MEDICAL GRAND ROUNDS

Parkland Memorial Hospital

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CHRONIC COR PULMONALE

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CASE #1: [redacted]

This [redacted] woman was first seen at [redacted] in [redacted], 1949, at which time she was 21 years old. She presented because of a tender lesion of the fifth rib which proved on excisional biopsy to be a noncaseating granuloma. She had lymphadenopathy, splenomegaly, and an extensive fluffy pulmonary infiltrate. P_2 was louder than A_2, but there was no overt cardiac problem. A lymph node biopsy also revealed noncaseating granuloma. A diagnosis of sarcoidosis was made.

The patient remained asymptomatic through 1954, except for several small papules on the skin which proved to be granulomas on biopsy. Repeated chest X-rays during these five years failed to reveal any change.

The patient first noted mild DOE in about 1955. She was followed for this by a private physician who treated her with ACTH and Cortisone during 1955 and 1956. Her course was stable until [redacted], 1959, when she was admitted to [redacted] with markedly progressive dyspnea of two months duration. During the month prior to admission she had developed marked pedal edema. On physical examination she was cyanotic, tachypneic, dyspneic, and tachycardic. She had harsh breath sounds, markedly increased P_2, hepatomegaly, questionable ascites, 3+ pedal edema, and clubbing. ECG revealed RAD and RVH; by chest X-ray the pulmonary infiltrates were unchanged from 1954, but she now had RVH. Venous pressure was 23.5 cm. H_2O, and circulation time was 18 seconds. The patient was treated with oxygen, Meticorten, bronchial hygiene, digitalis, diuretics, and salt restriction. On this regimen she became markedly improved, diuresed 19 pounds, and cyanosis disappeared. The blood gas studies in the chart were done at this time. She was discharged on maintenance digitalis, but steroids were discontinued.

In the ensuing months she continued to have dyspnea on mild exertion and a chronic cough, but there was no return of overt right heart failure. She received another course of Meticorten, but since there was no obvious change objectively or subjectively, this medication was not continued.

In [redacted], 1961, the patient had a sudden marked increase in dyspnea and cough; on admission to [redacted] she again was cyanotic, but there was no pedal edema. Venous pressure was 11 cm. H_2O, and circulation time was 14 seconds. The patient was again started on steroids. She had a dramatic improvement of her symptoms, although there were no objective changes.

Since the patient's 1961 hospitalization, she has been maintained on from 5 - 40 mgms. of Meticorten daily. There has been no change in her DOE, and she has had no recurrence of her right ventricular failure. ECG's and X-rays are unchanged, and several VP - CT's have been normal.

	Normal Values for This Patient	[redacted]-60	[redacted]-60 (On Steroids)	[redacted]-60	[redacted]-61
FVC (L)	2.90	1.80	1.94	2.02	2.00
$FEV_{0.5}$ (L)	1.76	1.25	1.34	1.20	1.20
$FEV_{1.0}$ (L)	2.175	1.60	1.60	1.50	1.40
	REST	REST	REST	REST	REST
SAT_{O_2} (%)	>94	70	84	82	88
pCO_2 (mmHg)	40	49	31	34	32
A-a (mmHg)	<15	61	51	52	34
N_2 Washout (%)	<2.5	6.0	8.3	5.5	
Cardiac output (L/min)					3.45
Membrane Diffusing Capacity (mlCO/min/mmHg)	41	6	6	7	7
Volume, Pulmonary Capillaries (cc)	52	28	31		16

CASE #2: [redacted]

This 44 y/O [redacted] woman was first admitted to [redacted]-61 because of thrombophlebitis of the left arm.

From about age 20 until age 42 the patient slowly gained approximately 100 pounds. During the 1½ years before hospitalization she gained over 100 more pounds, and at the time of admission she weighed greater than 300 pounds. For about 6 months prior to admission the patient noted progressive DOE, fatigability and orthopnea. She developed frequent episodes of somnolence and fell asleep during such times as talking on the telephone. She had frequent nightmares, fell from bed several times, and awoke confused in the mornings. Pedal edema developed during this period. Before admission she had been seen transiently in the Outpatient Department where the dyspnea, a BP of 250/130, and cardiomegaly by X-ray had led to the diagnosis of HCVD. She was digitalized for this without any great change in symptoms.

