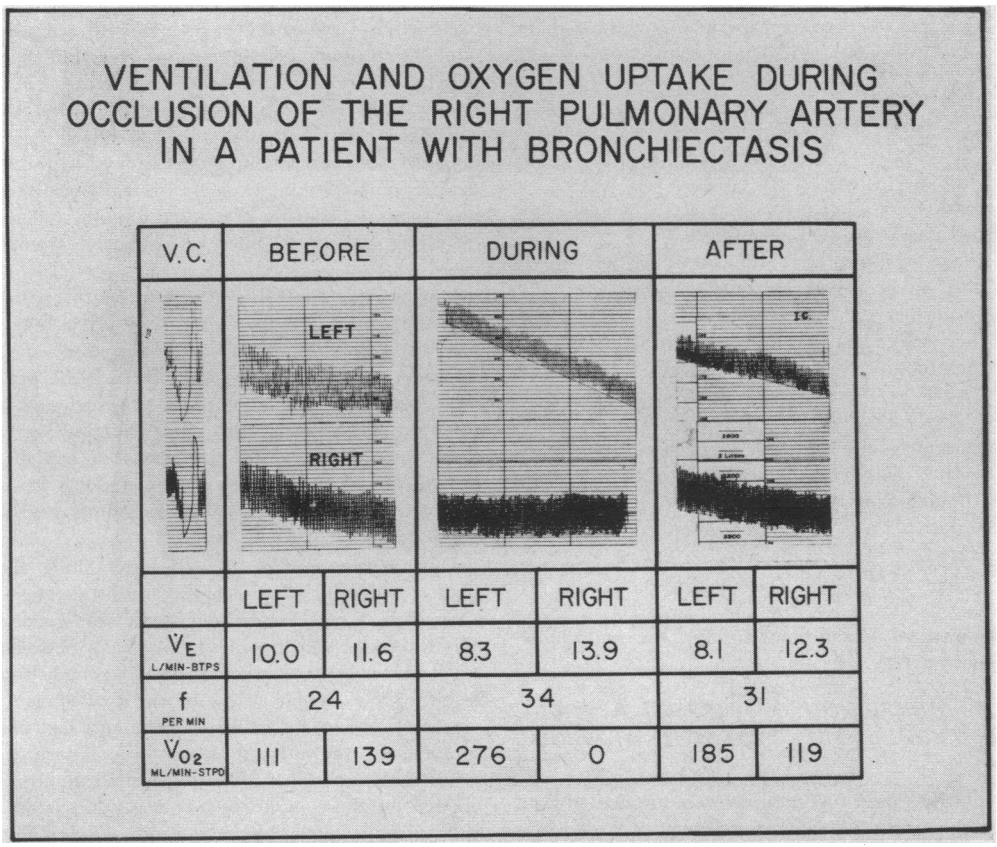

FIG. 7. SPIROGRAMS FROM EACH LUNG SEPARATELY, BEFORE, DURING, AND AFTER OCCLUSION OF A MAIN PULMONARY ARTERY BY INFLATING A BALLOON IN ITS LUMEN

During the period of occlusion, the oxygen uptake on the occluded side becomes imperceptible; following relief of the obstruction, the oxygen uptakes by each side return toward control levels. Abbreviations are as follows: V. C. = vital capacity; $\dot{V}_E$ = minute ventilation; f = respiratory frequency; $\dot{V}_{O_2}$ = oxygen uptake.

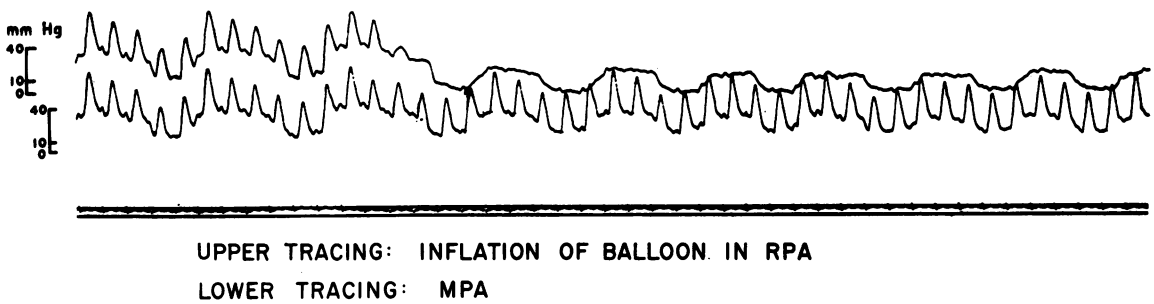

FIG. 8. PRESSURE PULSES RECORDED FROM TWO SITES IN THE PULMONARY ARTERY PRIOR TO, AND FOLLOWING, INFLATION OF AN OCCLUDING BALLOON

