EXPERIMENTAL TYPE III PNEUMOCOCCUS PNEUMONIA IN MONKEYS

I. Production and Clinical Course

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(Received for publication, February 1, 1934)

Blake and Cecil (1) were the first investigators who regularly produced experimental lobar pneumonia in monkeys. *Macacus syrichtus* was used in the majority of experiments, while *Cebus capucinus* and *M. rhesus* were found to be less satisfactory. In most instances, Type I Pneumococcus was employed; in the three cases in which pneumonia was produced by the inoculation of Type III Pneumococcus, spontaneous recovery occurred. Schöbl and Sellards (2) obtained similar results with Type I Pneumococcus in the same species of animal. Stuppy, Falk, and Jacobson (3) attempted to produce pneumonia with Type I Pneumococcus in monkeys of the *M. rhesus* and *C. capucinus* species, but found animals of these species to be resistant to infection, and the authors therefore considered them unsuitable for such an experimental study.

The present study was begun as an effort to induce experimental lobar pneumonia with Type III Pneumococcus in monkeys. Dubos and Avery (4) described, in 1931, an enzyme of bacterial origin which possessed the capacity of decomposing the type-specific capsular polysaccharide of Type III Pneumococcus *in vitro*. The enzyme was shown, in addition, to have a distinct therapeutic action upon Type III pneumococcus infections in mice and rabbits (5–7). Consequently, it was thought that if experimental Type III pneumococcus pneumonia could be successfully produced in monkeys, a study of the effect of specific enzyme in the therapy of this infection could be made. The scope of this paper, however, is limited to the production of experimental pneumonia with Type III Pneumococcus in monkeys.

Materials and Methods

1. Experimental Animal.—The Java monkey (*M. cynomolgos*) was used throughout the study. In several ways the choice was fortunate, for animals

of this species are hardy, and, in our experience, relatively free from tuberculosis and intestinal disturbances. No instance of spontaneous pneumonia occurred in any of the animals during the period of study. Most of the animals were young adults, the size of which varied over a considerable range. The stock animals were kept in large cages and overcrowding was avoided. Before infection the animals were observed for several days for evidence of any abnormality. During the course of an experiment, they were kept in individual cages, out of contact with normal or other infected animals. An effort was made to maintain an even temperature in all quarters in which animals were kept.

2. Type III Pneumococcus.—A strain of Type III Pneumococcus, virulent for rabbits, was selected. Organisms recovered in culture from the blood of an infected animal were used in subculture for the pulmonary inoculation of subsequent animals, and, in addition, occasional direct passages through monkeys by intraperitoneal or intravenous injection were made. Broth cultures of the organism in the active growth phase were used. The amount of culture inoculated varied from 0.05 to 2.0 cc., but the more common range was from 0.25 to 0.5 cc.

3. Starch.—The solutions of soluble starch and the suspensions of corn-starch were made in plain meat infusion broth pH 7.8, as described by Terrell, Robertson, and Coggeshall (8).

4. Morphine.—Morphine sulfate, in amounts of 16 to 32 mg., was given subcutaneously 1 to 2 hours preceding inoculation. The intensity of effect of the drug appeared to be subject to considerable variation in the individual animals. When necessary, additional amounts were administered just before inoculation. Smaller amounts were given when ether anesthesia was employed.

5. Technique of Inoculation.—Because of the tendency of *M. cynomolgos* to store food in the pharyngeal pouches, the animals were given no food for several hours before inoculation.

(*a*) *Intratracheal Method.*—In the first part of the study inoculations were made by the intratracheal route. With the animal on its back a light ether anesthesia was induced. A mouth gag was fixed in position and the tongue drawn forward with a rubber-tipped lingual clamp. The mouth was dried with absorbent cotton. A No. 8 radiopaque rubber catheter was used. The distal tip was rounded and in the proximal end a blunt needle, to serve as an adapter, was bound with silk thread. A good view of the larynx was obtained and the catheter inserted into the trachea until resistance was encountered. A syringe containing the desired dose of organisms in 0.5 cc. of 5 per cent soluble starch was attached to the adapter and the material allowed to flow in. When the syringe had emptied itself it was detached, partly filled with air, attached again and the air allowed to flow into the trachea so as to empty the catheter. The animal was held upright and tilted to one side in order to localize the injected material. The animal was kept on the board until consciousness returned, then replaced in the cage. In some instances, periods of excitement and hyperventilation followed, while occasionally cessation of respiration required stimulative manipulation.

(*b*) *Intrabronchial Method.*—In the latter part of the work the intrabronchial method described by Terrell, Robertson, and Coggeshall (8) was employed (Figs. 1 to 6). In general, larger preparatory doses of morphine were given than with the previous method. The animal was placed with a small sand bag under the lumbar spine so as to throw the head backward. With mouth gag and tongue forceps in place, the mouth was cleaned and dried. When the method was first used, the throat was cocainized, but later cocaine was dispensed with as unnecessary, thus eliminating any danger of aspiration through removal of reflex activity. With this method a No. 5 or No. 6 radiopaque catheter was used. The catheter was inserted into the trachea, and the sand bag removed from the board. Under the fluoroscopic screen, the catheter was introduced into a secondary bronchus of a pulmonary lobe with the least possible manipulation and trauma. There was apt to be a brief coughing spell when the catheter reached the bronchus. The syringe, containing 0.5 cc. of a mixture of organisms in corn-starch suspension and sufficient excess to allow for the capacity of the catheter, was attached to the adapter. The material was injected slowly while under fluoroscopic observation. The catheter could usually be seen to retreat as injection progressed. The catheter was quickly removed, the animal tilted upright and toward the injected side for 10 to 15 minutes, then returned to its cage. It was found that if the catheters were coated with bakelite, or, still better, a heat-resisting varnish, they retained their form for long periods. When the catheters became very flexible, it was difficult to guide them into position.