Physical examination revealed (besides the thrombophlebitis) a somnolent, massively obese colored female whose BP was 160/80. The diaphragms were high; breath sounds were diminished. Heart size was indeterminant, but P_2 was much louder than A_2. She had 2-3+ pretibial edema. All other physical findings were immersed in the fat.

Laboratory studies revealed a hematocrit of 45 and a CO_2 content of 38 meq/L. ECG showed RAD and nonspecific ST - T wave changes. Chest X-rays were always of poor quality; of diagnostic value one could only say that the pulmonary outflow tract was enlarged. Pulmonary function studies are tabulated below.

The patient became more somnolent on oxygen; oxygen with assisted ventilation was well tolerated, however, and this was her major therapy during hospitalization. Digitalization was continued, and diuretics were given about 10 days out of the total hospitalization of 43 days. Weight reduction was not entirely successful except for delivery of edema fluid; the patient's discharge weight was 283 pounds.

This regimen greatly benefited the patient in that symptoms of CO_2 retention disappeared; her ECG reverted to normal; P_2 became equal to A_2; edema disappeared, and the patient's exercise tolerance increased markedly.

After hospitalization, the digitalis was stopped without change. The patient continued to lose weight to a low of 225 pounds. During this time she was asymptomatic, and her ECG, chest X-ray, and CO_2 content were normal. During Feb. '62, she became despondent, and since that time her weight has climbed to 295 pounds. All of her symptoms have recurred, but she refuses to reduce or to be admitted for treatment.

	[redacted]-51		[redacted]	[redacted]		
PVC 3.45		ABD	ABD	ABD		
FVC (L)		1.275	2.375	1.755		
$FEV_{0.5}$ (L)		0.110	1.40	1.185		
$FEV_{1.0}$ (L)		0.950	1.765	1.365		
	REST	100% O_2	REST	REST	100% O_2	EXERCISE
SAT_{O_2} (%)	82	100	-	90	100	85
pCO_2 (mmHg)	71	74	45	60	68	57
pH	7.36	7.33	7.40	7.39	7.25	7.36
A-a (mmHg)	22	147	-	24	221	44
Hct.	52	48	48	50		
N_2 Wash-out	1.25%		2.1%			
Cardiac output	8.28 L		4.50 L			
D_M	46 (60%)		70 (91%)			
V_C	74 (115%)		60 (94%)			
EKG	RAD - Non Spec T Wave		Normal	Normal		
Weight	> 300 Pounds		225	295		

CASE #3: [redacted]

The patient was first seen at [redacted] in 1956 at which time he was a 61 y/o [redacted] man. He gave a history of heavy cigarette smoking his entire adult life. During middle life he had the onset of frequent episodes of bronchitis that finally developed into a chronic cough productive of thick sputum. In 1947-48 he noted the onset of DOE, and this progressed over the next few years to dyspnea on mild activity.

The physical exam at that time was classical for severe pulmonary emphysema. ECG showed RAD and peaked P waves in I and III. Chest x-ray was compatible with emphysema, and the pulmonary outflow tract was enlarged. Detailed pulmonary evaluation is in the chart below.

The patient did not adopt a treatment program and was not seen again until [redacted], 1958. During the two years of absence he had at least three episodes of peripheral edema associated with high venous pressures and ECG's showing right ventricular strain; these episodes occurred during periods of acute respiratory infection. At the time of this visit the physical was unchanged; the x-ray showed probable RVH; the ECG was unchanged. Venous pressure was 8 cm. H_2O and circulation time was 14 seconds. Other evaluation data is in the chart.

The patient had three more [redacted] admissions. On one of these admissions he had frank CO_2 narcosis with coma, RVH by ECG, peripheral edema, and a venous pressure of 20 cm. H_2O. On each admission he responded to vigorous bronchopulmonary hygiene.

After discharge the patient again failed to follow a rational treatment program.