As the balloon is inflated, the tracing distal to the occlusion (upper tracing) loses its arterial contour and is replaced by an undulating line which reflects phasic respiratory variations; the pressure pulse in the main pulmonary artery (lower tracing) retains its usual character.

artery blood. For reasons explained under Principles, the calculation was reserved for experiments with systemic hypoxemia and utilized the following formulation:

$$\dot{Q}_O = \frac{\dot{V}o_{2_O}}{(\text{Art. } O_2 \text{ Cap.} - 0.6) - Ca_{O_2}},$$

where,

$\dot{Q}_O$ = the rate of "effective" collateral blood flow through Lung O in liters per minute

$\dot{V}o_{2_O}$ = the oxygen uptake by Lung O, in ml. per minute

Art. O_2 Cap. = the oxygen capacity of systemic arterial blood in ml. per 100 ml.

Ca_{O_2} = the oxygen content of systemic arterial blood in ml. per 100 ml.

b) The fraction of total pulmonary blood flow

The fraction of total pulmonary blood flow contributed by the "effective" collateral blood flow is expressed, in per cent, from the following relationship:

$$\frac{\dot{Q}_O}{\dot{Q}_O + \dot{Q}_P} \times 100,$$

where,

$\dot{Q}_P$ = the rate of blood flow through the unoccluded pulmonary artery.

GROUP II. PERFUSION OF A LUNG BY BOTH MIXED VENOUS AND SYSTEMIC ARTERIAL BLOOD

The calculations used for Group I were applied to data obtained in this group following temporary occlusion of a pulmonary artery.

GROUP III. PERFUSION OF BOTH LUNGS SOLELY BY SYSTEMIC ARTERIAL BLOOD

The rate of "effective" blood flow from the systemic arteries to the gas-exchanging surface of both lungs ($\dot{Q}_T$) was calculated as:

$$\frac{Vo_{2_T}}{(\text{Art. } O_2 \text{ Cap.} - 0.6) - Ca_{O_2}},$$

where,

Vo_{2_T} = the oxygen uptake of both lungs, in ml. per minute.

EXPERIMENTAL PROCEDURE

All subjects were studied in the postabsorptive state, without premedication.

GROUP I. PERMANENT OCCLUSION OF A MAJOR PULMONARY ARTERY

Cardiac catheterization, with placement of the catheter tip in the main pulmonary artery, was done in the usual manner. Atropine sulfate, 0.43 mg., was administered through the catheter lumen. A Carlens tracheobronchial, double-lumen tube was then introduced under local anesthesia. The proper position of the tube was established by fluoroscopy. Following inflation of the occluding bronchospirometric cuffs, the presence of gross leaks was excluded by connecting each lumen to a separate closed circuit containing a six liter spirometer, and then attempting to displace air from one spirometer to the other. After the absence of gross leaks had been established, the brachial artery cannula was introduced. Following a respite from these manipulations, oxygen uptake, minute ventilation and vital capacity were determined for each lung separately, using the closed circuits and the six liter recording spirometers filled with slightly enriched ambient air.

During the control and experimental periods which followed, open circuits were used: Each lung was now part of a circuit which included a tank of oxygen in nitrogen, an anesthesia bag interposed between the reducing valve, and a specially designed, low-resistance, three-way valve[5] and a thirty liter Douglas Bag. Through these open circuits, different inspired oxygen mixtures were delivered to each lung and expired gas was separately collected for sampling and measurement of minute ventilation.

During the control periods, each lung breathed a slightly different mixture of oxygen in nitrogen (ambient air versus 25 per cent oxygen in nitrogen); this difference facilitates the detection of minor leaks between the two tracheobronchial airways from a comparison of the respiratory exchange ratios of the two lungs (24). For reasons explained in Principles, the enriched mixture was supplied to the lung in which a collateral circulation presumably existed. After at least 10 minutes of equilibration on these mixtures, expired gas, systemic arterial and mixed venous blood samples were simultaneously collected for the calculation of blood flow by the Fick principle.