At first, injections were usually made into the right lower lobe. This portion of the monkey's lung lies almost entirely below the level of the diaphragmatic dome, and renders X-ray interpretation comparatively difficult. Subsequently, the injections were made into the middle and upper lobes, where the shadow produced by pulmonary consolidation can be seen more clearly in the X-ray plates.

6. X-Ray Technique.—All roentgenograms were taken with a Victor-Snook X-ray machine and a radiator-type Victor tube. The readings were: 115 volts (50 kv. peak), 100 ma., 0.1 second exposure at a distance of 38 inches. Cassettes with double intensifying screens were used. The animals were routinely placed in the prone position with arms extended above their heads, and posterior-anterior exposures made.

7. Clinical Records.—

(*a*) *Rectal Temperatures.*—Records were usually made three times daily. From the average of a number of temperature readings of normal monkeys, a base line of 101.5° was adopted.

(*b*) *White Blood Counts.*—Counts were made before infection and usually at least once daily thereafter.

(*c*) *Blood Cultures.*—Blood was obtained from arm or leg veins. Cultures were made at least once daily using 0.5 to 1.0 cc. of blood in poured agar plates for enumeration of colonies; similar amounts were also cultured in broth. When the septicemia was known to be high, smaller amounts were used. When the

animals were quite sick, it was sometimes possible to obtain only small amounts of blood, and rapid clotting was a disturbing feature.

(*d*) *Symptoms.*—The animals were observed closely for degree of activity, appetite, strength, cough, character of respirations, and thoracic tenderness.

(*e*) *Diet.*—The monkeys were fed banana, orange, and bread and milk. During the period of illness they not infrequently refused the standard diet but accepted substitutes such as greens, carrots, prunes, and water. Diarrhea was an infrequent occurrence.

(*f*) *X-Rays.*—Roentgenograms of the chest were made before infection and at least once daily during the course of the disease.

(*g*) *Autopsies.*—Performed under sterile conditions as soon as possible after death. Frequently, the trachea was clamped before the chest was opened. Cultures were made of the heart's blood, of pleural and pericardial fluid, and of the pulmonary lobe chiefly involved. Stained preparations of the pneumonic exudate were sometimes examined for evidence of phagocytosis. At times the lungs were inflated with air. The heart and lungs were removed *in toto*.

TABLE I

*Mortality in Experimental Type III Pneumococcus Pneumonia in Monkeys**

Diagnosis	No. of animals	No. recovered	No. died	Mortality
				per cent
Pneumonia without septicemia	20	20	0	0
Pneumonia with septicemia (1–250 colonies per cc.)	20	11	9	45
Pneumonia with septicemia (250–2000 per cc.)	12	3	9	75
Pneumonia with septicemia (2000 or greater)	16	0	16	100
Total	68	34	34	50

* Classified on the basis of height of septicemia in first 3 days.

RESULTS

This report comprises an analysis of the data obtained in 68 monkeys, in which the experimentally induced Type III pneumococcus pneumonia was allowed to run its course without therapeutic interference. In the entire group, the mortality rate was 50 per cent. In Table I, the series is divided into groups on the basis of the height of the septicemia present during the first 3 days after infection. In animals in which pneumonia occurred without demonstrable septi-

cemia, recovery invariably resulted. It can readily be seen, however, that in the presence of septicemia the mortality rate rises progressively as the number of organisms in the circulating blood increases. In Chart 1 are shown the height of septicemia in the first 3 days after

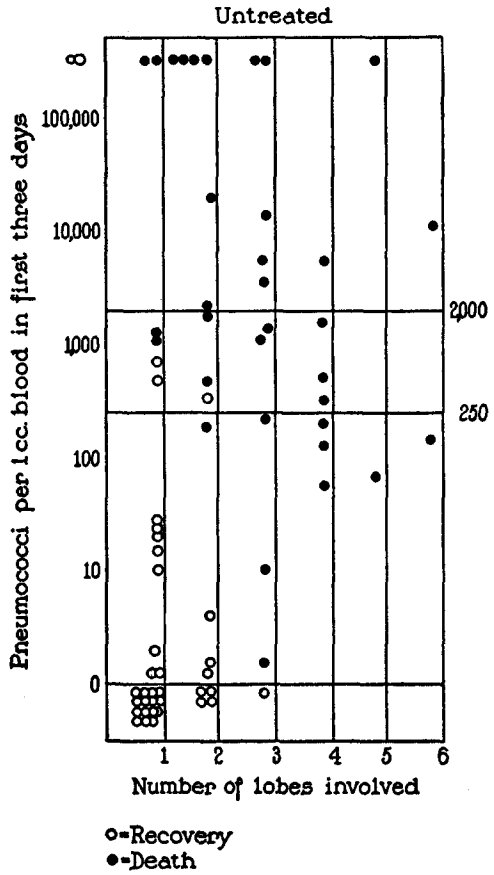

CHART 1. The relation of the height of septicemia and the amount of pulmonary involvement to the outcome of the disease.

infection and the number of pulmonary lobes involved during the disease in relation to the outcome of the disease. In the majority of animals which recovered, one or part of one lobe was involved, and in only one instance were three lobes affected. In all but one

