THE OXYGEN OF THE ARTERIAL AND VENOUS BLOOD IN PNEUMONIA AND ITS RELATION TO CYANOSIS.

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PLATES 13 TO 15.

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In the recent epidemic of influenza with its accompanying pneumonia the unusual frequency of cyanosis was striking, and was in fact one outstanding feature of the epidemic. To find the cause, if possible, of the cyanosis a group of pneumonia cases at the Hospital of The Rockefeller Institute was studied during the past winter, with particular reference to cyanosis and its relation to the arterial and venous blood oxygen.

Studies of the venous blood have been made, notably by Lundsgaard[1] in cardiac insufficiency, and Harrop[2] in pneumonia; but the interpretation of the results is difficult, because of the undeterminable factors which affect the venous oxygen, such as variations in the rates of circulation and metabolism in the parts from which the blood is drawn. It appeared that satisfactorily complete data on which to base an explanation of the cyanosis could be expected only from analyses of arterial as well as venous blood. A group of 33 cases of pneumonia is here presented in which the oxygen of both arterial and venous blood has been determined.

Method.

Technique of Arterial Puncture.—Hürter[3] has shown that puncture of the radial artery is a safe procedure. At the Hospital of

[1] Lundsgaard, C., *J. Biol. Chem.*, 1918, xxxiii, 133; *J. Exp. Med.*, 1918, xxvii, 179, 219.

[2] Harrop, G. A., *Bull. Johns Hopkins Hosp.*, 1919, xxx, 10.

[3] Hürter, *Deutsch. Arch. klin. Med.*, 1912, cviii, 1.

The Rockefeller Institute arterial puncture has been done six times on one patient without injury. In all, about 90 punctures have been done and no ill results have been observed. The possible dangers are hemorrhage, thrombosis, embolism, or aneurysm, but in this series these have never been observed, even after 4 to 5 months observation. Occasionally if proper precautions are not observed, an undue amount of blood extravasation occurs; this has been observed here once, but the blood was rapidly absorbed and no after effects were seen.

An ordinary 20 cc. all glass Luer syringe is used with a Luer needle 1 to 2 mm. in diameter. The point of the needle is beveled at an angle of about 45° and must be very sharp. To prevent the blood from coming in contact with air, 1 or 2 cc. of sterile albolene are poured into the barrel of the syringe, the plunger is inserted, and the syringe with the attached needle inverted. The plunger is forced upward, and the air in the dead space at the distal end of the syringe and needle is expelled. The excess of albolene is then forced out so that only a small amount remains in the needle and in the small dead space. The patient's arm is laid horizontally upon a pillow, the hand is flexed backwards, and the region over the radial artery is sterilized with tincture of iodine. The end of the left index finger of the operator is then sterilized with iodine and, by using this finger in palpation, the best site for the puncture is determined. (Since the position of the artery is determined solely by palpation, it is advantageous to avoid gloves and use the bare finger.) The skin at the site of the proposed puncture is anesthetized with novocaine. The syringe and needle are held at an angle of about 45° to the surface, the needle is then pushed through the skin, and, after carefully relocating its position, the needle is entered into the artery. It is essential that the position of the artery should be sharply located and the point of maximum pulsation chosen (usually opposite the radial styloid); then the artery is easily entered, the pressure of the blood stream forces up the plunger so that suction is unnecessary, and within 15 to 60 seconds from 10 to 20 cc. of blood can be obtained. The needle is then quickly withdrawn, and by means of a compress, firm pressure is immediately applied over the artery for 1 or 2 minutes, so as to obliterate it temporarily and prevent extravasation. The

wrist is then bandaged with three or four thicknesses of compress to get greater pressure, and at the end of about 2 to 3 hours the bandage may be removed. If the artery is missed at the first puncture, and especially if a hematoma begins to form or blood extravasates around the needle, the operator should desist at once.

The blood thus collected is transferred to a tube 2.5 by 10 cm. in which a layer of albolene at least 2 cm. deep has previously been placed (to prevent contact with air) with some potassium oxalate to prevent coagulation.

Not all cases are suitable for arterial punctures, especially where repeated punctures are contemplated. Many women and some men have small radial arteries deeply situated, and hence difficult to puncture. The more rapid and bounding the pulse, the easier the puncture; and cases with pulse rates of 70 or below are difficult. Occasionally when the artery has been touched with the point of the needle it becomes almost pulseless, due no doubt to reflex vasoconstriction, but after 15 to 60 seconds it relaxes and the puncture may be finished.

Following the puncture there is a numbness of the radial side of the hand, but this wears off rapidly. About 50 per cent of the subjects complain of very slight dull pain at the wrist lasting about 12 to 24 hours, but this is without significance.

In two cases which were autopsied the radial arteries, which had been punctured several times, were dissected out. In one case the sites of the punctures were difficult to determine, and there was only a small amount of extravasation of blood. In the second case one puncture had been made 4 or 5 hours before death, when the patient was almost pulseless and the puncture difficult; here there was a moderate amount of extravasated blood in the tissues surrounding the artery, and the site of the puncture was marked by a pin-head point of extravasation of blood in the wall of the artery.

Technique of Venous Puncture.—The venous blood was obtained without stasis by the technique devised by Lundsgaard.[1]

Determination of Oxygen Content, Oxygen Capacity, and Oxygen Unsaturation.[1]—The method of Van Slyke[4] was used. The arterial

[4] Van Slyke, D. D., *J. Biol. Chem.*, 1918, xxxiii, 127.

TABLE I.

Determination of Oxygen Content, Oxygen Capacity, and Oxygen Unsaturation.

