Effect of venesection on arterial gas values and ventilatory function in patients with chronic bronchitis

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The physician faced with a patient seriously ill with chronic bronchitis often feels obliged to use all therapeutic measures, including those of doubtful value. When such patients have received therapy to promote bronchial cleansing, to increase airway patency, to control infection and to improve cardiac function by the use of digitalis, diuretics, and salt restriction, serious disability may still continue. In this situation additional therapeutic manoeuvres are frequently attempted although the evidence for their usefulness may be tenuous. Since some of these subjects have raised haematocrits, venesection is often considered a justifiable procedure. Although much has been written about venesection, there is no unanimity about its usefulness in this situation.

In order to make a sound judgment concerning this mode of therapy one must weigh the beneficial effects of venesection against the possible dangers of this procedure, and in addition consider the consequences of allowing the haematocrit to remain raised. To assist in this evaluation it is necessary to have some knowledge of the effect of venesection, if any, on pulmonary function in these individuals.

The choice of parameters to evaluate the consequences of venesection, or various haematocrit levels, on lung function is difficult. Since the main purpose of the lung is to oxygenate the blood and remove metabolically produced CO_2 without undue effort, it appeared that simple, easily reproducible tests, designed to measure the adequacy of gas exchange and the degree of mechanical impairment should be used. Thus this study is concerned with the effects of venesection, as well as the effects of naturally occurring alterations in haematocrit, on the arterial gas values and ventilatory studies of subjects with chronic lung disease, who, in the main, had haematocrits which varied between 50 and 60%.

METHODS AND MATERIALS

SUBJECTS The subjects were men ranging in age from 44 to 74 years, with a mean age of 60 years. All except one were followed by one physician for more than six months. All were considered to be free of any acute infection or clinical change when studied. A diagnosis of chronic bronchitis was made in each subject on the basis of the presence of a cough productive of mucoid or purulent sputum daily for more than three years, in the absence of other chronic pulmonary disease likely to produce this symptom. Emphysema was tentatively diagnosed in all subjects on the basis of the clinical, radiological, and pulmonary function studies.

PULMONARY FUNCTION STUDIES Oxygen uptake and carbon dioxide output were calculated using the values from the Scholander analysis of expired air and the measured expired volume (Scholander, 1947). From these values the respiratory quotient, minute ventilation, and physiological dead space were calculated. The vital capacity, timed vital capacity, and maximum breathing capacity were determined using a Wedge spirometer and a two-channel recorder. The functional residual capacity was determined by the open-circuit nitrogen washout technique (Darling, Cournand, and Richards, 1940).

Arterial gas analysis consisted of the determination of the oxygen capacity and content in the Van Slyke apparatus and a calculation of the oxygen saturation (Van Slyke and Neill, 1924). Oxygen tension was determined directly with the Clark electrode using the adaptation of Severinghaus and Bradley (1958), while the carbon dioxide tension was determined using the Severinghaus PCO_2 electrode and an Instrumentation Laboratories meter. The pH was measured using a glass electrode in a Metrohm compensator. All gas tension and pH determinations were carried out at 37° C. in duplicate.

The alveolar ventilation ($\dot{V}_A$) was calculated from the $\dot{V}_{\text{CO}_2}$ and Paco_2 , whereas dead space ventilation ($\dot{V}_D$) represented the difference between the measured minute ventilation ($\dot{V}_E$) and the calculated $\dot{V}_A$. The alveolar oxygen tension was calculated from the

alveolar air equation and was used to arrive at the alveolar-arterial (A-a) gradient.

The red cell mass was determined using ^{51}Cr and a figure of 0.9 to correct the venous haematocrit as previously described by Read (1954). Venous blood for haematocrit determination was placed in heparinized capillary tubes and spun in a micro-haematocrit centrifuge for 10 minutes.