TABLE II

Experimental Type III Pneumococcus Pneumonia in Monkeys

No.	Weight	Dose	Route*	Date		Days after infection 1	2	3	4	5	6	7	Remarks
						Pneumonia without septicemia							
	gm.	*cc.*											
5	2725	0.5	i.t.	11–10–31	Bl. cult.† X-ray‡ WBC§	0 1/2 RLL	0 Same	0 Same	0 Same		0 Same	0 Same	Recovered 4th day
6	1575	0.5	i.t.	11–17–31	Bl. cult. X-ray WBC	0 1/2 RLL	0 Spread	0 Clearing	 Clearing				Recovered 3rd day
1-3	950	0.5	i.t.	1–12–32	Bl. cult. X-ray WBC	0 1/2 RML	0 Spread	0 Clearing	0 Clearing				Recovered 3rd day
1-5	1450	1.0	i.t.	1–19–32	Bl. cult. X-ray WBC	0 1/2 RLL	0 3/4 RLL	0 RLL	0 RLL	0 Clearing		 Clearing	Recovered 3rd–4th day
2-5	1775	0.2	i.t.	2–15–32	Bl. cult. X-ray WBC 10.8	0 1/3 LLL 21.3	0 1/3 LLL 14.3	0 Clearing LLL New in RLL 6.5	0 Clearing 10.5				Recovered 4th day
3-2	1500	0.3	i.t.	3–21–32	Bl. cult. X-ray WBC 10.0	0 1/3 LLL 9.4	0 Spread 13.0	0 Clearing	0 9.2	0			Recovered 3rd day
3-7	2290	0.4	i.t.	4–18–32	Bl. cult. X-ray WBC 24.2	0 1/3 RLL 21.2	0 Spread 13.2	0 1/2 RLL 13.2	0 Spread 14.0	0 3/4 RLL 16.5		0 RLL 16.2	Recovered 7th day

4-4	1825	0.4	i.t.	5–2–32	Bl. cult.	0	0	0	0	0			Recovered 3rd day
					X-ray	1/2 RLL	Same	Same	Clearing				
					WBC 10.7	25.8	9.7	5.4	6.0	6.0			
6-4	1250	1.0	i.t.	8–2–32	Bl. cult.	0	0	0					Recovered 4th day
					X-ray	Mottled	Mottled	Confluent	Clearing				X-ray: Mottled density 1/2 RML and RUL
					WBC 12.2	17.0							
7-1	2450	0.1	i.b.	10–17–32	Bl. cult.	0	0	0					Recovered 3rd day
					X-ray	1/3 RLL	2/3 RLL	Clearing					
					WBC 15.2	26.9	16.6	10.2					
7-9	2400	0.25	i.b.	12–12–32	Bl. cult.	0	0	0	0	0			Recovered 3rd–4th day
					X-ray	1/3 RLL	Same	Clearing					
					WBC 22.4	24.2	11.3	14.6	25.6	28.2			
8-3	1950	0.25	i.b.	12–19–32	Bl. cult.	0	0	0	0				Recovered 4th day
					X-ray	1/3 RLL	2/3 RLL	Same	Clearing				
					WBC 20.0	31.6	55.7	25.8	15.1				
8-9	2000	0.3	i.b.	1–16–33	Bl. cult.	0	0	0	0	0	0		Recovered 12th day
					X-ray	1/2 RUL	Spread	RUL	Same	Dense		Same	X-ray: RUL cleared as RLL became consolidated
					WBC 24.1	15.7	27.5	12.5	11.1	22.3	20.8		
9-3	2125	0.3	i.b.	1–30–33	Bl. cult.	0	0	0	0	0		0	Recovered 8th day
					X-ray	1/3 RML	Spread	Spread	RML			RUL	X-ray: RML cleared as RUL became consolidated
					WBC 27.8	24.5	14.6	30.2	14.2	28.3			
1-08	1540	0.3	i.b.	4–24–33	Bl. cult.	0	0	0	0				Recovered 3rd–4th day
					X-ray	Mottled	Same	Same	Same	Clearing			Irregular slight mottled density midportion right lung
					WBC 17.6	33.8	27.0	28.0	16.8				

* i.t. = intratracheal inoculation; i.b. = intrabronchial inoculation.

† Number of pneumococci obtained in poured plate culture per 1 cc. of blood; + = growth occurred in broth cultures of blood; C = contaminated.

‡ RUL, RML, RLL, LUL, LML, LLL = right upper, right middle, right lower, left upper, left middle, left lower lobes, respectively. (Cardiac lobe not included.)

§ White blood cells in thousands per c.mm. of blood.

TABLE II—*Continued*

No.	Weight	Dose	Route*	Date		Days after infection 1	2	3	4	5	6	7	Remarks
Pneumonia without septicemia—*Concluded*													
	gm.	*cc.*											
1-15	1500	0.4	i.b.	5–15–33	Bl. cult.	0	0	0	0				Recovered 3rd–4th day
					X-ray	1/3 RLL	1/2 RLL	Same	Clearing				
					WBC 17.3	18.4	26.5	11.5	13.5				
1-16	1800	0.4	i.b.	5–15–33	Bl. cult.	0	0	0	0				Recovered 3rd day
					X-ray	RML	Spread	Clearing	Clearing				
					WBC 21.1	40.6	31.0	18.1	13.7				
1-21	1800	0.45	i.b.	5–23–33	Bl. cult.	0	0	0	0				Recovered 3rd day
					X-ray	1/3 RUL	Same	Clearing	Clearing				
					WBC 20.8	29.7	23.5	14.6	23.5				
1-22	1750	0.45	i.b.	5–28–33	Bl. cult.	0	0	0	0				Recovered 3rd day
					X-ray	2/3 RUL	Same	Clearing	Clearing				
					WBC 31.0	41.7	50.0	24.8	23.7				
1-25	1750	0.45	i.b.	5–29–33	Bl. cult.	0	0	0	0				Recovered 4th day
					X-ray	1/3 RUL	Spread	RUL	Clearing	Clearing			
					WBC 20.6	21.2	13.0	9.5	13.9				
Pneumonia with septicemia (1–250 colonies per cc. in first 3 days after infection													
2	1650	0.5	i.t.	10–26–31	Bl. cult.	0	15	4	0				Recovered 4th day
					X-ray	1/2 RLL 1/2 RML	Spread	3/4 RLL RML	Clearing				
					WBC								
7	3180	1.0	i.t.	11–28–31	Bl. cult.	0	0	1	0	0			Recovered 4th day
					X-ray	1/2 LLL	LLL	LLL	Same	Clearing			
					WBC								