Case No.	Day of disease.	Diagnosis and clinical notes.	Result.	Cyanosis.						Oxygen content.		Oxygen capacity per 100 cc. of blood.	Oxygen unsaturation.			
				General.	Cheeks.	Nose.	Lips.	Ears.	Fingers.	Arterial, per 100 cc. of blood.	Venous, per 100 cc. of blood.		Arterial.		Venous.	
													Per 100 cc. of blood.	Per cent.	Per 100 cc. of blood.	Per cent.
										cc.	*cc.*	*cc.*	*cc.*		*cc.*	
3	6th	Lobar pneumonia.	R.*	0†	0	0	0	0	0	18 4	14.8	20.1‡	1.7	8.5	5.3	26 4
	8th	Acutely ill.		0	0	0	0	0	0	17 7	15 0	20.1‡	2 4	11 9	5.1	25.4
	11th			2	1	0	0	0	2	17.7		20.6	2.9	14.1		
	14th	After crisis; much better.		1	1	0	0	0	1	19.1	17.5	21.0	1.9	9.0	3.5	16.7
	20th	Convalescing.		0	0	0	0	0	0	18.9	15.1	20.1	1.2	6.0	5.0	24.9
	30th	"		0	0	0	0	0	0	19.9	17.8	19.9	0.0	0.0	2.1	10.5
4	7th	Influenza; bronchopneumonia. Extremely ill.	D.	3	3	2	1	1	3	15.1	5.3	20.3	5.2	25.6	15.0	73.9
5	10th	Influenza; bronchopneumonia. Heart's blood, 5 p.m.	"	4	4	4	4	4	4		3.6	23.2			19.6	84.5
				During illness.												
8	24th	Influenza; bronchopneumonia.	R.	0	0	0	0	0	0	17.1	12.0	18.6	1.5	8.1	6.6	35.5
9	9th	Bronchopneumonia.	D.	4	4	3	1	2	4	7.9	3.6	24.8	16.9	68.2	21.2	85.5
10	18th	"	R.	0	0	0	0	0	0	22.7	18.5	23.8	1.1	4.6	5.3	22.3
11	7th	Influenza; bronchopneumonia; pleuritic effusion.	"	2	2	0	0	1	2	23.1	20.1	25.7	2.6	10.1	5.6	21.8
	22nd			0	0	0	0	0	0	21.5	16.1	23.6	2.1	8.9	7.5	31.8

14	9th	Lobar pneumonia; influenza.	D.	3	2	1	1	1	3	21.1	10.6	26.6	5.5	20.7	16.0	60.2
15	3rd	Influenza; bronchopneumonia.	R.	1	1	0	0	0	1	20.0	16.7	21.7	1.7	7.8	5.0	23.0
	11th			0	0	0	0	0	0	19.1	16.4	20.6	1.5	7.3	4.2	20.4
16	4th	Bronchopneumonia.	D.	3	3	2	0	2	3	20.7	13.8	24.1	3.4	14.1	10.3	42.8
17	13th	Lobar pneumonia.	R.	1	1	0	0	0	1	16.9	16.2	20.2	3.3	16.3	4.0	19.8
	15th			1	1	1	1	0	0	16.1	9.0	18.2	2.1	11.5	10.2	56.0
18	23rd	" "	D.	2	2	1	1	0	2	19.6	17.7	23.5	3.9	16.6	5.8	24.7
	24th	Influenza; empyema.		3	3	2	1	2	3	19.8	17.1	23.7	3.9	16.5	6 6	27.8
	26th			4	4	3	2	3	4	14.4	1.3§	23.3	8.9	38.2	22.0	94.5§
19	4th	" bronchopneumonia.	R.	0	0	0	0	0	0	21.0	17.5	22.8	1.8	7.9	5.3	23.2
	5th			0	0	0	0	0	0	21.7	17.2	23.4	1.7	7.3	6.2	26.5
	13th			0	0	0	0	0	0	20.7	17.2	20.7	0.0	0.0	3.5	16.9
20	11th	" "	"	1	1	0	1	0	1	18.1	15.7	20.9	2.8	13.4	5.2	24.9
21	7th	" "	D.	4	4	4	2	3	4	10.8	4.7	22.5	11.7	52.0	17.8	79.2
	7th	Heart puncture (p.m.; 1½ hrs.).									1.8	22.5			20.7	
22	11th	Lobar pneumonia.	"	2	2	1	1	0	2	18.6	9.3	23.1	4.5	19.5	13.8	59.8
	13th			2	2	1	1	1	2	16.7	12.7	22.3	5.6	25.1	9.6	43.0

* R. indicates recovered, D. died.

† The numbers in this column indicate plus signs; *i. e.*, 0 indicates no cyanosis, 1 indicates + (slight cyanosis), 2 indicates ++ (moderate cyanosis), 3 indicates +++ (marked cyanosis), and 4 indicates ++++ (intense cyanosis).

‡ Determined colorimetrically (Palmer method—Palmer, W. W., *J. Biol. Chem.*, 1918, xxxiii, 119).

§ Postmortem heart's blood.

TABLE I—*Concluded.*

Case No.	Day of disease.	Diagnosis and clinical notes.	Result.	Cyanosis.						Oxygen content.		Oxygen capacity per 100 cc. of blood.	Oxygen unsaturation.			
				General.	Cheeks.	Nose.	Lips.	Ears.	Fingers.	Arterial, per 100 cc. of blood.	Venous, per 100 cc. of blood.		Arterial.		Venous.	
													Per 100 cc. of blood.	Per cent.	Per 100 cc. of blood.	Per cent.
										cc.	*cc.*	*cc.*	*cc.*		*cc.*	
23	6th	Influenza; bronchopneumonia.	R.	1	1	1	1	0	1	18.5	11.3	21.8	3.3	15.1	10.5	48.2
	7th			1	1	1	1	0	1	21.6	9.2	23.7	2.1	8.9	14.5	61.2
24	6th	" "	"	0	0	0	0	0	0	17.9	16.7	18.6	0.7	3.8	1.9	10.2
	11th			0	0	0	0	0	0	20.5	11.4	21.0	0.5	2.4	9.6	45.7
	25th			0	0	0	0	0	0	19.1	15.9	19.9	0.8	4.0	4.0	20.1
25	9th	" "	D.	3	3	2	1	2	3	15.7	12.6	28.1	12.4	44.1	15.5	55.2
29	14th	Lobar pneumonia.	R.	0	0	0	0	0	0	19.9	14.8	20.4	0.5	2.5	5.6	27.5
30	6th	Influenza; bronchopneumonia.	D.	3	3	1	2	2	3	17.2	7.9	22.9	5.7	24.9	12.0	48.3
31	4th	Multiple pulmonary abscesses; empyema.	"	2	1	1	0	1	2	17.1	15.7	20.2	3.1	15.3	4.5	22.3
	9th			1	0	0	0	0	2	17.8		19.6	1.8	9.2		
32	6th	Influenza; bronchopneumonia.	"	1	0	1	1	1	2	20.7	9.7	24.7	4.0	16.2	15.0	60.8
	7th			3	2	2	1	2	4	19.9	11.8	26.2	6.3	24.0	14.4	55.0
33	8th	" "	"	2	1	1	0	1	2	17.0	13.5	22.2	5.2	23.4	8.7	39.2
34	10th	Bronchopneumonia.	"	3	3	1	1	2	3	12.9		17.1	4.2	24.6		
	13th			3	3	2	1	2	3	11.3		16.2	4.8	29.6		