On the patient's return in [redacted], 1959, more successful treatment was carried out. The patient was then evaluated for a RUL bullectomy. Cardiac catheterization revealed a PA pressure of 24/13 (mean 18), Right atrial pressure 4, Wedge pressure of 5-7, Cardiac Index 2.48 L/m^2, and pulmonary vascular resistance 2.7 units. Pulmonary angiography revealed compression of blood vessels into the lower lobes by the bullae.

Surgery was performed on the right lung [redacted], 1959, and the patient recovered without incident. The patient was much improved, and he continued to improve until [redacted]., 1960. At that time he developed an interstitial infiltrate thought to be a viral pneumonia. During this illness he had a grand mal convulsion thought to be due to anoxia. After this episode his pulmonary status deteriorated, and he never regained his previous level of activity.

In [redacted], 1960, the patient developed acute ECG changes of a myocardial infarct. These findings recurred in [redacted]t, 1960, and the patient expired.

PVC 4.2	[redacted] 1956 BBD	ABD	[redacted] 1958 ON ADM.	AFTER HOSP. BBD	ABD	[redacted].'59	[redacted]'59	[redacted]'59 (Post Op)	[redacted].'59	[redacted].'60	[redacted].'60
FVC	900	1100	750	1860	2100		1900	2475	2100	2600	
$FEV_{0.5}$	300	400	200	520	640		400	815	570	650	
$FEV_{1.0}$	500	700	400	830	1000		650	1150	730	850	

	[redacted] 1956 REST	EXER.	100% O_2	[redacted] 1958 REST	100% O_2	[redacted]'59 REST	[redacted].'59 REST	[redacted].'59 REST	[redacted].'60 35% O_2
SAT_{O_2} (%)	90%	79%	100%	85	100	92	83	91	100
pCO_2 (mmHg)	44	47	61	57	66	38	43	30	58
pH	7.40	7.36	7.23			7.53	7.45	7.58	7.38
A-a(mmHg)	35	47	176				52		
Hct.	51			43		42	39	35	49

REFERENCES

REVIEWS

1. Cournand, Andre: Some aspects of the pulmonary circulation in normal man and in chronic cardiopulmonary diseases. Circ. 2:641, 1950.

2. Harvey, Rejane M., Ferrer, M. Irene, Richards, Dickinson W., Jr., and Cournand, Andre: Influence of chronic pulmonary disease on the heart and circulation. Am. J. Med. 10:719, 1951.

3. Mack, Irving, and Snider, Gordon L.: Respiratory insufficiency and chronic cor pulmonale. Circ. 8:419, 1956.

4. Hecht, Hans H.: Heart failure and lung disease. Circ. 14:265, 1956.

5. Motley, Hurley L.: The mechanisms of chronic pulmonary heart disease (cor pulmonale) with and without arterial hypoxemia. Progr. in Cardiov. Dis. 1:326, 1959.

6. Mack, Irving: Cor pulmonale. Clinical Cardiopulmonary Physiology. Grune and Stratton, 1960.

7. Davidson, Paul: Functional aspects of the cor pulmonale syndrome. Brit. J. Dis. Chest 54:186, 1960.

8. Harvey, Rejane, and Ferrer, M. Irene: A clinical consideration of cor pulmonale. Circ. 21:236, 1960.

9. Mack, Irving, Anderson, Milton W., Goldberg, Harry, and Mattingly, Thomas W.: Chronic cor pulmonale, panel discussion. Dis. Chest 41: 477, 1962.

For a general review of the entire subject of cor pulmonale, the chapter by Irving Mack in Clinical Cardiopulmonary Physiology (#6) is probably as good as can be found. Motley's review (#5) uses a different approach that isn't as well organized, but the material contained is very good.

RIGHT VENTRICULAR ANATOMY AND PHYSIOLOGY

10. Rushmer, Robert F., and Crystal, Dean K.: Changes in configuration of the ventricular chambers during the cardiac cycle. Circ. 4:211, 1951.

11. Rushmer, Robert F., Crystal, Dean K., and Wagner, Clyde: The functional anatomy of ventricular contraction. Circ. Res. 1: 162, 1953.

12. Lafontant, Robert R., Feinberg, Harold, and Katz, Louis N.: Pressure - volume relationships in the right ventricle. Circ. Res. 11:699, 1962.