Between control periods, a measured quantity of T-1824 was injected into the main pulmonary artery, through the cardiac catheter, for the estimation of the cardiac output by the Stewart-Hamilton principle (19). Blood samples were collected from the brachial artery, before and after injection, by a constant-drive fractionating device; approximately twenty consecutive samples of blood were gathered over a one minute period. These samples were centrifuged and their plasma analyzed in a Beckman spectrophotometer for their respective concentrations of T-1824. The construction of time-concentration curves and the calculation of cardiac output were then done in the usual manner (19).

After the second control period, and without the patient's knowledge, the low oxygen mixture was substituted for ambient air as the inspired gas mixture to the normal lung; the affected lung continued to receive the *hyperoxic* mixture. After at least fifteen minutes of re-equilibration, the first of two consecutive test periods was terminated by collecting expired gas, arterial and mixed venous blood as in the control periods. The injection of T-1824 and the collection of systemic arterial blood were repeated before the final test period was begun.

[5] Manufactured by Respiration Aids, 255 East 148 Street, New York, N. Y.

GROUP II. PERFUSION OF A LUNG BY BOTH MIXED VENOUS AND SYSTEMIC ARTERIAL BLOOD

In each of the five subjects with unilateral pulmonary lesions (Table I), the pulmonary artery to the *diseased* lung was occluded by inflating a balloon situated on the end of a cardiac catheter. In the sixth subject (J. G.), without a demonstrable pulmonary lesion, the right pulmonary artery was occluded.

The procedure and sequence was that described for Group I, except for the use of a balloon-tipped cardiac catheter to transiently occlude a major pulmonary artery. The catheter contained three lumens; the middle one opened into a latex balloon which was subsequently filled with diodrast, under fluoroscopic control, so as to occlude one pulmonary artery while sparing the main pulmonary artery. Completeness of occlusion was established by briefly substituting the closed circuits described above, for the open circuits. By this device, the cessation of oxygen uptake on the side of occlusion, and the contralateral augmentation, could be directly visualized.

The use of a triple rather than a double lumen catheter afforded several advantages: *1*) Blood pressures in the right ventricle and in the distal pulmonary artery could be monitored as the balloon was inflated; *2*) blood samples could be procured for analysis of blood gas composition proximal and distal to the balloon; and *3*) the dye T-1824 could be injected proximal to the balloon for measurements of blood flow by the Stewart-Hamilton principle.

One threat to the subject during inflation of a balloon in a pulmonary artery is inadvertent encroachment of the balloon on the main pulmonary artery. This possibility was obviated by: *1*) fluoroscopic control of the position of the swelling balloon; *2*) oscilloscopic monitoring of right ventricular blood pressure, particularly during inflation; and *3*) continuous supervision of an electrocardiographic lead on the oscilloscopic screen.

GROUP III. BOTH LUNGS PERFUSED BY SYSTEMIC ARTERIAL BLOOD

All of these subjects had previously undergone diagnostic cardiac catheterization and brachial artery cannulation in the same laboratory. For the calculation of "effective" collateral blood flow, the oxygen uptake was measured in the usual way (31), using an open circuit for the administration of the inspired gas mixture, *i.e.*, 25 per cent oxygen in nitrogen, and a Tissot-type spirometer for the collection of expired gas. An arterial blood sample was drawn during the collection of expired gas.

GENERAL PROCEDURES

In the patients subjected to bronchospirometry and cardiac catheterization, the blood pressures in the pulmonary and brachial arteries were monitored throughout control and test periods. These blood pressures were transduced by Statham strain gauges and were displayed on the oscilloscopic face of a multi-channel apparatus containing high sensitivity carrier amplifiers.

The oxygen content and capacity of whole blood were determined by the Van Slyke-Neill manometric apparatus; the fractions of oxygen in inspired and expired gas were analyzed by the 0.5 ml. Scholander apparatus. All analyses were done in duplicate. From the analyses of inspired and expired gas, the oxygen uptake, the carbon dioxide output, and the respiratory exchange ratios were calculated for each lung, and for both lungs.

RESULTS

The three groups of patients are listed in Table I. For the sake of convenience, the first two groups, *i.e.*, with permanent or temporary occlusion of a pulmonary artery, will be considered together.