35	16th	Bronchopneumonia.	R.	3	3	1	2	2	3	12.8	10.2	19.1	6.3	33.0	8.9	46.7
	17th			2	3	1	0	1	2	13.7	9.7	17.9	4.2	23.5	8.2	45.7
	23rd			3	3	2	1	2	3	11.7		15.8	4.1	25.9		
	38th			1	0	0	0	0	1	13.3		14.9	1.6	10.7		
36	9th	"	"	1	0	0	0	0	1	22.8	17.7	26.3	3.5	13.3	5.6	21.3
37	7th	"	"	0	0	0	0	1	1	20.5		21.8	1.3	6.0		
	8th			0	0	0	0	0	0	20.4	18.8	22.0	1.6	7.3	3.2	14.4
38	4th	Lobar pneumonia.	"	0	0	0	0	0	1	17.4	12.5	19.0	1.6	8.4	6.5	34.2
39	5th	Bronchopneumonia.	"	2	2	2	2	2	2	18.3	12.9	21.4	3.1	14.5	8.5	39.7
40	7th	"	D.	3	2	2	2	1	3	16.2		22.3	6.1	27.3		
41	9th	"	"	3	2	1	1	3	3	20.7		28.6	7.9	27.6		
42	9th	"	"	4	2	2	3	2	4	8.1		17.8	9.7	54.5		

and venous samples were taken under albolene to prevent contact with air and analyzed in duplicate immediately for oxygen content. A portion of the blood was saturated with oxygen and the total oxygen capacity determined, as described by Van Slyke. Thus are obtained (1) arterial oxygen content (cubic centimeters of oxygen combined with hemoglobin in 100 cc. of arterial blood), (2) venous oxygen content (a similar value for venous blood), (3) total oxygen capacity (cubic centimeters of oxygen combined with the hemoglobin of 100 cc. of blood when fully saturated).

The difference between oxygen content and total oxygen capacity has been named by Lundsgaard[1] the oxygen unsaturation, and we have followed his usage of the term. The unsaturation may be expressed either as cubic centimeters of oxygen per 100 cc. of blood, or as percentage of the total oxygen capacity. In the latter case the data represent the per cent of total hemoglobin in the form of reduced hemoglobin. An example will make this clear.

	cc.	*per cent*
Arterial oxygen content	18.0	90.0
Venous oxygen content	14.0	70.0
Total oxygen capacity	20.0	100.0
Arterial oxygen unsaturation	2.0	10.0
Venous oxygen unsaturation	6.0	30.0

RESULTS.

Table I gives the results obtained in the 33 cases of pneumonia studied.

38 cases were studied which were divided as indicated in Table II.

TABLE II.

Classification of Cases.

Diagnosis.	No
Pneumonia, lobar	7
Postinfluenzal bronchopneumonia	25
Multiple pulmonary abscesses	1
Normal individuals	5
Total	38
Complications, empyema	3

Results in Normal Controls.—Table III gives the results obtained in five normal resting men. All these subjects were up and about, but were punctured 15 to 30 minutes after resting in bed.

The range of arterial oxygen content is from 17.9 to 22.1 cc. per 100 cc. of blood. The arterial unsaturation varies from 2.8 to 6.3 per cent. The venous unsaturation varies from 22.7 to 33 per cent. The arterial blood is usually assumed to be approximately saturated, but in the five individuals given in Table III the mean value is 95 per cent. The values found for the venous oxygen unsaturation are in close accord with those of Lundsgaard in normal individuals.

TABLE III.

Arterial and Venous Oxygen, Total Oxygen Capacity, and Arterial and Venous Oxygen Unsaturation in Five Normal Individuals.

Individual No.	Oxygen content.		Oxygen capacity per 100 cc. of blood.	Unsaturation.			
				Arterial.		Venous.	
	Arterial, per 100 cc. of blood.	Venous, per 100 cc. of blood.		Per 100 cc. of blood.	Per cent.	Per 100 cc. of blood.	Per cent.
	cc.	*cc.*	*cc.*	*cc.*		*cc.*	
1	17.9	12.8	19.1	1.2	6.3	6.3	33.0
2	21.0	16.7	21.6	0.6	2.8	4.9	22.7
3	22.1	17.2	23.3	1.2	5.2	6.1	26.2
4	20.2	15.6	21.6	1.4	6.5	6.0	27.8
5	19.5	15.4	20.3	0.8	3.9	4.9	24.1
Mean.....	20.2	15.6	21.2	1.0	5.0	5.6	26.8

Arterial and Venous Oxygen in the Pneumonia Cases.—That the arterial and venous oxygen content and unsaturation in the pneumonia cases show striking contrasts to the normal individuals is seen at once from Table IV.

TABLE IV.

Maximum and Minimum Arterial and Venous Oxygen Content and Arterial and Venous Oxygen Unsaturation in Pneumonia Cases.

Arterial content per 100 cc. of blood.		Arterial unsaturation.		Venous content per 100 cc. of blood.		Venous unsaturation.	
Maximum.	Minimum.	Maximum.	Minimum.	Maximum.	Minimum.	Maximum.	Minimum.
cc.	*cc.*	*per cent*	*per cent*	*cc.*	*cc.*	*per cent*	*per cent*
22.9	7.9	68.2	0.0	20.1	3.6	85.5	14.4

The arterial oxygen unsaturation ranges up to 68.2 per cent as contrasted to 6.3 per cent for normal individuals. For the venous unsaturation the variations are just as marked.

Oxygen Unsaturation in Fatal and Non-Fatal Cases.—If the cases are divided according to the outcome, equally characteristic differences are obtained. Table V shows that the maximum arterial unsaturation

TABLE V.

Arterial and Venous Oxygen Unsaturation in Sixteen Non-Fatal Cases.

Case No.	Maximum* unsaturation.	
	Arterial.	Venous.
	per cent	*per cent*
3	14.1	60.1
8	8.1	35.5
10	4.6	22.3
11	10.1	31.8
15	7.8	23.0
17	16.3	56.0
19	9.8	26.5
20	13.4	24.9
23	15.1	61.2
24	4.0	45.7
29	2.5	27.5
35	33.0	46.7
36	13.3	21.3
37	7.5	14.4
38	8.4	34.2
39	14.5	39.7
Mean.....	13.9	36.3

* Where more than one determination was made the maximum observed value is given.

in the recovered cases is 33 per cent, while the mean value (13.9 per cent) is more than twice the normal mean. In one case (No. 35), however, the arterial unsaturation was 33 per cent. This patient was desperately ill and the outcome for some time appeared hopeless, but she made a remarkable recovery.

Table VI shows that the arterial unsaturation in the fatal cases is much greater, the mean value being 32 per cent. Fourteen of the

sixteen fatal cases, but only one of sixteen non-fatal cases, had an arterial unsaturation greater than 20 per cent. Hence the fatal outcome of pneumonia is usually associated with a great degree of arterial unsaturation, and the arterial oxygen unsaturation offers a valuable prognostic sign. Rarely does a patient with a value greater than 20 per cent recover (one case out of 33).