13. Fulton, R. M., Hutchinson, E. C., and Jones, A. Morgan : Ventricular weight in cardiac hypertrophy. Brit. Med. J. 14: 413, 1952.

14. Altschule, Mark D.: Cor pulmonale: a disease of the whole heart. Dis. Chest. 41:398, 1962.

The two papers by Rushmer (10, 11) give a clear picture of the right ventricle as a thin walled muscular appendage of the thick walled, conical left ventricle; one can easily visualize why the right ventricle is a good volume pump but functions badly against high pressures.

Since the left ventricle normally greatly outweighs the right ventricle, the weight of the whole heart is a poor index of right ventricular hypertrophy. Furthermore, the measurement of ventricular wall width is frequently difficult. Fulton's (13) method of ventricular dissection is not necessarily the best, but this approach to the problem seems reasonable.

Altschule (14) is included as representative of one viewpoint; namely, that the left ventricular hypertrophy that exists in most cases of cor pulmonale indicates a functional derangement of the left ventricle. Measurements of left atrial or pulmonary capillary wedge pressures during life do not support this concept.

NORMAL PULMONARY CIRCULATION PRESSURES

15. Hickam, John B. and Cargill, Walter H.: Effect of exercise on cardiac output and pulmonary arterial pressure in normal persons and in patients with cardiovascular disease and pulmonary emphysema. J. Clin. Inves. 27:10, 1948.

16. Riley, R. L., Himmelstein, A., Motley, H. L., Weiner, H. M., and Cournand, A.: Studies of pulmonary circulation at rest and during exercise in normal individuals and in patients with chronic pulmonary disease. Am. J. Physiol. 152:372, 1948.

17. Cournand, Andre, Riley, R. L., Himmelstein, A., and Austrian, R.: Pulmonary circulation and alveolar ventilation - perfusion relationships after pneumonectomy. J. Thor. Surg. 19:80, 1950.

18. Dexter, L., Whittenberger, J. L., Haynes, F. W., Goodale, W. T., Gorlin, R., and Sawyer, C. G.: Effect of exercise on circulatory dynamics of normal individuals. J. Appl. Physiol. 3:439, 1951.

19. Slonim, N. B., Ravin, A., Balchum, O. J., and Dressler, S. H.: The effect of mild exercise in the supine position on the pulmonary arterial pressure of five normal human subjects. J. of Clin. Inves. 33:1022, 1954.

The normal pulmonary vasculature has such a large reserve that it can accommodate several times the normal cardiac output with only a very small rise in pulmonary artery pressure. This is probably done both by increasing the size of functioning vessels and by opening up vessels that are not always patent. Slonim (19) has repeated the experiments of the earlier workers in this field with more elaborate techniques. This work has demonstrated that the earlier statements of no PA pressure rise during exercise may be a mild overstatement; he confirms, however, that PA pressure rises in normals are minimal.

DISEASES WITH REDUCTION OF THE PULMONARY VASCULAR BED

20. Carroll, Douglas: Chronic obstruction of major pulmonary arteries. Am. J. Med. 9:175, 1950.

21. McKeown, Florence: The pathology of pulmonary heart disease. Brit. Ht. J. 14:25, 1952.

22. Owen, William R., Thomas, Wilbur, A., Castleman, Benjamin, and Bland, Edward W.: Unrecognized emboli to the lungs with subsequent cor pulmonale. N. Eng. J. of Med. 249:919, 1953.

23. Heilman, Richard S., Tabakin, Burton S., Hanson, John S., and Naeye, Richard L.: Alterations in circulatory and ventilatory dynamics in pulmonary vascular obstruction secondary to recurrent pulmonary emboli. Am. J. Med. 32:298, 1962.

24. Langfield, Stephen B., Hopkins, F. Thomas, and Theurkauf, Edward A., Jr.: Chronic cor pulmonale due to multiple pulmonary emboli and accompanied by diffuse interstitial fibrosis. Am. J. Med. 27:494, 1959.

25. Scadding, J. G.: Sarcoidosis, with special reference to lung changes. Brit. Med. J. 1:745, 1950.

26. Parmley, Loren F., Jr., Jones, Francis S.: Primary pulmonary arteriosclerosis. Arch. Int. Med. 90:157, 1952.

27. Andrews, E. C., Jr.: Five cases of an undescribed form of pulmonary interstitial fibrosis caused by obstruction of the pulmonary veins. Bull. J. Hop. Hosp. 100:28, 1957.