PLAN OF STUDY Ten studies before and after venesection were performed on eight different subjects. About half the subjects were studied as out-patients, while the remainder were electively admitted to hospital for the procedures but were maintained on the same medications as they had had before admission. The subjects were brought to the cardiopulmonary laboratory fasting, without premedication, having refrained from smoking for eight hours. A Courmand needle was placed in the brachial artery and the pulmonary function studies were performed. About 40 ml. of arterial blood was removed. Four hours later blood volume studies were performed, and the subject was then bled over a two-day period beginning the day after the initial pulmonary function studies. Blood, 400 to 1,000 ml., was removed (Table I). On the second or third day after the last venesection the pulmonary function and blood volume studies were repeated. Three of the patients studied had, in addition to the more acute studies, several blood volume or haematocrit determinations and pulmonary function tests performed over several months.

RESULTS

The oxygen saturation fell in six subjects and rose in four after venesection. The pH was unchanged in eight subjects, fell in one, and rose in the other. Oxygen tension fell four times, rose on five occasions, and was unchanged in one subject. A rise in Paco_2 was noted on three occasions, a fall twice, while no significant change occurred in five experiments. The A-a gradient narrowed in six patients, widened in one, and was essentially un-

changed in three patients (Tables I, II, and III). None of these individual parameters, when considered before and after venesection for the entire group (Table IV), changed significantly.

The respiratory quotients indicated a fairly steady state before and after venesection. Seven subjects exhibited a rise in respiratory equivalent, and a fall or no change occurred in three after venesection. The expired volume rose in seven subjects and fell in three, and alveolar ventilation rose in three and fell in seven patients. Dead space ventilation rose in seven subjects and fell in three, and the physiological dead space rose in six and fell in four patients. The $\dot{V}_D/\dot{V}_E$ ratio rose in eight subjects and fell in two. When each of these parameters was considered for the entire group (Table IV) before and after venesection no statistically significant changes were noted.

Lung volume and dynamic ventilatory studies (Tables III and IV), although showing some variation before and after venesection, also failed to show any consistent or significant changes. In those subjects studied both acutely and over several months (Table V) no consistent trend was noted between alterations in haematocrit and pulmonary function.

DISCUSSION

When considered apart from its effects on pulmonary function, as indicated by arterial gases and ventilatory tests, a raised haematocrit seems to impose certain physiological disadvantages on the subject. Thus when the haematocrit is raised, especially above 60%, an increase in blood viscosity is known to occur (Burch and De Pasquale, 1963). Richardson and Guyton (1959) showed that, although there was no significant change in dogs in right atrial and mean pulmonary artery pressure, a fall in cardiac output associated

TABLE I
PATIENTS STUDIED BEFORE AND AFTER VENESECTION

Patient	Age (yrs)	Height (cm.)	V'eight (kg.)	B.S.A. (m. ²)	Before Venesection			Blood Withdrawn (ml.)	After Venesection		
					R.C.M. (ml./kg.)	P.V. (ml./kg.)	Hct (%)		R.C.M. (ml./kg.)	P.V. (ml./kg.)	Hct (%)
T.I.	63	168	67.0	1.76	28.3	27.9	56.0	400			50.0
C.G.	67	168	61.0	1.69			63.0	1,000			55.0
D.C.	74	163	69.0	1.73	24.0	30.0	49.7	600	15.9	25.2	43.0
R.M.	71	173	73.0	1.86	33.0	33.0	56.0	600	29.5	32.0	53.0
S.I.	45	181	73.0	1.93	35.0	38.0	53.0	1,000			50.0
H.C.	58	181	85.0	2.06	30.2	30.2	57.0	1,000	22.9	26.9	51.5
J.M.	44	165	62.3	1.68	23.0	25.0	52.5	500	17.0	31.0	39.0
C.E.	62	173	74.0	1.88	36.0	31.0	59.5	500	31.0	34.0	53.0
T.L.	63	168	64.0	1.73	39.3	26.2	66.9	800	33.9	29.0	59.8
C.G.	67	168	61.0	1.69	43.0	43.0	55.0	1,000	37.0	37.0	55.0