Groups I and II. Permanent and temporary occlusion of a pulmonary artery

Control periods. Measurements of gas exchange and blood gas composition in these subjects appear in Table III. Each datum in this table is the average of two consecutive samples, except in Subject J. S. (one control period) and Subject T. C. (one test period). As may be seen in this table, average values for total minute ventilation ($\dot{V}_{E_T}$), for oxygen uptake ($\dot{V}o_{2_T}$), and for carbon dioxide output ($\dot{V}co_{2_T}$) were similar in the subjects with permanent and with temporary occlusion. Although these values are somewhat high, they are consistent with measurements generally obtained during bronchospirometry (24). Since the increase in total carbon dioxide output paralleled the increase in metabolism, the average respiratory exchange ratio for both lungs was almost normal, averaging 0.81. Arterial blood was well-oxygenated with oxyhemoglobin saturations ranging from 97 to 100 per cent of capacity.

The partition of ventilation and gas exchange differed in the subjects with *temporary* occlusion from those with *permanent* occlusion of a pulmonary artery. Thus, in those with permanent occlusion of a pulmonary artery, both the uptake of oxygen ($\dot{V}o_{2_o}$) and the output of carbon dioxide ($\dot{V}co_{2_o}$) by the affected lung were abnormally low. Indeed, in Subject A. B. with less than six months of occlusion by carcinoma, gas exchange was negligible. On the other hand, in Subject O. B., with eleven years of occlusion, the oxygen uptake by the affected lung was only four per cent of the total

TABLE III

Ventilation, gas exchange and blood gas composition in subjects with occlusion of one major pulmonary artery

Subject	Side of occluded pulmonary artery*	Experimental state	Gas exchange in lungs													Blood gas composition		
			$F_{I_{O_2}}$†		$\dot{V}_E$‖			$\dot{V}_{O_2}$¶			$\dot{V}_{CO_2}$**			R_E††			Arterial blood		Mixed venous blood
			Lung O‡	Lung P§	Lung O	Lung P	Total	Lung O	Lung P	Total	Lung O	Lung P	Total	Lung O	Lung P	Total	O_2 Cont.	O_2 Sat.	O_2 Cont.
					L./min.			*ml./min.*			*ml./min.*						*ml./100 ml.*	*per cent*	*ml./100 ml*
			Permanent occlusion of a major pulmonary artery																
O. B.	Left	Control	0.25	0.21	5.58	5.16	10.74	13	285	298	54	161	215	4.20	0.57	0.72	19.0	95	15.4
		Hypoxemia	0.25	0.12	8.01	5.93	13.94	61	185	246	57	144	201	0.94	0.78	0.82	12.7	64	10.3
A. B.	Left	Control	0.27	0.21	4.68	9.92	14.60	3	211	214	<1	204	204		0.97	0.95	13.6	100	9.4
		Hypoxemia	0.27	0.12	4.84	9.83	14.67	3	238	241	<1	198	198		0.83	0.82	10.5	82	6.9
			Temporary occlusion of a major pulmonary artery																
J. S.	Right	Control	0.25	0.21	5.16	8.76	13.92	93	190	283	89	160	249	0.96	0.84	0.88	22.4	100	18.4
		Hypoxemia	0.25	0.12	5.58	8.17	13.75	<1	276	277	2	198	200		0.72	0.72	16.9	82	12.8
J. Mc.	Left	Control	0.27	0.21	4.68	5.64	10.32	83	190	273	77	159	236	0.93	0.84	0.86	18.1	95	14.3
		Hypoxemia	0.27	0.12	5.50	8.41	13.91	<1	246	246	12	253	265		1.03	1.08	13.6	72	10.4
P. C.	Right	Control	0.27	0.21	5.74	4.20	9.94	109	156	265	87	140	227	0.80	0.90	0.86	18.4	96	12.9
		Hypoxemia	0.27	0.12	5.59	7.36	12.95	4	226	230	<1	219	220		0.97	0.97	12.9	70	10.6
J. C.	Right	Control	0.27	0.21	6.62	3.79	10.41	160	155	315	126	111	237	0.79	0.72	0.75	19.9	100	15.3
		Hypoxemia	0.27	0.12	6.40	3.74	10.14	22	232	254	43	138	181	1.95	0.60	0.71	13.0	65	9.7
T. C.	Right	Control	0.25	0.21	4.67	3.92	8.59	169	158	327	117	119	236	0.69	0.75	0.72	19.0	96	14.2
		Hypoxemia	0.25	0.12	6.67	6.80	13.47	26	316	342	64	210	274	2.46	0.67	0.80	12.5	64	8.4
J. G.	Right	Control	0.25	0.21	5.14	4.76	9.90	160	185	345	133	148	281	0.83	0.80	0.81	21.9	96	17.6
		Hypoxemia	0.25	0.12	7.51	10.74	18.25	22	347	369	23	324	347	1.00	0.93	0.94	16.0	72	11.8