1-2	1300	1.0	i.t.	12–16–31	Bl. cult.	0	0	0		0			Regarded as recovered. Sacrificed 6th day
					X-ray	LLL	LLL	Same		Same	LLL 1/3 LUL		Autopsy: Pneumonia LLL, 1/3 LUL
					WBC								HB culture: Pn. III
5-8	2000	0 75	i.t.	7–12–32	Bl. cult.	0	2	6	0				Recovered 4th–5th day. Sacrificed 7th day
					X-ray	1/3 LLL	1/2 LLL	LLL	LLL 1/2 LUL		LLL LUL		Autopsy: Pneumonia LLL (beginning resolution), 2/3 LUL (grey)
					WBC 26.3	41.6	9.4	4.3	7.1				
6-0	2300	0.85	i.t.	7–27–32	Bl. cult.	0	20	0	0				Recovered 4th day
					X-ray	1/3 LLL	3/4 LLL	Same	Clearing				
					WBC 13.0	13.1	7.5	11.7	13.0				
4-7	2200	0.5	i.b.	9–12–32	Bl. cult.	1	—	1	0				Recovered 4th day
					X-ray	1/2 RLL	Same	Same					
					WBC 20.6	13.1	8.8	10.6	9.3				
4-5	2050	1.0	i.b.	9–22–32	Bl. cult.	0	23	6	5	0			Recovered 5th day
					X-ray	1/3 RLL	RLL		Denser	Same			
					WBC 20.4	52.8	21.3	21.0	25.3	23.3			
9-7	2700	0.33	i.b.	2–20–33	Bl. cult.	0	1	2	10	4	1	0	Recovered 6th day
					X-ray	1/2 RUL	RUL 1/3 RML	RUL 1/2 RML	Same	Clearing		Clearing	
					WBC 27.9	47.0	45.0	30.9	28.0	17.8	25.6	22.6	
1-07	1750	0.3	i.b.	4–24–33	Bl. cult.	0	0	10	0	0			Recovered 4th day
					X-ray	1/2 RLL	1/2 RLL	Spread	Clearing	Clearing			
					WBC 19.6	12.3	10.8	9.3	11.1	22.4			
1-28	1500	0.5	i.b.	6–5–33	Bl. cult.	1	6	27	25	2		0	Recovered 6th day. Sacrificed 8th day
					X-ray	1/3 RLL	1/2 RLL	RLL	Same	Clearing			
					WBC 16.2	24.8	19.2	10.2	14.3	70.0		20.0	Autopsy: Pneumonia RLL resolving
1-32	1650	0.5	i.b.	6–5–33	Bl. cult.	0	3	2	0				Recovered 4th day
					X-ray	1/3 RLL	Spread	1/2 RLL	Clearing	Clearing			
					WBC 13.5	63.6	38.6	24.8	10.6				

TABLE II—*Continued*

No.	Weight	Dose	Route	Date		Days after infection 1	2	3	4	5	6	7	Remarks
Pneumonia with septicemia (1–250 colonies per cc. in first 3 days after infection)—*Concluded*													
	gm.	*cc.*											
4	2450	0.5	i.t.	11–4–31	Bl. cult.	12	+	185		653	1728	+	Died 7th day
					X-ray	1/2 RLL	RLL	Spread		Denser	RLL RML	Same	Autopsy: Pneumonia RLL, RML. Injection lower margin RUL
					WBC								
1-0	1650	1.0	i.t.	12–9–31	Bl. cult.	+	+	+	−				Died 5th day
					X-ray	1/2 RLL Lt. hilus	RLL Lt. hilus	Spread	−				Autopsy: Pneumonia 1/2 RLL, 1/2 LLL, most of LML and LUL
					WBC								
1-1	1300	1.0	i.t.	12–9–31	Bl. cult.	10	0	+		+			Died 5th day
					X-ray	2/3 LLL	LLL	LLL LML		LLL LML 1/2 LUL			Autopsy: Pneumonia LLL, LML, 1/2 LUL
					WBC								Culture: Pericardial fluid = Pn. III
1-6	1275	1.0	i.t.	1–19–32	Bl. cult.	6	133	38	37	3500 Post mortem			Died 5th day
					X-ray	1/3 RLL	2/3 RLL 1/3 RML 1/2 RUL	RLL RML 1/2 RUL	Spread	Spread			Autopsy: Pneumonia RLL, 2/3 RML, 2/3 RUL, 2/3 LLL (mottled)
					WBC								Culture: Pericardial fluid = Pn. III
1-7	1250	1.0	i.t.	1–26–32	Bl. cult.	−	140 Post mortem						Died 2nd day
					X-ray	Diffuse							Autopsy: Left empyema; pneumonia, all lobes extending from right and left hilus. (Included here because of p. m. culture)
					WBC 20.0								
4-1	1975	0.4	i.t.	4–26–32	Bl. cult.	1	4	75	1800				Died 5th day
					X-ray	1/3 RLL 1/3 LLL	Spread	Spread	Spread				Autopsy: Empyema, right and left. Pneumonia LLL, LML, 2/3 RUL, RLL, 1/2 RML; RUL (patchy)
					WBC 20.7	26.0	2.2	3.2	1.7				