R.C.M., P.V., and Hct indicate the red cell mass, plasma volume, and haematocrit

TABLE II

EFFECT OF VENESECTION ON ARTERIAL GASES, RESPIRATORY GAS EXCHANGE, AND ALVEOLAR RESPIRATORY FUNCTION

Patient		SaO ₂ (%)	PaO ₂ (mm. Hg)	pH	Paco ₂ (mm. Hg)	Vo ₂ (ml./min.)	Vco ₂ (ml./min.)	R.Q.	Resp. Equiv.	VE (l. min.)	VA (l./min.)	VD (l./min.)	D.S. (ml.)	VD/VE	A-a (mm Hg)
T.L.	Before	73.8	44	7.28	78	217	182	0.84	32.7	7.10	2.00	5.07	226	0.72	14
	After	71.8	40	7.29	83	197	229	0.87	34.2	7.83	2.04	5.78	222	0.75	17
C.G.	Before	84.0	53	7.33	62	263	216	0.81	27.0	7.02	3.00	4.02	235	0.56	27
	After	83.0	57	7.29	57	206	176	0.86	36.0	7.33	2.67	4.66	228	0.64	20
D.C.	Before	92.1	68	7.44	50	221	175	0.79	37.0	8.05	3.05	5.00	229	0.62	32
	After	94.5	80	7.42	52	184	153	0.84	39.0	8.77	2.07	4.61	212	0.65	10
R.M.	Before	82.8	62	7.37	62	192	172	0.90	31.8	6.10	2.39	3.71	240	0.61	19
	After	84.7	57	7.38	54	198	172	0.86	33.4	6.09	2.63	3.87	250	0.59	31
S.L.	Before	80.1	58	7.39	51	237	273	0.87	29.0	7.91	4.01	3.88	222	0.49	35
	After	78.7	49	7.38	54	225	266	0.84	30.0	7.95	3.54	4.41	230	0.57	37
H.C.	Before	84.5	52	7.33	54	309	259	0.84	31.5	9.72	4.16	5.56	178	0.58	35
	After	80.8	57	7.32	59	340	283	0.84	31.0	10.40	4.14	6.22	197	0.60	24
J.M.	Before	91.4	68	7.42	45	204	165	0.81	35.4	7.20	3.16	4.04	262	0.57	27
	After	95.1	69	7.41	47	187	154	0.83	38.5	7.15	2.86	4.29	296	0.60	23
C.E.	Before	90.5	56	7.36	52	278	242	0.87	33.8	10.59	4.02	5.31	109	0.57	34
	After	85.8	49	7.39	54	252	205	0.82	33.2	8.34	3.28	5.05	216	0.61	37
T.L.	Before	83.4	53	7.34	61	201	166	0.83	38.5	7.15	2.21	5.07	235	0.73	27
	After	85.2	56	7.34	63	206	165	0.81	35.6	7.28	2.28	5.00	218	0.69	19
C.G.	Before	85.0	52	7.31	49	201	165	0.83	36.0	7.12	2.91	4.21	203	0.59	39
	After	84.0	59	7.32	49	194	162	0.84	37.0	7.13	2.88	4.75	227	0.60	30

R.Q. = respiratory quotient; D.S. = dead space

with normovolaemic polycythaemia resulted in a marked increase in pulmonary vascular resistance. In addition these authors found that when the maximum number of red cells available each minute for oxygen transport (the product of the cardiac output per kilogram and the haematocrit) is determined, this value is at a maximum at a haematocrit of 40. This haematocrit value was within 0.6% of the mean control haematocrit in the dogs studied. Howarth, McMichael, and Sharpey-Schafer (1947) found in subjects with chronic heart failure due to pulmonary disease that an immediate reduction in right atrial and pulmonary artery pressure as well as cardiac output follows venesection. Auchincloss and Duggan (1957) made similar observations. However, because studies of pulmonary haemodynamics repeated over a prolonged period of time are not available, the duration of these changes is unknown. Since several subjects in the present study had a rather rapid re-expansion of their blood volume, mainly through a rapid rise in plasma volume, it would appear, in subjects in whom

viscosity is not an important factor, that these haemodynamic changes will be short-lived. Hecht, Gaylor, and Stein (1955) found that venesection had no predictable effect on the vascular alterations of cor pulmonale. From the studies just cited it appears that a lowering of markedly raised haematocrits might improve pulmonary circulatory function. It is unlikely that the correction of moderately raised haematocrits in the 50 to 60% range would be of significant benefit for any significant length of time.