* In Group II, control periods were completed prior to inflation of the occluding balloon.

† $F_{I_{O_2}}$ = the fraction of oxygen in inspired gas.

‡ Lung O = lung with occluded pulmonary artery.

§ Lung P = lung with patent pulmonary artery.

‖ $\dot{V}_E$ = minute ventilation, in liters per minute.

¶ $\dot{V}_{O_2}$ = oxygen uptake, in ml. per minute.

** $\dot{V}_{CO_2}$ = carbon dioxide output, in ml. per minute.

†† R_E = respiratory exchange ratio.

whereas carbon dioxide production averaged 25 per cent. It is noteworthy that in Subject A. B., the minute ventilation on the affected side ($\dot{V}_{E_O}$) was unduly low. This deficiency was ascribed to injury of the left phrenic nerve during exploratory thoracotomy, one month prior to the study. Although this level of minute ventilation is low, it should presumably suffice to provide an appreciable gas exchange in a lung with an unobstructed pulmonary artery.

In the other subjects, prior to occlusion of a pulmonary artery, the partition of minute ventilation and gas exchange approximated normal values. The lung with the artery to be occluded accounted for 50 per cent of the total ventilation and effected approximately 43 per cent of both the total oxygen uptake and the total carbon dioxide output.

For reasons indicated in Principles, the "effective" collateral blood flow could not be calculated for the control periods.

The average blood flow through the intact pulmonary artery was 6.86 liters per minute when calculated by the mixing formula illustrated in Figure 5. The corresponding value by the Stewart-Hamilton method was 7.23 liters per minute, a difference of 5 per cent.

Test periods. These are designated in Table III as hypoxemia. During these periods, the oxyhemoglobin saturation of systemic arterial blood dropped to an average of 71 per cent, with a range from 64 to 82 per cent. The average total minute ventilation for the eight subjects increased, on the average, by 30 per cent whereas the average oxygen uptake and carbon dioxide output remained virtually unchanged from control, *i.e.*, minus 5 per cent and plus 1 per cent, respectively. The respiratory exchange ratio for the eight subjects changed on the average by 0.4 from control.

Although the total oxygen uptake ($\dot{V}_{O_{2_T}}$) and the total carbon dioxide production remained virtually unchanged during the test periods, the partition between the occluded and nonoccluded sides changed considerably in some subjects. Thus, in Patient O. B., with closure of the left pulmonary artery eleven years previously, there was a fivefold increase in oxygen uptake ($\dot{V}_{O_{2_O}}$) above control values to 61 ml. per minute, whereas carbon dioxide output by the same side ($\dot{V}_{CO_{2_O}}$) remained essentially unchanged. Furthermore, in three of the subjects with temporary occlusion of the right pulmonary artery (J. C., T. C. and J. G.), oxygen uptake on the ipselateral side continued after occlusion but decreased to an average value of 23 ml. per minute. In these subjects, carbon dioxide was also put out by the affected lung ($\dot{V}_{CO_{2_O}}$) at a lower rate, averaging 43 ml. per minute, approximately one-third of control values.

By way of contrast, neither the subject with recent occlusion of the left pulmonary artery by carcinoma (A. B.) nor the three subjects with bronchogenic carcinoma in whom the pulmonary artery was temporarily occluded (J. S., J. Mc. and P. C.), manifested an appreciable gas exchange during the test periods.