A study of the venous unsaturation shows a far less degree of uniformity, and indicates the presence of factors difficult to control,

TABLE VI.

Arterial and Venous Oxygen Unsaturation in Sixteen Fatal Cases.

Case No.	Maximum* unsaturation.	
	Arterial.	Venous.
	per cent	*per cent*
4	25.6	73.9
9	68.2	85.5
14	20.7	60.2
16	14.1	42.8
18	38.2	
21	52.0	79.2
22	25.1	59.8
25	44.1	55.2
30	24.9	48.3
31	15.3	22.3
32	24.0	60.8
33	23.4	39.2
34	29.6	
40	27.3	
41	27.6	
42	54.5	
Mean	32.0	57.0

* Where more than one determination was made the maximum observed value is given.

which make the determination of the venous unsaturation of less prognostic significance than the arterial. However, in the fatal cases the mean value is 20 per cent higher than in the non-fatal cases. Eight of the eleven cases, or 72 per cent, showing a venous unsaturation over 47 per cent were fatal, while thirteen out of sixteen, or 81 per cent, showing less than 47 per cent venous unsaturation recovered.

Table VII gives briefly a summary of the above discussion with the maximum and minimum arterial and venous oxygen unsaturation in the fatal and non-fatal cases.

TABLE VII.

Maximum and Minimum Arterial and Venous Oxygen Unsaturation in Fatal and Non-Fatal Cases.

Type of case.	No. of cases.	Arterial unsaturation.			Venous unsaturation.		
		Maximum.	Minimum.	Mean.	Maximum.	Minimum.	Mean.
		per cent	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
Fatal cases.....	16	68.2	14.1	32.0	85.5	22.3	57.0
Non-fatal cases.....	16	33.0	1.6	13.9	61.2	14.4	36.3
Normal individuals..	5	6.5	2.8	5.0	33.0	22.7	26.8

Cyanosis.

Cyanosis may be caused by one of three factors or any combination of these three.

1. Disturbance of the Capillary Bed.—If there is a constriction of the arterial precapillaries, or a dilatation of the capillaries due to any cause, there is a stagnation of blood in the capillaries which, in the superficial or distal parts of the body, such as the lips, nose, ears, or fingers, gives cyanosis. For example, the cyanosis after prolonged exposure to cold is undoubtedly due to this cause. Cyanosis associated with various vasomotor paralyses, as in hemiplegia and poliomyelitis, may also be explained in this way.

2. Change in the Hemoglobin.—Certain intoxications change the hemoglobin into substances which do not contain labile oxygen, and therefore reduce the oxygen capacity of the blood. These substances are methemoglobin and sulfhemoglobin, and they are found in the blood associated with the cyanosis of acetanilide, phenacetin, potassium chlorate, or nitrobenzol poisoning.[5]

Enterogenous cyanosis due to methemoglobin or sulfhemoglobin, and cases of cyanosis in which the presence of these substances can

[5] Hammarsten, O., Text book of physiological chemistry, New York, 7th edition, 1914, 283.

be shown, and in which there is a reduction of the total oxygen capacity of the blood, would fall into this class.

It is possible that the cyanosis associated with pneumonia, more particularly in the very severe cases with a marked septicemia, may in some measure be caused by this factor. Butterfield and Peabody[6] have shown that the growth of pneumococci *in vitro* results in the formation of a substance with the optical properties of methemoglobin. Further, Peabody,[7] in rabbits in which he induced an overwhelming septicemia with pneumococci, found a rapid and marked fall in the total oxygen capacity of the blood, and also observed that the blood was of a brownish color and took up oxygen slowly. However, he was rarely able to demonstrate the presence of methemoglobin in such blood, and it may be pointed out that such overwhelming septicemias as were produced in his rabbits (direct films of the blood showed numerous organisms) are never found in man. Peabody[8] and Harrop[2] found, in a few severe cases of pneumonia, a diminution in the total oxygen capacity of the blood, but were unable to demonstrate the presence of methemoglobin in the blood.

3. Admixture Cyanosis.—The third factor in the production of cyanosis is a deficient or incomplete oxygenation of the blood as it passes through the pulmonary capillaries, or the passage of but part of the blood through the lungs (as in congenital heart disease), so that there is an abnormally low percentage of oxyhemoglobin in the peripheral circulation. Obviously the study of the arterial blood oxygen would determine this.

Degree of Cyanosis and the Oxygen Unsaturation.—Cyanosis, to a greater or less degree, was observed in 28 cases out of 33. In order to compare cyanosis in different parts from time to time the following scale was used. ± indicates very slight, + slight, ++ moderate, +++ marked, and ++++ intense cyanosis.

In the five cases (Nos. 8, 10, 19, 24, and 29) of pneumonia in which no cyanosis was observed at any time, the maximum arterial un-

[6] Butterfield, E. E., and Peabody, F. W., *J. Exp. Med.*, 1913, xvii, 587.
[7] Peabody, F. W., *J. Exp. Med.*, 1913, xviii, 1.
[8] Peabody, F. W., *J. Exp. Med.*, 1913, xviii, 7.

saturation was 8.1 per cent, slightly greater than normal (Table VIII). The mean value is 5.4 per cent, only 0.4 per cent greater than for the normal individuals. The venous unsaturations follow in the same order, but are more irregular.

In the twenty-seven cases showing cyanosis during their illness (Table IX), the difference is at once apparent. Here the variations are from 7.3 to 68.2 per cent of arterial unsaturation, and all but three of the values are above 10 per cent. The mean, 24.7 per cent, is five times greater than in normal individuals. Similarly the values

TABLE VIII.

Maximum Arterial and Venous Oxygen Unsaturation in Cases without Cyanosis.*

Case No.	Arterial unsaturation.		Venous unsaturation.	
	Per 100 cc. of blood.	Per cent.	Per 100 cc. of blood.	Per cent.
	cc.		*cc.*	
8	1.5	8.1	6.6	35.5
10	1.1	4.6	5.3	22.3
19	1.8	7.9	6.2	26.5
24	0.8	4.0	9.6	45.7
29	0.5	2.5	5.6	27.5
Mean.....	1.1	5.4	6.7	31.5

*Where more than one determination was made the maximum observed value is given.

for the venous unsaturation are higher and the mean, 44.5 per cent, is greater than in the cases without cyanosis.

Not only is there a greatly increased arterial and venous unsaturation in the cases with cyanosis, but there is a definite relation between the degree of cyanosis and the degree of unsaturation. In Table X the observations are divided into five groups according to whether there was no, slight, moderate, marked, or intense cyanosis at the time the blood was obtained. There is a gradual increase in both arterial and venous unsaturation as the associated cyanosis increases. This is strikingly brought out by Text-fig. 1 which shows as a curve the relation between unsaturation and cyanosis. The curve for the venous unsaturation parallels that for the arterial unsaturation.