Stroebel, Hall, and Pease (1951) have shown that subjects with polycythaemia vera are predisposed to angina pectoris and myocardial infarction. However, these subjects frequently have thrombocytosis which complicates the situation. Burch and De Pasquale (1963) have called attention to the higher haematocrit levels in subjects with acute myocardial infarction as compared with age-matched controls. These authors have tentatively suggested, although published controlled studies are not available, that venesection should be used in patients with erythrocytosis and symptomatic

TABLE III
EFFECT OF VENESECTION ON STATIC AND DYNAMIC LUNG VOLUMES

Patient	T.L.C. (ml.)	V.C. (ml.)	F.R.C. (ml.)	R.V. (ml.)	M.B.C. (l. min.)	T.V.C. 3 sec. (%)
T.L. Before	6,055	1,232	5,097	4,823	18.0	52
T.L. After		1,513			14.7	52
C.G. Before		1,860			22.0	57
C.G. After		1,790			35.0	55
D.C. Before		1,495			21.5	76
D.C. After		1,899			25.3	63
R.M. Before		2,040			17.6	46
R.M. After		1,850			19.8	54
S.L. Before	9,140	2,610	7,240	6,640	37.0	71
S.L. After	7,930	2,400	6,420	5,520	57.0	74
H.C. Before	4,085	1,817	2,785	2,239	19.4	65
H.C. After	3,700	1,765	2,488	1,935	21.3	66
J.M. Before		1,620			15.1	41
J.M. After		1,460			15.5	43
C.E. Before		2,170			44.3	64
C.E. After		2,760			51.3	51
T.L. Before		1,332	3,809		18.7	62
T.L. After	6,171	1,486	4,796	4,685	21.2	59
C.G. Before	4,120	1,170		2,970	14.9	68
C.G. After	4,490	1,220		3,270	17.2	82

T.L.C. = total lung capacity; V.C. = vital capacity; F.R.C. = functional residual capacity; R.V. = residual volume; M.B.C. = maximum breathing capacity; T.V.C. 3 sec. = timed vital capacity third second

TABLE IV

Parameter	Mean Value Pre- venesection	Mean Value Post- venesection	p ¹
O ₂ saturation (%)	84.8	84.4	> 0.9
PaCO ₂ (mm. Hg)	56.4	57.2	0.9
PaO ₂ (mm. Hg)	56.6	57.3	0.9
pH	7.36	7.35	0.9
A-a gradient (mm. Hg)	28.9	24.8	0.3
Respiratory equivalent	33.3	34.8	0.3
V _A (l./min.)	3.09	2.84	0.4
V _D (l./min.)	4.59	4.86	0.3
V _E (l./min.)	7.80	7.83	> 0.9
V _D /V _E	0.60	0.63	0.3
Physiological dead space (l.)	0.214	0.230	0.3
Vital capacity (l.)	1.73	1.81	0.8
M.B.C. (l. min.)	22.8	27.8	0.4
Timed vital capacity third sec. (%)	60.2	59.9	> 0.9

¹ p value obtained from the standard deviation of the difference of the means

ischaemic heart disease. It is curious and of interest that, while erythrocytosis of a mild to moderate degree is common in subjects with chronic lung disease, myocardial infarction is uncommon (Nonkin, Dick, and Baum, 1964).

In attempting to evaluate the effects of venesection on pulmonary function in subjects with

chronic lung disease several things may be considered. First, subjects with polycythaemia vera, in the absence of intrinsic lung disease or damage to the medullary respiratory centre, rarely have abnormal ventilatory function or gas exchange (Ratto, Briscoe, Morton, and Comroe, 1955). Secondly, since the raised haematocrit is presumably a compensatory mechanism to provide additional haemoglobin for oxygen transport, could its reduction adversely affect gas exchange? Evidence is available to indicate that correction of anaemia results in an increase in the diffusing capacity of the lung of human subjects (Rankin, McNeill, and Forster, 1961). Mochizuki, Anso, Goto, Hamamoto, and Makiguchi (1958) found in dogs that the calculated diffusing capacity of the lung for oxygen increased proportionately to an increase in haematocrit when other conditions remained constant. Burrows and Niden (1963) reported that haemorrhagic shock induced a marked fall in pulmonary diffusing capacity for carbon monoxide in dogs. Anderson and Gray (1962) noted a fall in the diffusing capacity for carbon monoxide when normovolaemic polycyth-