5-2	1475	1.0	i.t.	6–9–32	Bl. cult.	0	22	60	+	30	26		Died 6th day
					X-ray	Rt. hilus Lt. hilus	3/4 RLL Lt. hilus	Spread	RML RUL 2/3 RLL	Same	Spread		Autopsy: Pneumonia 2/3 RLL, RML, 1/2 RUL, 2/3 LUL
					WBC 17.7	26.6	10.4	10.1	29.1	33.9	20.0		Culture: Pericardial fluid = Pn. III
9-0	1950	0.3	i.b.	1–23–33	Bl. cult.	38	32	236	174	106	1200	∞	Died 8th day
					X-ray	2/3 RLL	2/3 RLL	Same	Spread	RL		RLL RML	Autopsy: Right fibrinopurulent pleurisy, pericarditis; pneumonia RLL, RML, 1/2 RUL
					WBC 23.2	13.5	27.0	10.5	11.7	18.0		10.0	
1-10	2520	0.3	i.b.	4–24–33	Bl. cult.	0	0	2	18				Died 5th day
					X-ray	1/2 RLL	RLL	RLL RML	RLL RML 1/2 LLL				Autopsy: Pneumonia RLL, RML, 1/2 LLL, congestion RUL. Bilateral maxillary sinusitis
					WBC 11.4	17.1	9.5	2.5	12.2				
Pneumonia with septicemia (250–2000 colonies per cc. in first 3 days after infection)													
2-7	1110	0.2	i.t.	2–19–32	Bl. cult.	208	700	580	78	50	352	72	Recovered 9th day. Sacrificed 10th day
					X-ray	1/2 RLL	Same	Spread	RLL	Same	Denser	Clearing	Pneumonia RLL. Early resolution
					WBC 13.5		3.5	6.8	8.5	13.5	6.8	5.1	Cultures sterile
6-6	3550	2.0	i.t.	8–16–32	Bl. cult.	468	64	172	0				Recovered 4th day. Sacrificed 5th day
					X-ray	RLL	Same	Denser	Same				Autopsy: Pneumonia RLL
					WBC 23.6	40.1	23.0	15.1	12.1				
1-27	1700	0.5	i.b.	6–5–33	Bl. cult.	140	36	366	2	0			Recovered 5th day. Sacrificed 8th day
					X-ray	2/3 RUL	Spread	RUL RML	Same	Clearing		Clearing	Autopsy: RUL resolving; RML, early resolution
					WBC 21.0	40.0	14.1	13.7	6.8	34.0			
1-4	1150	1.0	i.t.	1–12–32	Bl. cult.	+	C	+					Moribund. Sacrificed 4th day.
					X-ray	1/2 RLL	Spread	RLL RML	RLL RML				Autopsy: Pneumonia RLL, RML Pericarditis (hem. strep.)
					WBC								HB culture: Pn. III and hem. strep.

TABLE II—*Continued*

No.	Weight	Dose	Route*	Date		Days after infection 1	2	3	4	5	6	7	Remarks
Pneumonia with septicemia (250–2000 colonies per cc. in first 3 days after infection)—*Concluded*													
	gm.	*cc.*											
2-0	1400	1.0	i.t.	2–8–32	Bl. cult.	0	1600	+					Died 3rd day
					X-ray	1/2 RLL	RLL RML	RLL RML 1/3 RUL					Autopsy: Calcified cysts lungs and abdomen. Pneumonia RLL, RML, center RUL
					WBC 16.0	5.3	3.4	2.3					HB culture: Pn. III and Gram-neg. bacillus
2-8	1875	0.3	i.t.	3–7–32	Bl. cult.	12	64	460	+				Moribund, sacrificed 5th day
					X-ray	1/2 RLL	2/3 RLL	RLL RML	RLL RML RUL	Same			Autopsy: Fibrinopurulent pleurisy right; pericarditis; pneumonia RLL, RML, RUL, part LLL
					WBC 23.0	18.5	8.0	4.2	13.5				
6-1	2625	1.0	i.b.	10–4–32	Bl. cult.	36	224	1440	2400	∞			Died 5th day
					X-ray	1/3 RLL	2/3 RLL	RLL RML 1/3 LML	RLL RML LML				Autopsy: Pneumonia RLL, RML, LML
					WBC 17.2	24.1	15.0	14.6	10.6	8.3			
6-3	2300	0.05	i.b.	10–10–32	Bl. cult.	0	19	1812	2240	4240			Died 5th day
					X-ray	1/3 RLL	3/4 RLL	RLL	Same	Same			Autopsy: Right fibrinopurulent pleurisy; pericarditis; pneumonia RLL
					WBC 52.0	31.2	20.9	15.7	29.7	36.9			
7-0	3750	1.0	i.b.	10–25–32	Bl. cult.	43	360	1208	∞				Died 5th day
					X-ray	1/3 RLL	RLL		RLL				Autopsy: Pneumonia RLL
					WBC 14.6	13.8	7.6	7.6	11.0				HB culture: Pn. III and Gram-neg. bacillus. Pericardial fluid: Pn. III

8-2	2000	0.25	i.b.	12–19–32	Bl. cult.	0	0	1320	∞	∞			Died 5th day
					X-ray	1/4 RLL	2/3 RLL	2/3 RLL	Same	Less dense			Autopsy: Fibrinopurulent pleurisy; pneumonic abscess; 1/3 RLL containing abscess 1 x 0.5 cm.
					WBC 9.1	13.9	19.8	25.8	4.9	2.6			
9-6	2600	0.33	i.b.	2–20–33	Bl. cult.	0	10	1220	∞				Died 4th day
					X-ray	1/3 RUL	3/4 RUL	RUL RML	Pneumothorax left side				Autopsy: Fibrinopurulent pleurisy, right; pneumonia RUL, RML, 1/3 RLL
					WBC 18.2	22.3	20.2	23.6	27.8				
4-6	1975	1.0	i.b.	9–27–32	Bl. cult.	170	120	345	64				Died 5th day
					X-ray	LLL	Spread	Same	LLL LML				Autopsy: Pneumonia LLL, LML, 1/3 LUL, 1/3 RML
					WBC 19.3	7.6	6.2	1.7	2.6				
Pneumonia with septicemia greater than 2000 colonies per cc. in first 3 days after infection													
1	1350	1.0	i.t.	10–20–31	Bl. cult.	∞							Died 1st day
					X-ray	RLL RML							Autopsy: Fibrinopurulent pleurisy; pericarditis; pneumonia RLL, RML
					WBC								
1-8	1350	1.0	i.t.	1–26–32	Bl. cult.	14,000							Died 2nd day
					X-ray	2/3 LLL 1/2 LML 1/2 LUL							Autopsy: Pneumonia inner 3/4 LLL, central 1/2 LML, median 1/3 LUL
					WBC 17.0								
2-3	1350	1.0	i.t.	2–8–32	Bl. cult.	12,100							Died 2nd day
					X-ray	Both lungs diffuse, patchy							Autopsy: Involvement of all lobes extending from hilus
					WBC 17.7	10.8							HB: Pn. III and Gram-neg. bacilli
2-2	1400	0.4	i.t.	2–24–32	Bl. cult.	220	∞						Died 2nd day
					X-ray	1/3 LLL 1/3 RLL	LLL LML RLL						Autopsy: Pneumonia LLL, LML, RLL, part RML
					WBC 21.0	22.0	7.5						HB: Pn. III and a few Gram-neg. bacilli