TABLE IX.

Maximum Arterial and Venous Oxygen Unsaturation in Cases with Cyanosis.*

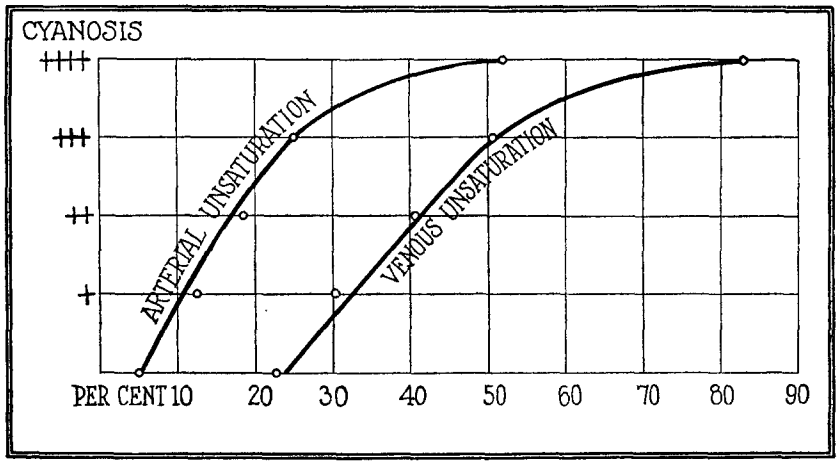
Case No.	Arterial unsaturation.		Venous unsaturation.	
	Per 100 cc. of blood.	Per cent.	Per 100 cc. of blood.	Per cent.
	cc.		*cc.*	
3	2.9	14.1	5.3	26.4
4	5.2	25.6	15.0	73.9
9	16.9	68.2	21.2	85.5
11	2.6	10.1	5.6	21.8
14	5.5	20.7	16.0	60.2
15	1.7	7.8	5.0	23.0
16	3.4	14.1	10.3	42.8
17	3.3	16.3	10.2	56.0
18	8.9	38.2	6.6	27.8
20	2.8	13.4	5.2	24.9
21	11.7	52.0	17.8	79.2
22	5.6	25.1	13.8	59.8
23	3.3	15.1	14.5	61.2
25	12.4	44.1	15.5	55.2
30	5.7	24.9	12.0	48.3
31	3.1	15.3	4.5	22.3
32	6.3	24.0	15.0	60.8
33	5.2	23.4	8.7	39.2
34	4.8	29.6		
35	6.3	33.0	8.9	46.7
36	3.5	13.3	5.6	21.3
37	1.6	7.3	3.2	14.4
38	1.6	8.4	6.5	34.2
39	3.1	14.5	8.5	39.7
40	6.1	27.3		
41	7.9	27.6		
42	9.7	54.5		
Mean.....	5.6	24.7	10.2	44.5

* Where more than one determination was made the maximum observed value is given.

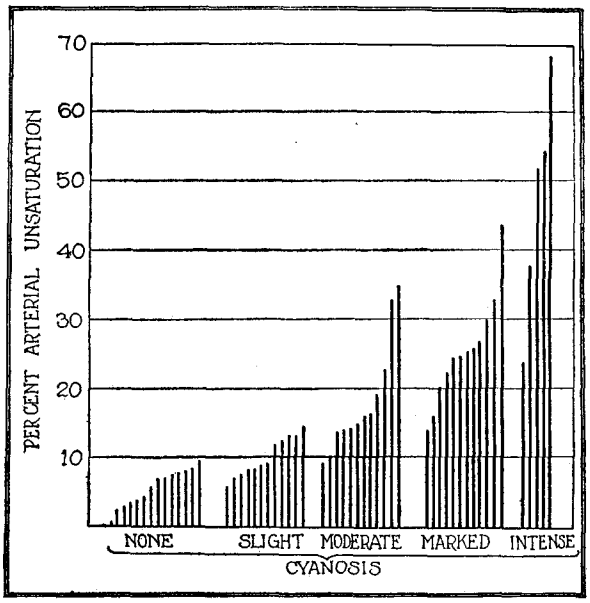
TABLE X.

Arterial and Venous Oxygen Unsaturation Associated with Cyanosis of Varying Degree.

Cyanosis.	No. of observations.	Unsaturation.	
		Mean arterial.	Mean venous.
		per cent	*per cent*
None.....	18	5.8	23.8
Slight.....	11	11.8	30.4
Moderate.....	10	17.2	41.8
Marked.....	13	26.0	51.2
Intense.....	4	53.2	82.3



TEXT-FIG. 1. Curves showing the relation between arterial and venous unsaturation and degree of cyanosis.

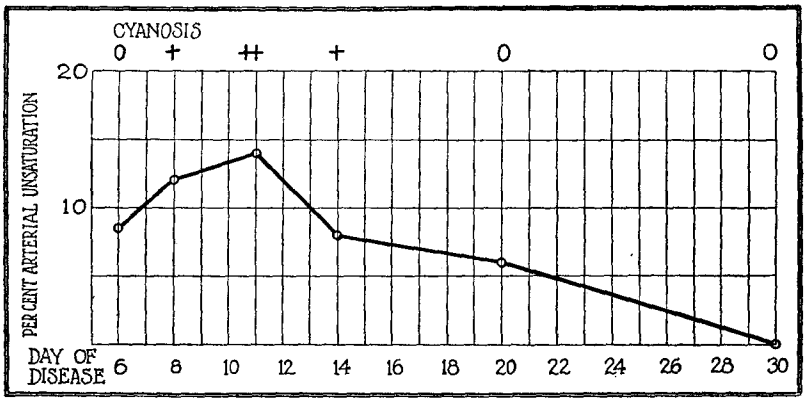


TEXT-FIG. 2. The observations of the per cent arterial unsaturation are plotted in groups according to the degree of cyanosis at the time of observation. The increase of the per cent oxygen unsaturation of the arterial blood with increasing cyanosis is striking.

In Text-fig. 2 the individual values for each observation are plotted in groups according to the degree of cyanosis. Here again the steadily increasing unsaturation with increasing cyanosis is apparent.

Again the relation of cyanosis to blood unsaturation is shown by a study of cases, in which repeated determinations were made on the same patient at different stages of the disease and with varying degrees of cyanosis.

Case 3 (Text-fig. 3) at the first observation (6th day) had no cyanosis, the arterial unsaturation being 8.5 per cent. He became much sicker and had a moderate cyanosis on the 11th day. The arterial unsaturation was then 14.1 per cent. With recovery the cyanosis disappeared, and on the 30th day the arterial unsaturation was 0.0 per cent.