28. Gross, Paul: The concept of the Hamman-Rich syndrome. Am. Rev. Resp. Dis. 85:828, 1962.

29. Seldin, D. W., Ziff, Morris, DeGraff, Arthur C., Fallis, B. D., and Burns, R. R.: Raynaud's phenomenon associated with pulmonary hypertension. Texas S. Jour. 58:654, 1962.

30. Renzetti, Attilio D., Jr., Eastmen, Gerard, Auchincloss, J. Howland, Jr.: Chronic disseminated histiocytosis X (Schüller-Christian Disease) with pulmonary involvement and impairment of alveolar-capillary diffusion. Am. J. Med. 22:834, 1957.

31. Casey, James F: Chronic cor pulmonale associated with lipoid pneumonia. J.A. M. A. 177:78, 1961.

32. Cortes, Felix M., and Winters, William L.: Schistosomiasis cor pulmonale. Am. J. Med. 31:808, 1961.

33. Moser, Kenneth M., and Shea, James G.: The relationship between pulmonary infarction, cor pulmonale, and the sickle states. Am. J. Med. 22:561, 1957.

This is not intended to be an extensive listing of all causes of cor pulmonale due to pulmonary vascular destruction. The variety of such causes, is, however, emphasized by the titles of the articles chosen. References 20-24 all deal with multiple pulmonary emboli; this subject is stressed because of its frequence, difficulty in diagnosis, potential prevention, and poor prognosis if untreated. The article by Heilman (23) is particularly good in pointing up many of the problems associated with the diagnosis and treatment of embolization.

RESPONSES OF THE CARDIOPULMONARY SYSTEM TO VARIOUS STIMULI

34. Aviado, Domingo M.: The pharmacology of the pulmonary circulation. Pharm. Rev. 12:159, 1960.

35. Fowler, Noble O.: Effects of pharmacologic agents on the pulmonary circulation. Am. J. Med. 28:927, 1960.

36. Fishman, A. P., McClement, J., Himmelstein A., and Cournand, A.: Effects of acute anoxia on the circulation and respiration in patients with chronic pulmonary disease studied during the "steady state". J. Clin. Invest. 31:770, 1952.

37. Aviado, Domingo M., Jr., Johnson, S. Ling, and Schmidt, Carl F.: Effects of anoxia on pulmonary circulation: reflex pulmonary vasoconstriction. Am. J. Physiol. 189:253, 1957.

38. Boahe, W. C., Daley, Raymond, and McMillan I. K. R.: Observations on hypoxic pulmonary hypertension. Clin. Sci. 31:1958.

39. Fishman, Alfred P., Fritts, Harry W., Jr., Cournand, Andre: Effects of acute hypoxia and exercise on the pulmonary circulation. Circ. 22:204, 1960.

This very complex subject is best covered by Aviado (34) in his extensive review (80 pages and 856 references). Fowler (35) is less extensive, but his review is certainly adequate. Fowler's explanation of the difficulties involved in measurements of pulmonary vascular resistance help explain the marked variation in results.

Of particular interest to the subject of cor pulmonale are the responses to hypoxia. There is general agreement that hypoxia causes increased pulmonary artery pressure, and increased cardiac output in normal

humans; patients with partial obliteration of the pulmonary vascular bed have even greater rises in PA pressure. Results of the effects of hypoxia on pulmonary vascular resistance, however, have been variable. The evidence probably favors an increase in this resistance with hypoxia. All of these changes are at least related to the degree of hypoxia present; saturations below 85% seem to be the most significant in eliciting response.

Cardiopulmonary responses to high CO_2 have been extremely varied.

DECREASED VENTILATION OR VENTILATORY DRIVE

40. Bergofsky, E. H., Turino, G. ,., and Fishman, A. P.: Cardiorespiratory failure in kyphoscoliosis. Medicine 38, 1959.

41. Seide, Morris J.: Heart failure due to extreme obesity. N. Eng. J. Med. 257:1227, 1957.

42. Richter, Tor, West, John R., and Fishman, Alfred P.: The syndrome of alveolar hypoventilation and diminished sensitivity of the respiratory center. N. Eng. J. Med. 256.1165, 1957.