The "effective" pulmonary collateral blood flow was calculated for the four subjects with appreciable oxygen uptakes during the hypoxemic periods. As may be seen in Table IV, the largest "effective" collateral blood flow, *i.e.*, 860 ml. per minute, occurred in Subject O. B. with long-standing occlusion of a pulmonary artery. Lesser flows, of 300 to 400 ml. per minute, were measured in the two subjects with bronchiectasis. Intermediate values, *i.e.*, 700 ml. per minute, were calculated for Subject J. G. with idiopathic clubbing of the digits. In Table V are listed the individual values for consecutive periods; these values are shown to be remarkably reproducible. This table also indicates that in none of these subjects did the "effective" pulmonary collateral blood flow exceed 8 per cent of the total pulmonary blood flow.

The blood flow through the unobstructed pulmonary artery increased during hypoxia, averaging 21 per cent above control in the eight subjects. The corresponding increase in total pulmonary artery flow by the Stewart-Hamilton method averaged 29 per cent. Although the direction of changes in flow were similar by both methods, this similarity in averages conceals individual discrepancies; the basis for these differences is not clear.

Considerable changes in pulmonary artery blood pressure occurred during the hypoxemic test periods. Indeed, in one instance (J. G.)

TABLE IV

The "effective" pulmonary collateral and pulmonary artery blood flow in subjects with occlusion of one pulmonary artery

Subject	Experimental state	"Effective" collateral blood flow through Lung O *L./min.*	Pulmonary artery blood flow by mixing formula* *L./min.*	Pulmonary artery blood flow by Dye-Dilution Method† *L./min.*
Permanent occlusion of a major pulmonary artery				
O. B.	Control		8.26	
	Hypoxemia	0.860	10.43	
A. B.	Control		5.32	5.46
	Hypoxemia	‡	6.62	6.46
Temporary occlusion of a major pulmonary artery				
J. S.	Control		7.08	7.69
	Hypoxemia	‡	7.16	8.10
J. Mc.	Control		7.18	8.34
	Hypoxemia	‡	7.68	9.76
P. C.	Control		4.81	5.96
	Hypoxemia	‡	9.93	
J. C.	Control		6.85	6.49
	Hypoxemia	0.315	7.70	9.61
T. C.	Control		7.39	7.67
	Hypoxemia	0.382	8.34	12.67
J. G.	Control		8.02	8.99
	Hypoxemia	0.352	8.79	9.22

* Calculated as the total oxygen uptake of both lungs ($\dot{V}_{O_{2T}}$) divided by the difference in oxygen content between systemic and pulmonary arterial blood (see Figure 5).

† Calculated on the basis of the Stewart-Hamilton mean circulation time method.

‡ Oxygen uptake (Table III) was too low for calculation of blood flow by the Fick Principle.

pulmonary artery blood pressure approximated systemic blood pressure. These changes will be analyzed in detail in a subsequent report.

Group III. Both lungs perfused by systemic arterial blood

The results on these subjects are summarized in Table VI. All four subjects were polycythemic. The minute ventilations ($\dot{V}_{ET}$) and oxygen uptakes ($\dot{V}_{O_{2T}}$) were greater than normal in all three subjects but the carbon dioxide outputs were correspondingly increased as reflected in approximately normal values for respiratory exchange ratio (R_{ET}). In this group, with congenital heart disease, the youngest child (A. K.) had a greater "effective" pulmonary collateral blood flow than did the adults in the groups with acquired or induced obstruction of a major pulmonary artery. In Subject W. Y., who was comfortable at rest but who manifested considerable exercise intolerance, the cardiac output at rest was approximately 80 per cent of predicted. During exercise the cardiac output remained virtually unchanged. On the other hand, Subject B. C., who became breathless only during strenuous exertion, manifested a normal increase in cardiac output during mild exercise.

DISCUSSION

Several aspects of the present study warrant further consideration. They will be discussed in the following sequence: *1*) the definition and significance of "effective" pulmonary collateral blood flow; *2*) the effects of systemic hypoxemia on the pulmonary collateral blood flow; *3*) the interpretation of the present results in the light of previous observations by others; and *4*) the contribution of the pulmonary collateral blood

TABLE V

Consecutive measurements of "effective" pulmonary collateral blood flow in four subjects

Subject	"Effective" collateral blood flow, through Lung O $\dot{Q}_O$ *L./min.*	"Effective" collateral plus pulmonary artery blood flow by mixing formula* $\dot{Q}_O+\dot{Q}_P$ *L./min.*	Ratio of "effective" collateral to total pulmonary blood flow† $\frac{\dot{Q}_O}{\dot{Q}_O+\dot{Q}_P}\times 100$ %
O. B.	0.946	11.61	8
	0.773	10.92	7
J. C.	0.411	8.81	5
	0.190	7.25	3
T. C.	0.382	8.72	4
J. G.	0.366	8.72	8
	0.338	9.49	7

* See Table IV for definition of terms.