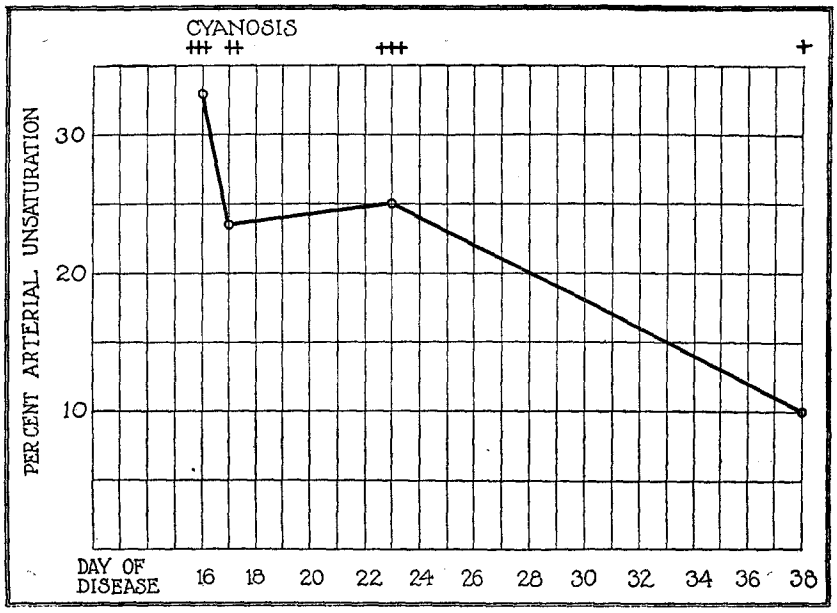
TEXT-FIG. 3. Curve of arterial oxygen unsaturation in Case 3. Note the increase in both cyanosis and arterial unsaturation as the patient became worse. After recovery the cyanosis disappeared and the arterial unsaturation became 0 per cent.

Case 35 (Text-fig. 4) was critically ill and markedly (+++) cyanotic on the 16th day; the arterial unsaturation was 33 per cent. For some time the outlook was desperate and the cyanosis continued associated with an arterial unsaturation of 23.5 and 25.9 per cent on the 17th and 23rd days. Subsequently the patient became much better; the cyanosis diminished until it was slight. The arterial unsaturation was then 10.7 per cent. After complete

recovery (95th day) when no cyanosis was present, the arterial unsaturation was 6.7 per cent.

On the other hand, Case 18 increased the arterial unsaturation from 16.6 per cent to 38.2 per cent as he became worse and the cyanosis increased (Text-fig. 5).

Discussion of Color.—The comparison of the colors of the cyanotic parts with the standard colors in "Répertoire de couleurs"[9] shows



TEXT-FIG. 4. Curve of arterial oxygen unsaturation in Case 35. There is a gradual decrease of the arterial unsaturation as the patient became better and the cyanosis diminished.

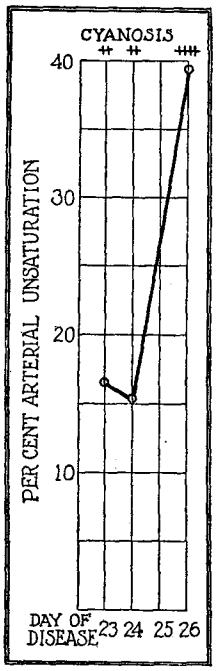
that there is considerable variation in the shades. The basic color is blue, but due to the varying admixtures with red, shades of heliotrope and mauve are frequent, especially in the fingers. On the cheeks a reddish heliotrope is not uncommon, but when the facial cyanosis is diffuse, the color is a leaden or plumbago-blue.

Distribution of Cyanosis.—The most constant and frequent site of the cyanosis was in the end of the fingers, especially under the

[9] Oberthür, R., Répertoire de couleurs, 1905.

nails. In cases with slight cyanosis a faint but definite bluish tinge could be observed here when no cyanosis could be made out elsewhere.

As the cyanosis became more intense it could next be observed over the entire end of the finger, being more marked on the dorsal aspect and fading gradually toward the first joint and toward the palmar surface.



TEXT-FIG. 5. Curve of arterial oxygen unsaturation in Case 18. The cyanosis increased from ++ to ++++ in 3 days, and the arterial unsaturation increased from 16.6 per cent to 38.2 per cent.

Fig. 1 shows the hand in Case 39 with a moderate (++) degree of cyanosis. This corresponded to 14.5 per cent of arterial unsaturation. The cyanosis is confined to the finger-nails and is of the heliotrope shade. In this case there was cyanosis of the lips, nose, and cheeks, but the color was less intense than in the finger-nails.

Fig. 2 shows the hand of a case with intense (++++) cyanosis with an arterial unsaturation of 44.1 per cent. The tips of the

fingers are a darker mauve-blue which is most intense under the nails. On the dorsum the color fades gradually beyond the terminal joint and also toward the palmar aspect.

The cyanosis of the toes is of the same order, but as a rule much less marked.

Second to the fingers the face shows cyanosis. Here it is of different types and distribution. At times even with a high degree of unsaturation, as in Case 34 (Fig. 3) with a marked (+++) degree of cyanosis, there is only a slight, dull, leaden blue, diffusely spread over the face from the forehead to and including the chin. In this case the fingers were darkly cyanotic (+++) and yet the face shows no marked accumulation of color at any one area, and seen alone would not lead one to suspect so high a degree of unsaturation.

Case 31 (Fig. 4) illustrates a second type. Here the 15.3 per cent of arterial unsaturation is accompanied by facial cyanosis in which the color is not diffuse but localized to the areas most frequently involved; namely, nose, chin, lips, ears, and cheeks.

When the cyanosis is slight it may be most marked over the malar bone. Frequently, despite a high arterial unsaturation and deep cyanosis of the fingers, the cyanosis is sharply limited to this area of the face and is of a dull cherry-red-blue at the center surrounded by a fading band of color similar to that seen in the fingers. Fig. 5 is an illustration of this type.

Even with a high arterial unsaturation the chin infrequently shows cyanosis, and the lips and ears, but occasionally. In fact the rarity and lesser degree of cyanosis of the lips in the pneumonia cases is in striking contrast to its frequency in cardiac cases.

Facial cyanosis is characterized also by its variability from day to day and from hour to hour. Often marked changes occurred within an hour. Change of position and coughing produced great changes in the intensity of the facial cyanosis. Therefore, as a measure of the degree of cyanosis from time to time the fingers are the best guide, for here the cyanosis remains most constant.

Total Oxygen Capacity.—A consideration of the oxygen capacity is important to determine whether there is methemoglobin production in pneumonia. In the entire series the total capacity varied from 14.9 to 28.6 cc. In the non-fatal cases (Table XI) there is

no unusually low capacity (except in Case 35) and the mean, 20.0 cc., is slightly lower than the normal mean. In Case 35 there was a drop in 6 days from 19.1 cc. to 15.8 cc. This patient's blood culture was negative and she was desperately ill with marked cyanosis. No examination was made for methemoglobin and the cause of this sudden drop is undetermined.