43. Zimmerman, Henry A.: Hemodynamics: studies on a group of patients who developed cor pulmonale following thoracoplasty. J Thor. Surg. 22:94, 1951.

44. Feltman, James A., Newman, Walter, Schwartz, Arthur, Stone, Daniel J., and Lovelock, Francis J.: Cardiac failure secondary to ineffective bellows action of the chest cage. J. Clin. Inves. 31:762, 1952.

45. Kilburn, Kaye H., Eagan, John T., Sieker, Herbert O., and Heyman, Albert: Cardiopulmonary insufficiency in myotonic and progressive muscular dystrophy. N. Eng. J. Med. 261:1089, 1959.

46. Steinborn, Kurt E., Zimdahl, Walter T., and Loeser, William D.: Chronic cor pulmonale in the respiratory poliomyelitis patient. Arch Int. Med. 110.249, 1962.

Any condition that leads to hypoventilation of a severe degree may ultimately cause cor pulmonale even if the pulmonary vasculature is normal. The more pulmonary parenchymal disease is present in addition to the hypoventilation, the more likely cor pulmonale is to ensue.

Causes of hypoventilation include deformed chest walls (40, 43), weak chest walls (45, 46), extreme obesity (41), and a failure of the respiratory center (42). This problem is best discussed in Bergofsky's brilliant article on 'the heart failure of the hunchback' (40).

EMPHYSEMA AND COR PULMONALE

47. Liebow, Averill A.; The bronchopulmonary venous collateral

circulation with special reference to emphysema. Amer. J. Path. 29:251, 1953.

48. Cromie, John B.: Correlation of anatomic pulmonary emphysema and right ventricular hypertrophy. Amer. Rev. Resp. Dis. 84:657, 1961.

49. Platts, Margaret M.: The arterial blood gases in pulmonary heart failure. Clin. Sci. 12:63, 1953.

50. Miller, Drew R., Fowler, Ward S., and Helmholz, H. Frederic, J.: The relationship of arterial hypoxemia to disability and to cor pulmonale with congestive failure in patients with chronic pulmonary emphysema. Proc. Staff Meet. Mayo Cl. 28:737, 1953.

51. Mounsey, J. P. D., Ritzmann, L. W., Selverstone, N. J., Briscoe, W. A., and McLemore, G. A.: Circulatory changes in severe pulmonary emphysema. Brit. Heart J. 14:153, 1952.

52. Yu, Paul N. G., Lovejoy, Frank W., Jr., Joos, Howard A., Nye, Robert E., Jr., and McCann, William S.: Studies of pulmonary hypertension. I. Pulmonary circulatory dynamics in patients with pulmonary emphysema at rest. J. Clin. Inves. 32:130, 1953.

53. Platts, Margaret M., Hammond, J. D. S., and Stuart-Harris, C. H.: A study of cor pulmonale in patients with chronic bronchitis. Quart. J. Med., N.S. 29:559, 1960.

54. Hammond, J. D. S.: The physical properties of the lungs in chronic cor pulmonale. Clin. Sci. 16:481, 1957.

55. Woolf, G. R., Gunton, R. W., and Paul, W.: Cardiac output and blood volume in chronic cor pulmonale. Canad. Med. Ass. J. 85:1271, 1961.

56. Fowler, Noble O., Westcott, Richard N., Scott, Ralph C., and Hess, Emily: The cardiac output in chronic cor pulmonale. Circulation 6:888, 1952.

Many of the papers in the other sections also deal with cor pulmonale due to emphysema, since this is the most frequent cause of cor pulmonale. In essence, this type of cor pulmonale is a mixture of the other two types; the pulmonary vascular bed is partially destroyed, but the destruction is not extensive enough to cause pulmonary hypertension. The added functional vascular restriction of hypoxia is also necessary to produce hypertension.

The paper by Liebow (47) discusses the pulmonary vasculature in emphysema. Cromie's study (48) shows statistically that there is no relationship between the amount of anatomical emphysema and the development of a hypertrophied right ventricle.