TABLE II—*Concluded*

No.	Weight	Dose	Route*	Date		Days after infection 1	2	3	4	5	6	7	Remarks
Pneumonia with septicemia greater than 2000 colonies per cc. in first 3 days after infection—*Concluded*													
	gm.	*cc.*											
2-6	1750	0.3	i.t.	2–29–32	Bl. cult.	340	1600	5280	2280				Moribund. Sacrificed 6th day
					X-ray	1/3 RLL 1/2 RML 1/2 RUL	Spread	Spread	RLL RML RUL	Spread 1/4 LLL			Autopsy: Pneumonia RLL, RML, RUL, inner 1/4 LLL
					WBC	15.0	10.0	7.2	6.1				
3-5	1450	0.5	i.t.	4–1–32	Bl. cult.	240	1390	5600					Moribund. Sacrificed 4th day
					X-ray	2/3 RLL 1/3 RML	RLL RML	RLL RML 1/2 RUL	Same				Autopsy: Small empyema, left; pneumonia RLL, RML, 1/2 RUL
					WBC 23 9	17.8	8.3	4.2					
3-6	1450	0.4	i.t.	4–11–32	Bl. cult.	6400	∞						Died 2nd day
					X-ray	2/3 RLL	RLL RML						Autopsy: Beginning empyema; pneumonia RLL, RML; congestion RUL
					WBC 11.1	4.8	1.2						
5-4	1600	1.0	i.t.	6–22–32	Bl. cult.	∞	∞						Found dead 3rd day
					X-ray	1/3 RLL 1/2 LLL	Spread						Autopsy: Pneumonia LLL, 1/2 LML, 1/3 RLL
					WBC	14.1	1.2						
5-5	1950	0.75	i.t.	7–5–32	Bl. cult.	+	3360						Died 2nd day
					X-ray	Diffuse on right	Spread						Autopsy: Pneumonia RLL, 2/3 RUL, 1/2 RML; hilus LLL
					WBC	7.5	3.1						

5-7	2253	1.0	i.t.	7–5–32	Bl. cult.	+	8736	20,800					Died 5th day
					X-ray	1/3 RLL	2/3 RLL	RLL	RLL RML				Autopsy: Empyema; pneumonia RLL, RML
					WBC 18.3	11.4	5.7	1.4	5.0				Pericardial fluid: Pn. III
5-9	2030	1.0	i.t.	7–19–32	Bl. cult.	3040	7500	∞					Died 4th day
					X-ray	Mottled shadow both lower lobes							Autopsy: Pneumonia RML, 1/2 RLL
					WBC 9.8	8.0	5.2	3.0					HB: Pn. III and Gram-neg. bacillus
6-5	1325	1.5	i.t.	8–9–32	Bl. cult.	∞							Died 2nd day
					X-ray	1/2 RLL							Autopsy: Pneumonia 1/2 RLL
					WBC 14.7	7.3							HB: Pn. III and Gram-neg. bacillus
6-8	2550	1.5	i.b.	9–6–32	Bl. cult.	∞							Died 1st day
					X-ray	RLL							Autopsy: Pneumonia 1/2 RLL
					WBC 13.8	3.6							
7-3	1800	0.5	i.b.	11–8–32	Bl. cult.	2240	∞						Died 2nd day
					X-ray	RLL (mottled)							Autopsy: Empyema. Pneumonia RLL; collapsed RML, congested RUL
					WBC 27.1	4.1	0.5						
7-4	1650	0.35	i.b.	11–14–32	Bl. cult.	∞							Died 2nd day
					X-ray	RLL RML							Autopsy: Pneumonia 2/3 RLL, 2/3 RML, patchy engorgement RUL
					WBC 20.7	10.3							
1-09	1400	0.3	i.b.	4–24–33	Bl. cult.	2200	1600	+	4000	+			Died 6th day
					X-ray	1/2 RUL 1/3 RML	3/4 RUL 1/2 RML	RUL RML	Same	Spread			Autopsy: Fibrinopurulent pleurisy right; pericarditis; pneumonia RUL, RML; congestion RLL
					WBC 21.0	29.6	19.6	9.3	8.5	11.4			

of the fatal cases with mild (1–250 colonies per cc.) septicemia, three or more lobes were involved. But with the higher degrees of septicemia, death frequently occurred when only one or two lobes were involved. In the latter animals, death occurred comparatively early in the disease, before sufficient time had elapsed for further spread to occur. The details of the disease in different groups of animals are given below.

Group A. Lobar Pneumonia without Septicemia

In this group are included 20 monkeys, all of which recovered.

The weights varied from 950 gm. to 2200 gm., with an average of 1850 gm. The amount of culture varied from 0.1 cc. to 1.0 cc., with an average dose of 0.42 cc. In 15 animals, only one, or part of one lobe, was involved. The average time of recovery was 4.3 days after infection. In those with only one lobe involved, recovery took place on an average of 3.4 days after infection, while in the others the duration of the disease averaged 6.4 days. Among the latter, there were 2 cases in which relapses occurred, but with ultimate recovery on the 8th and 12th days respectively. In the entire group, there was a tendency, as shown by roentgenograms, for a lesion which was well localized on the 1st day, to extend on the 2nd day, and to show evidence of beginning resolution on the 3rd day. The white blood cell count tended to increase on the day after infection, and to remain at a relatively high level throughout the course of the disease.

The charts and protocols of cases illustrative of this group are presented.

Monkey 1-16 (Chart 2) represents an example of pneumonia without septicemia, in which the disease was of brief duration. The temperature fell by crisis on the 2nd day after infection, and resolution was evident in the roentgenogram taken on the 3rd day.