† Flow through collateral blood vessels, expressed as per cent of total pulmonary artery flow. For this calculation, the collateral blood flow for J. G. to Lung 0 was doubled, since both lungs are presumably equally affected; the other patients, with unilateral pulmonary lesions, required no such correction.

flow to the increment in pulmonary artery pressure elicited by acute hypoxia.

1) The definition and significance of "effective" pulmonary collateral blood flow

The collateral blood supply to the lung originates from intercostal and pericardiophrenic, as well as bronchial, arteries. The use of the Fick principle to measure the blood flow through the pulmonary collateral vessels identifies only that fraction of systemic arterial blood which reaches the alveolar-capillary interface to participate in gas exchange. It does not take into account the volume of blood which by-passes the gas exchanging surface of the lung. Consequently, the Fick principle affords only a minimal estimate of the hemodynamic burden imposed upon the left heart by the collateral blood flow.

2) The effects of systemic hypoxemia on the pulmonary collateral blood flow

Systemic arterial hypoxemia is required for the measurement of "effective" pulmonary collateral blood flow by the Fick principle. Since arterial oxyhemoglobin unsaturation is associated with an increase in both cardiac output and in pulmonary artery pressure (32,20), the effects of these hemodynamic changes on the pulmonary collateral blood flow merit assessment.

The increment in cardiac output should not, *per se*, affect the volume rate of pulmonary collateral blood flow. On the other hand, it is to be expected that an increase in pulmonary artery pressure may, by diminishing the perfusion gradient, decrease the rate of blood flow through the systemic-pulmonary arterial communications (33). However, in experiments with unilateral obstruction of a pulmonary artery, the obstruction spares the zone of communications from the pressor response induced in the proximal pulmonary artery by the systemic hypoxemia. Indeed, the blood pressure in this area tends to be unusually low, favoring an augmentation rather than a diminution in collateral blood flow.

It would be of interest to extrapolate from volume rates of collateral blood flow measured

TABLE VI

"Effective" pulmonary collateral blood flow in four patients with congenital atresia of the main pulmonary artery

Subject	State	$\dot{V}_{E_T}$ *L./min.*	$\dot{V}_{O_{2T}}$ *ml./min.*	R_{E_T}	Arterial blood: O_2 Cont. *ml./100 ml.*	Arterial blood: O_2 Cap. *ml./100 ml.*	$\dot{Q}_T$* *L./min.*
J. W.	Rest	9.53	222	0.83	14.8	24.1	2.54
	Exercise	33.28	382	0.98	12.6	24.5	3.22
A. K.	Rest	4.03	127	0.80	18.4	28.4	1.35
W. Y.	Rest	8.44	221	0.72	20.2	26.6	3.79
B. C.	Rest	5.32	165	0.80	18.3	22.0	5.00
	Exercise	18.40	494	0.94	16.6	22.5	9.30

* The "effective" pulmonary collateral blood flow, $\dot{Q}_T = \frac{\dot{V}_{O_{2T}}}{(\text{Art. } O_2 \text{ Cap.} - 0.6) - (\text{Art. } O_2 \text{ Cont.})}$.

during systemic hypoxemia to corresponding rates of blood flow during ambient-air breathing. Unfortunately, such attempts are complicated by: *1*) uncertainty as to the effects of acute hypoxemia on the collateral blood flow, and *2*) anatomic demonstrations (34) that the collateral blood vessels may not be regarded as passive conduits since they are muscular structures with anatomic potential for altering blood flow, independent of the blood pressure gradients measured at the entrances and exits of these vessels.

3) The interpretation of the present results in the light of observations by others

There is ample anatomic evidence that a variety of chronic pulmonary diseases is associated with large pulmonary collateral circulations (3). Moreover, there is little question that some of these systemic vessels communicate with the precapillary segments of the pulmonary artery (7,11). The present studies in subjects with bronchiectasis and cystic disease of the lungs, by measuring appreciable "effective" collateral blood flows, confirm the presence of precapillary communications in these types of pulmonary disease.