TABLE XI.

Oxygen Capacity of Non-Fatal Cases.

Case No.	Oxygen capacity per 100 cc. of blood.	Degree of cyanosis.
	cc.	
3	19.9	++
8	18.6	0
10	18.5	0
11	23.6	++
15	20.6	+
17	17.5	+
19	17.2	0
20	20.9	+
23	21.8	+
24	18.6	0
29	20.4	0
35	14.9	+++
36	26.3	+
37	21.8	+
38	19.0	+
39	21.4	++
Mean.....	20.0	

In the fatal cases (Table XII) all had marked cyanosis and should show low capacities if the formation of methemoglobin played an important part in the cyanosis. However, values even slightly below normal were shown only by Case 34. This patient was cyanotic throughout, and during a 3 day period her capacity decreased 0.9 cc. Her blood culture was sterile. With the exception of this the capacities are high and the mean, 23 cc., is higher than the normal.

Again a consideration of the changes in total oxygen capacity (Table XIII) shows that for the fatal cases there was during the illness but slight loss, and many cases show a gain. These changes

are no greater than for the non-fatal cases (Table XIV), particularly those which showed no cyanosis. Case 35 was the only case of the series which showed an unusual fall of capacity (4.2 cc.) associated with marked cyanosis.

It may be said, however, that but four cases, two of which were fatal, had positive blood cultures of pneumococci. Only one (No. 22) had an infinite number of colonies per cc. of blood; the others had but a few. This might explain why, unlike Peabody and Harrop, we failed to find occasional cases with greatly reduced oxygen capacity.

It seems unlikely, therefore, that methemoglobin formation plays any important part in the production of the cyanosis here observed, or had any part in the fatal outcome of the sixteen cases.

TABLE XII.

Oxygen Capacity of Fatal Cases.

Case No.	Time before death.	Oxygen capacity (gasometric) per 100 cc. of blood.	Degree of cyanosis.
		cc.	
4	7 hrs.	20.3	+++
5	Heart puncture (p.m.).	23.2	++++ during illness.
9	20 min.	24.8	+++
14	2 days.	26.6	+++
16	4 "	24.1	+++
18	3 "	23.7	+++
21	8 hrs.	22.5	++++
22	12 "	22.3	++
25	1 day.	28.1	+++
30	1 "	22.9	+++
31	6 days.	19.6	++
32	1 day.	26.2	+++
33	1 "	22.2	++
34	1 "	16.2	+++
40		22.3	+++
41		28.6	+++
42		17.8	++++
Mean		23.0	

A striking feature is the unusually high values for the oxygen capacities of some of the very ill or fatal cases. Cases 9, 14, 16, 25, 32, and 41 show this characteristic, but the exact cause of this high capacity is still unknown.

TABLE XIII.

Change in Oxygen Capacity in Fatal Cases.

Case No.	Change in capacity per 100 cc. of blood.	Interval.
	cc.	*days*
18	−0.2	3
22*	−0.8	2
31	−0.6	5
32	+1.7	1
34	−0.9	3

* Blood culture, Pneumococcus Type II colonies ∞ per cc.

TABLE XIV.

Change in Oxygen Capacity in Non-Fatal Cases.

Case No.	Change in capacity per 100 cc. of blood.	Interval.	Remarks.
	cc.	*days*	
3	−0.0	7	
11	−2.1	16	
15	−1.1	8	
17	−2.0	21	
19	−2.1	9	No cyanosis.
23	+2.0	1	
24	+1.3	19	No cyanosis.
35	−4.2	24	
37	+0.2	1	No cyanosis.

Oxygen Consumption and Heart Failure.

Lundsgaard[1] pointed out that the oxygen consumption, *i.e.* the difference between the arterial and venous oxygen content, increases in cardiac insufficiency. It is also increased by exercise, and presumably by other factors, such as fever, which accelerate the metabolism, unless an equivalent acceleration in circulation occurs.

The oxygen consumption in the series of pneumonia cases presented here is from 0.7 to 10.5 cc. of oxygen per 100 cc. of blood, the average values ranging from 3 to 5 cc., which is the usual range in normal individuals. As a rule, the values for the oxygen consumption in the fatal cases or in the extremely sick were no greater than those in the non-fatal cases, or in the less acutely ill. This would indicate that in the types of pneumonia (chiefly post influenza) represented by our cases the cardiac output does not fall below that normal for the resting organism.

SUMMARY.

1. A simple method for arterial puncture is given which does no permanent injury to the artery. Arterial and venous punctures have been done on 33 cases of pneumonia and five normal subjects, and the blood thus obtained has been studied with reference to the oxygen capacity and arterial and venous unsaturation.

2. In five normal subjects the mean arterial unsaturation was 5 per cent of the total oxygen capacity; the mean venous unsaturation was 26.8 per cent.

3. In the pneumonia cases the arterial oxygen unsaturation varied over a wide range. The arterial unsaturation varied from 0.0 to 68.2 per cent, the venous from 14.4 to 85.5 per cent. In the fatal cases as opposed to the non-fatal cases of pneumonia, the mean arterial oxygen unsaturation was 32 per cent as against 13.9 per cent. As a rule, an arterial unsaturation of over 20 per cent was associated with a fatal outcome. Similarly, the mean venous oxygen unsaturation was 57 per cent in the fatal cases and 36.3 per cent in the non-fatal cases.

4. In five cases in which no cyanosis was observed at any time the mean arterial oxygen unsaturation was 5.4 per cent, the mean venous oxygen unsaturation 31.5 per cent. In cases which showed cyanosis of varying degree during the course of the illness, the mean arterial unsaturation was 24.7 per cent, and the mean venous unsaturation 44.5 per cent. Cases without cyanosis have an arterial unsaturation close to the normal.

5. There is a definite relation between the degree of cyanosis and the per cent of arterial unsaturation. With increasing cyanosis

the arterial unsaturation becomes greater. The venous unsaturation varies similarly.

6. In individual cases with marked cyanosis associated with high arterial unsaturation, the clinical improvement of the patient and the diminution of the cyanosis are accompanied by a similar diminution in the arterial and venous unsaturation. Conversely, an increase of cyanosis is accompanied by an increase in arterial unsaturation.

It is evident that the cyanosis of pneumonia patients is due to the incomplete saturation of venous blood with oxygen in the lungs, and that the various shades of blue observed in the distal parts are caused by an admixture of reduced hemoglobin and oxyhemoglobin in the superficial capillaries.