TABLE V
PULMONARY FUNCTION VALUES ASSOCIATED WITH SPONTANEOUS CHANGE IN HAEMATOCRIT AND RED CELL MASS

Patient	Date	SpO ₂ (%)	PaO ₂ (mm. Hg)	pH	Paco ₂ (mm. Hg)	R.Q.	R.E.	V _A (l./min.)	V _D (l./min.)	V _D /V _E	D.S. (ml.)	A-a (mm. Hg)	V.C. (l.)	M.B.C. (l./min.)	Hct (%)	R.C.M. (ml./kg.)	P.V. (ml./kg.)	T.B.V.
C.G.	20. 9.62	84.0	53	7.33	62	0.81	27	3.00	4.02	0.56	235	27	1.86	22.0	63.0	43.3	41.6	85.0
	13.12.62	86.4	59	7.34	63	0.83	29	2.46	3.89	0.61	243	19	1.20	21.0	57.0	43.0	43.0	86.0
	18. 3.63	85.0	52	7.31	49	0.83	36	2.91	4.21	0.59	205	39	1.17	14.9	55.0			
S.L.	4. 6.62	80.7	54	7.39	54	0.89	31	3.84	4.46	0.54	225	38	2.18	37.0	60.0	35.0	38.0	73.0
	31.10.62	80.1	58	7.39	51	0.87	29	4.00	3.88	0.49	222	35	2.61	31.0	51.0	53.0	61.0	114.0
	18. 2.63	83.0	54	7.39	56	0.84	23	4.22	3.15	0.43	172	32	2.41	59.0	50.5			
C.E.	2. 5.62	90.0	59	7.40	47	0.86	39	3.68	5.37	0.59	225	35	2.25					
	4.10.62	92.0	59	7.38	46	0.79	36	3.61	5.40	0.60	234	28	2.58	43.0	48.0	38.8	33.8	72.6
	25. 2.63	87.5	54	7.36	46	0.81	36	3.92	5.22	0.56	240	41	1.94	39.0	59.0			

T.B.V. = total blood volume

aemia was induced in dogs. However, in this experiment the polycythaemia was associated with a fall in cardiac output.

Thus, although it seems well documented that the diffusing capacity is directly related to the haematocrit, the extent to which this becomes a practical consideration in making a decision to lower the haematocrit in subjects with chronic lung disease is limited. Indeed, if polycythaemia is associated with a smaller cardiac output than would be present at a lower haematocrit, the pulmonary diffusing capacity might rise with a fall in haematocrit. Other alterations, in addition to changes in diffusion, are probably brought into play by venesection. Changes in ventilation-perfusion relationships and the degree of venous admixture would be expected to take place if alterations in cardiac output were produced.

Although all these changes probably do occur in a complex fashion, their ultimate effect on gas exchange seems to be minimal. Thus Auchincloss and Duggan (1957) found in rather severely polycythaemic subjects with chronic lung disease little change in arterial gas values after venesection. The present study confirms these findings in a group of patients seen more commonly, those whose haematocrit is between 50 and 60%, due to the hypoxaemia of chronic lung disease. Likewise, the lack of any significant changes in the pH of the arterial blood after venesection in both studies indicated the ability of these subjects to compensate for the loss of some buffering material.

Although difficult to evaluate and fraught with emotional overtones, the patient's subjective response to venesection is of interest. Most subjects with very high haematocrits generally feel better after venesection. The subjects in this study whose haematocrits were only moderately raised, uniformly felt more weak and tired after as compared with before venesection.

SUMMARY AND CONCLUSIONS

The effect of venesection on pulmonary gas exchange and ventilatory function was studied in eight subjects with chronic bronchitis. No significant changes were found after venesection. Spontaneous fluctuations in haematocrit or red cell mass were also unassociated with significant changes in arterial gas tensions, pH or ventilatory function.

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