A particularly useful experimental device for stimulating the development of a large pulmonary collateral circulation, has been the ligation of a major pulmonary artery in dogs (8). The luxuriant overgrowth of systemic vessels in the young animals stands in sharp contrast to the meager collateral circulation which develops when the same procedure is performed in adult dogs. It is consequently of considerable interest to note that *children* with congenital atresia of the pulmonary artery may develop larger collateral blood flows than do *adults* with long-standing acquired occlusion of a pulmonary artery.

Physiologic measurements and anatomic observations are far less consistent in the subjects with bronchogenic carcinoma. Thus, although anatomists have repeatedly demonstrated a systemic arterial blood supply to primary carcinomas of the lung (35), the present studies failed to demonstrate an "effective" collateral blood flow to the lung containing the tumor. This discrepancy may be resolved on the ground that the blood supply to the tumor is either exceedingly small or else does not participate in gas exchange, thereby escaping detection by the Fick principle.

Of particular interest with respect to the pathogenesis of clubbed digits is the large "effective" collateral blood flow in the subject with long-standing, idiopathic clubbing of the fingers and toes (35). However, interpretation here is tempered by: *1*) the absence of "effective" collateral blood flow in other subjects with clubbed digits (Table I); *2*) the lack of anatomic basis for an extensive collateral circulation in idiopathic clubbing; and *3*) the inability to define the "ineffective" component of collateral blood flow by the Fick principle.

A final word is in order concerning the hemodynamic significance of the collateral blood flow in patients with acquired pulmonary disease. It has been proposed that the augmented pulmonary venous return effected by the collateral blood flow may strain the left heart (7,36). Two lines of evidence suggest that the left heart strain is not a usual consequence of an augmented pulmonary collateral blood flow: *1*) the diminutive "effective" collateral blood flow recorded above in subjects with intrinsic pulmonary disease, and *2*) the lack of clinical, X-ray, electrocardiographic or postmortem (32, 7) evidence of left ventricular enlargement despite anatomic display of an extensive pulmonary collateral circulation.

4) The contribution of the pulmonary collateral blood flow to the increment in pulmonary artery pressure elicited by acute hypoxia

It has now been well established that acute hypoxemia of moderate degree elicits an increment in pulmonary artery pressure (37,20). This response is exaggerated by decrease in the extent and expansibility of the pulmonary vascular tree (38) and is reflected in the present study by the markedly hypertensive levels proximal to the occlusion. It is noteworthy that the pressor response occurs even though the area of enlarged collateral-pulmonary artery communications has been isolated by the obstructing balloon. Such observations would suggest that the collateral circulation is not an essential contributor to the pressor response.

By way of contrast, hypotensive levels exist distal to the balloon at a time when this area is perfused by hypoxemic blood from the systemic circulation and ventilated by an enriched oxygen mixture. The hypotensive levels in the distal pulmonary artery may stem from: *1*) a decrease in blood volume and flow as inflow of blood from the pulmonary artery is arrested; *2*) a lack of vasoconstriction when the hypoxic stimulus is confined, as in the present experiments, to the precapillary segments of the pulmonary vascular bed; and *3*) a combination of *1* and *2*. Further analysis of this phenomenon will be deferred to a subsequent report.

SUMMARY

1) The "effective" pulmonary collateral blood flow was measured in human subjects, with various types of pulmonary and cardiac abnormalities, by special adaptations of the Fick principle.

2) In support of previous anatomic demonstrations of precapillary communications in the lung, "effective" collateral blood flows were demonstrated in a subject with long-standing ligation of a pulmonary artery and in others with bronchiectasis, with cystic disease of the lung, and with idiopathic clubbing of the digits. However, these blood flows did not exceed 8 per cent of the total pulmonary blood flow. No "effective" collateral blood flow could be measured in subjects with either primary carcinoma of the lung or short-term obstruction of a pulmonary artery.

3) By way of contrast, subjects with atresia of the main pulmonary artery displayed large "effective" pulmonary collateral blood flows, which approximated normal values for cardiac output at rest. During exercise, the "effective" collateral blood flow either remained unchanged or increased.

4) These observations are considered with respect to: *a*) the hemodynamic burden imposed on the left heart by the collateral circulation, and *b*) the contribution of the collateral circulation to the pulmonary hypertension elicited by acute hypoxemia. They emphasize the distinction between "effective" and total pulmonary collateral blood flow.

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