7. No unusually low total oxygen capacities were observed, even in fatal cases with intense cyanosis. On the contrary, in these cases the total oxygen capacity was unusually high, pointing toward a concentration of the blood. Again in only one case was there any marked fall in the oxygen capacity during the illness. Therefore, methemoglobin formation, in these cases, can hardly have occurred to such an extent as to be an important factor in the production of cyanosis. Of the 33 cases studied, however, only seven were lobar pneumonia, the rest being of types ordinarily unusual, which have accompanied the recent influenza epidemic; and of the seven, not all were in all respects typically lobar. The possibility still remains, therefore, that in typical lobar pneumonia caused by the pneumococcus methemoglobin may play a part in the cyanosis.

8. The oxygen consumption, *i.e.* difference between arterial and venous contents, was within normal limits, indicating that the cardiac output was not diminished in the cases (chiefly post influenza) of pneumonia studied.

EXPLANATION OF PLATES.

PLATE 13.

FIG. 1. Case 39. Arterial unsaturation 14.5 per cent. There is a moderate cyanosis which is confined to the finger-nails. The color is heliotrope.

FIG. 2. Case 25. In this case there is an intense (++++) cyanosis of the fingers associated with an arterial unsaturation of 44.1 per cent. Cyanosis extends as high as the terminal joint and then fades out imperceptibly.

PLATE 14.

FIG. 3. Case 34. Bronchopneumonia; influenza. Arterial unsaturation 29.6 per cent. The entire face is diffusely cyanotic with no especial localization. The color is a leaden blue. The fingers in this case were markedly blue.

FIG. 4. Case 31. Multiple pulmonary abscesses (*Staphylococcus aureus*). Arterial unsaturation 15.3 per cent. There is a marked cyanosis of cheeks, nose, lips, and ears. On the cheek the color is a cherry-red-blue at the center, fading at the periphery to a heliotrope.

PLATE 15.

FIG. 5. Case 35. Bronchopneumonia. Arterial unsaturation 33 per cent. There is a sharply localized area of cyanosis of the cheek. The rest of the face is relatively free. The fingers had a +++ cyanosis.

FIG. 1.

FIG. 2.

(Stadie: Oxygen of the blood in pneumonia.)

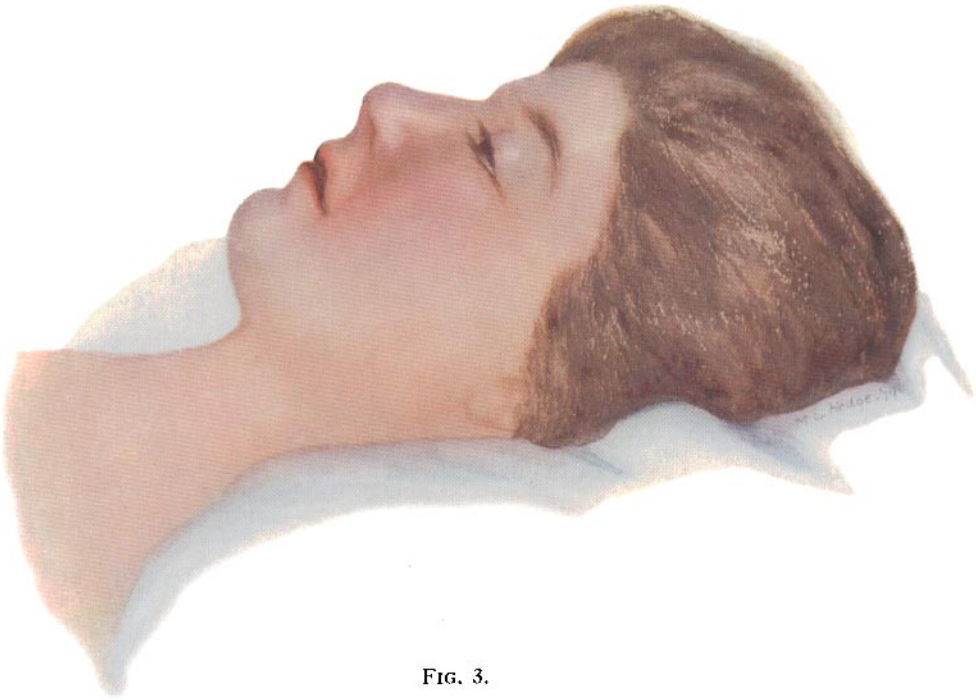


FIG. 3.

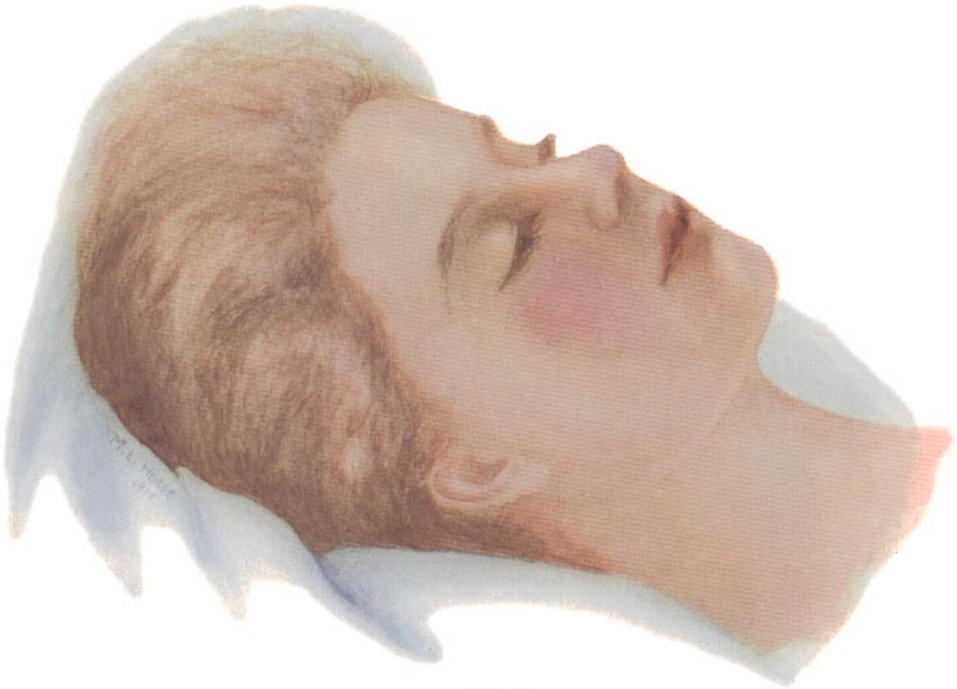


FIG. 4.

(Stadie: Oxygen of the blood in pneumonia.)

FIG. 5.

(Stadie: Oxygen of the blood in pneumonia.)