References 49 - 56 point out that the patients with emphysema who develop cor pulmonale have lower oxygen saturations and higher P_{CO_2}'s than those who do not; in addition, at the time of right heart

failure the Sat. O_2 is even lower and the P_{CO_2} even higher than when failure is not present. Cardiac output is noted to be high, normal or low at the time of failure depending on many variables.

TREATMENT

57. Harvey, Rejane M., Ferrer, Irene, and Cournand, Andre: The treatment of chronic cor pulmonale. Circulation 7:932, 1953.

58. Fishman, Alfred P., Richards, Dickinson W.: The management of cor pulmonale in chronic pulmonary disease, with particular reference to the associated distrubances in the pulmonary circulation. Amer. Heart J. 52:149, 1956.

59. Taquini, Alberto C., and Fernandez, Jose M. Gonzales: The factors involved in the maintenance of the oxygen tension of the tissues in patients with chronic cor pulmonale. Acta Physiol. Lat. Amer. 2:217, 1951.

60. Taquini, Alberto C.: Physiopathological basis for the clinical interpretation of chronic cor pulmonale. Cardiologia 21:393, 1952.

61. Barach, Alvin L.: Possibilities for prevention of cardiac failure in pulmonary emphysema. Dis. Chest 37:687, 1960.

62. Sieker, Herbert O., Manfredi, Felice: The use of oxygen therapy and of mechanical aids in the treatment of cor pulmonale. Progr. Cardiov. Dis. :176, 1960.

63. Effersoe, P., Kristensen, H. Sund, and Lassen, H.C.A.: Effect of oxygen therapy on oedema in patients with cor pulmonale. Brit. Med. J. :1469, 1960.

64. Cotes, J. E., Pisa, Z., and Thomas, A. J.: Effect of breathing oxygen upon cardiac output, heart rate, ventilation systemic and pulmonary blood pressure in patients with chronic lung disease. Clin. Sci. 25:305, 1963.

65. Ferrer, M. Irene, Harvey, Rejane M., Cathcart, Richard T., Webster, Charles A., Richards, Dickinson W., Jr., and Cournand, Andre: Some effects of digoxin upon the heart and circulation in man, digoxin in chronic cor pulmonale. Circulation 1:161, 1950.

66. Gray, Frank D., Jr., Williams, M. Henry, Jr., and Gray, Frieda: Changes in chronic pulmonary disease as affected by lanatoside C. Amer. Heart J. 44:517, 1952.

67. Davis, James D., Howell, David S., Hyatt, Robert E.: Effects of acute and chronic digoxin administration in dogs with right sided congestive heart failure produced by pulmonary artery constriction. Circulat. Res. 3:259, 1955.

68. Baum, George L., Dick, Morris M., Shotz, Sylvia, and Gumpel, Roy C.: Digitalis toxicity in chronic cor pulmonale. Southern Med. J. 49:1037, 1956.

69. Baum, George L., Dick, Morris M., Blum, Alvis, Kaupe, Arthur, and Carballo, Jose: Factors involved in digitalis sensitivity in chronic pulmonary insufficiency. Amer. Heart J. 57:460, 1959.

70. Ferrer, M. Irene, Conroy, Richard J., and Harvey, Rejane M.: Some effects of digoxin upon the heart and circulation in man, digoxin in combined (left and right) ventricular failure. Circulation 21:372, 1960.

71. Bliss, Harry A., Fishman, William E., and Smith, Philip M : Effect of alterations of blood pH on digitalis toxicity. J. Lab. Clin. Med. 62:53, 1963.

72. Lewis, Ceylon S., Samuels, Arthur J., Daines, Merrill C., and Hecht, Hans H.: Chronic lung disease, polycythemis and congestive heart failure. Circulation 6:874, 1952.

73. Auchincloss, J. Howland, Jr., and Duggan, John J.: Effects of venesection on pulmonary and cardiac function in patients with chronic pulmonary emphysema and secondary polycythemia. Southern Med. J. 49:1037, 1956.