Monkey 8-9 (Chart 3) is another instance of pneumonia without septicemia. The pulmonary involvement spread through the right upper lobe and right middle lobe during the first 4 days, after which resolution began, and recovery apparently took place on the 6th day. The following day the temperature rose again and a new pneumonic process was noted in the right lower lobe. Extension occurred during the next 3 days, although there was no demonstrable septicemia, and leukocytosis persisted. Recovery finally occurred on the 12th day.

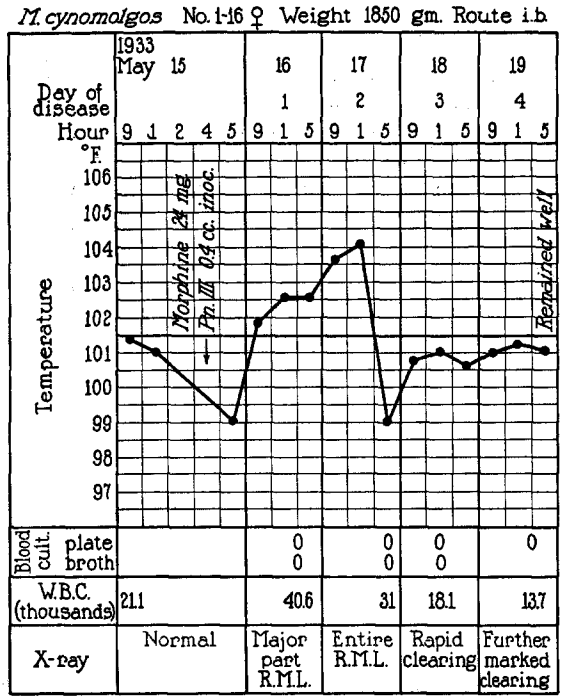

CHART 2. Experimental pneumonia showing an abortive course.

Lobar Pneumonia with Septicemia

Since the height of the septicemia accompanying experimental pneumonia in monkeys appears to bear a relation to the outcome of the disease, the remainder of the cases have been subdivided on the basis of the number of pneumococci in the circulating blood during the first 3 days after infection: 1 to 250 colonies per 1 cc. of blood—mild to moderate septicemia; 250 to 2000 colonies per cc.—heavy septicemia; 2000 colonies or more per cc.—extreme septicemia.

Group B. Lobar Pneumonia with Septicemia (1–250 Colonies per Cc.)

This group comprises 20 monkeys. Of these, 11 recovered and 9 died, a mortality of 45 per cent.

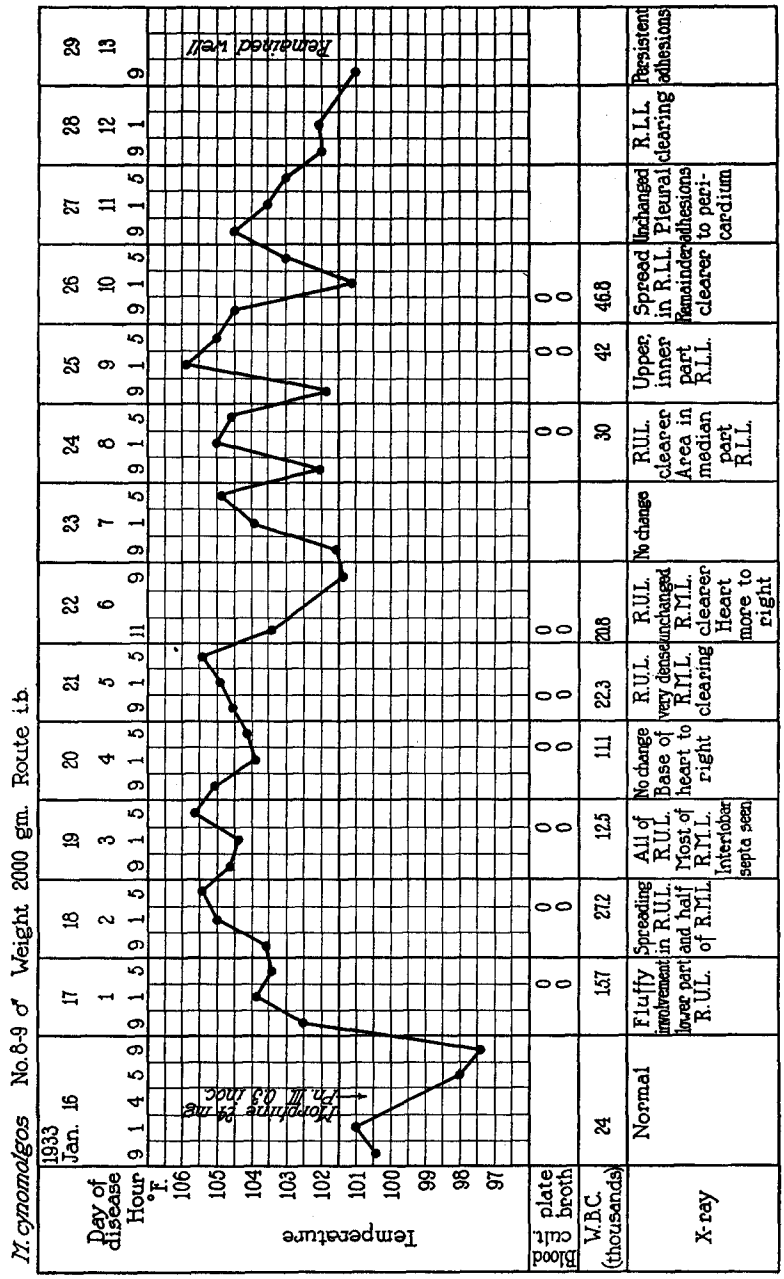

CHART 3. Experimental pneumonia with a relapse and prolonged course.