The use of oxygen in the treatment of cor pulmonale cannot be overemphasized. Tissue needs for oxygen must be met. By the use of increased inspired oxygen, this goal can be accomplished with less cardiac output. The decreased cardiac output and perhaps a decrease in pulmonary vascular resistance result in a lowering of the pulmonary arterial hypertension, and hence, the work load of the right ventricle is decreased. If CO_2 retention is caused by the administration of oxygen, assisted ventilation or respiratory stimulants are necessary to correct this induced hypoventilation. (57-64).

Digitalis increases cardiac output in patients with cor pulmonale, and it may therefore be useful in the type of disease with a low cardiac output. However, it does not attack the basic problem of increased pulmonary vascular resistance. In addition, the incidence of digitalis toxicity is higher in the presence of hypoxia. (65 - 71).

Studies of the effects of venesection on cor pulmonale conflict. Although most physicians feel moderate phlebotomies may be useful, others feel that tissue oxygenation is adversely affected (72). One must conclude, with Auchincloss, that phlebotomy is not usually necessary to compensate right heart failure (73).

MISCELLANEOUS

74. Sokolow, M., and Lyon, T. P.: The ventricular complex in right ventricular hypertrophy as obtained by unipolar precordial and limb leads. Am. Heart J. 38:273, 1949.

75. Milnor, W. R.: Electrocardiogram and vectorcardiogram in right ventricular hypertrophy and right bundle branch block. Circulation 16:348, 1957.

76. Mounsey, J. P. D., Ritzmann, L. W., and Selverstone, N. J.: Cardiographic studies in severe pulmonary emphysema. Brit. Heart J. 14:442, 1952.

77. Roman, Gonzalo T., Jr., Walsh, Thomas J., and Massie, Edward: Right ventricular hypertrophy, correlation of electrocardiographic and anatomical findings. Amer. J. Cardiol. 7:481, 1961.

78. Spodick, David H., Hanger-Klevene, Julia H., Tyler, John T., Muench, Hago, and Dorr, Constance A.: The electrocardiogram in pulmonary emphysema. Amer. Rev. Resp. Dis. 88.14, 1963.

Several criteria for the electrocardiographic diagnosis of right ventricular hypertrophy have been proposed. Any one set of criteria have a fairly high percentage of false positive and false negative diagnoses when correlated with pathological findings. The easiest criteria to remember are those of the St. Louis group (77). If RAD, an R/S amplitude ratio in $V_1 > 1$, or an R/S amplitude ratio in V_6 = or < 1 is present, RVH is probable. If two of these findings are present, it is claimed that 87% of the cases of RVH will be diagnosed, and there will be 38% false positives. P pulmonale (P $>$ 2.5 mm.) almost always means RVH when present, but its occurrence is $<$ 50% of the cases. The electrocardiogram in emphysema is frequently abnormal with or without anatomical RVH.

79. Fishman, Alfred P., Maxwell, Morton H., Crowder, Charles H., and Morales, Pablo: Kidney function in cor pulmonale. Circulation 3:703, 1951.

80. Stuart-Harris, C. H., Mackinnon, J., Hammond, J.D.S., and Smith, W. D.: The renal circulation in chronic pulmonary disease and pulmonary heart failure. Quart. J. Med. N. S. 25:389, 1956.

Despite a normal or high cardiac output, patients with congestive heart failure due to cor pulmonale have a decreased glomerular filtration rate and renal blood flow similar to patients with heart failure due to other causes.

81. Gray, Frank D., Jr., Lurie, Paul R., and Whittemore, Ruth: Circulatory changes in chronic pulmonary disease, a study of pulmonary collateral circulation. Yale J. Biol. Med. 23:380, 1951.

82. Marks, Matthew O., and Zimmerman, H. A.: The roentgen and differential diagnosis of chronic cor pulmonale. Amer. J. Roentgenol. 66:9, 1951.

83. Whitaker, W.: Pulmonary hypertension in congestive heart failure complicating chronic lung disease. Quart. J. Med. N. S. 23:57, 1954.

84. Rose, Leonard B., and Hoffman, David L.: The coronary blood flow in pulmonary emphysema and cor pulmonale. Circulat. Res. 4:130, 1956.

The coronary blood flow was found to be normal despite the presence of cor pulmonale.