There is one case in which enumeration of colonies was not made, but which is included because the course of the disease is typical of that occurring in this group, and another case in which, although no estimates of the height of septicemia were made during life, the blood culture made post mortem contained 140 colonies of pneumococci per 1 cc. of blood. The average weight of the animals of this series was 1923 gm., the average dose of pneumococci employed was 0.68 cc., while the range of dosage in both the recovered and fatal cases was from 0.3 cc. to 1.0 cc.

Of the 11 recovered cases, only 3 had involvement of two lobes, while in the others there was only one lobe or part of one lobe involved. The average duration of the disease was 4.5 days. There was a tendency for the lesion to spread during the first 3 days. In recovered cases, the white blood count generally reached its lowest level at the time when the number of bacteria in the blood and the extent of the pulmonary involvement were greatest. A subsequent rise of the white blood cell count occurred during recovery.

In one of the 9 fatal cases, there was involvement of two lobes, in the other 8 fatal cases of three or more lobes. The average time of death was 5.4 days after infection. In 4 of these cases, Pneumococcus III was obtained from the pericardial fluid at autopsy, and in 3 empyema was found. In the 4 instances in which white blood counts are available, there was a decrease in the number of circulating leukocytes as the pneumonic process spread.

The charts of typical cases of this group are shown.

Monkey 4-5 (Chart 4) represents a case of pneumonia which recovered by crisis on the 5th day of the disease; a mild septicemia was present from the 2nd to 4th days. No depression of the leukocyte counts occurred.

Monkey 9-7 (Chart 5) serves as an example of pneumonia with mild septicemia from which the animal recovered spontaneously on the 6th to 7th day. Resolution of the pneumonic process had commenced before the septicemia had completely subsided. The leukocytes were increased in number throughout the course of the disease.

Monkey 1-6 (Chart 6) represents the type of case in which a progressively spreading pneumonia with a relatively mild septicemia terminated fatally on the 5th day. The animal showed only a slight febrile reaction. Autopsy revealed the presence of consolidation of the entire right lower lobe, two-thirds of the right middle and right upper lobes, and irregular consolidation of two-thirds of the left lower lobe.

Monkey 9-0 (Chart 7) illustrates the course of the disease in an animal in which the persistently spreading pneumonia is accompanied by a moderately severe septicemia increasing to a terminal, heavy septicemia. There was only moderate depression of the circulating leukocytes. Death resulted on the 8th day. On the day of death, a line suggesting pleural effusion was noted in the X-ray. Consolidation of the entire right lower and middle lobes and of one-half the right

M. cynomolgos No. 4-5 ♀ Weight 2050 gm. Route i.b.

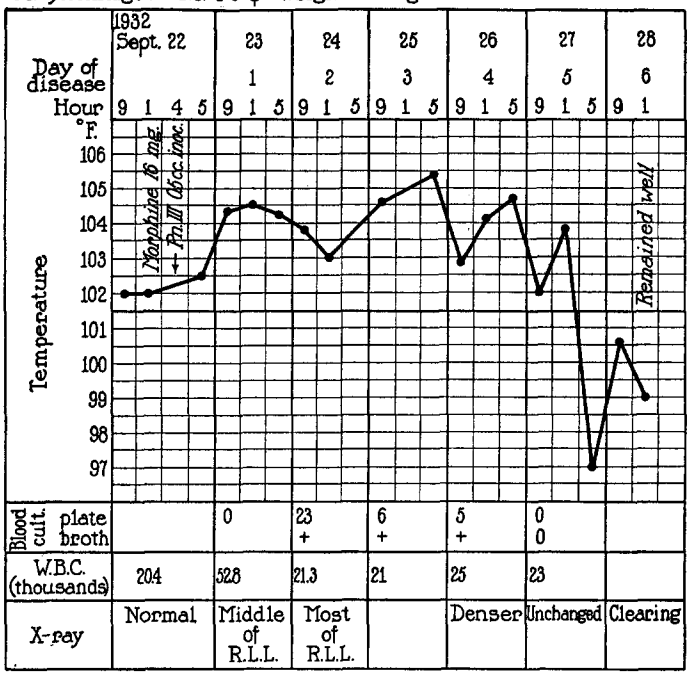

CHART 4. Experimental pneumonia with a mild septicemia followed by crisis.

M. cynomolgos No. 9-7 ♀ Weight 2700 gm. Route i.b.

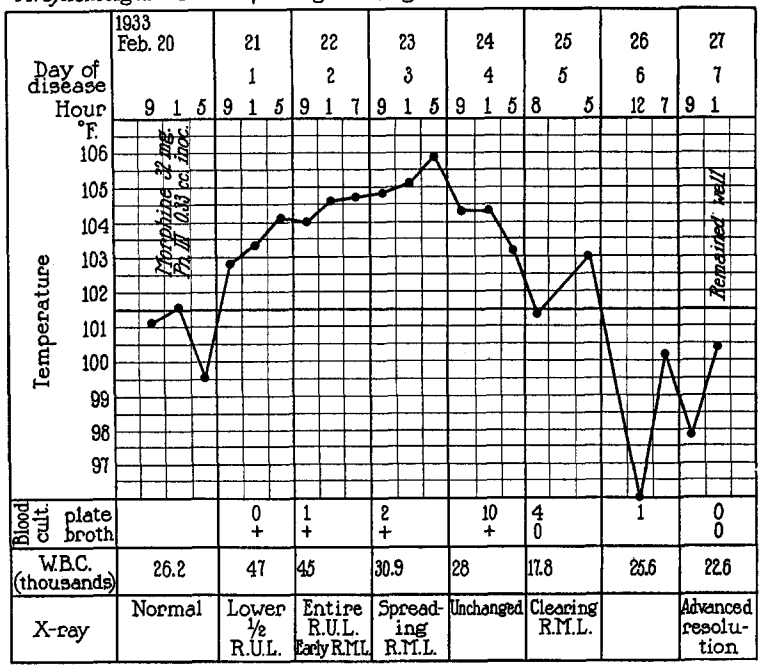

CHART 5. Experimental pneumonia with a mild septicemia followed by recovery.

M. cynomolgos No. 1-6 ♂ Weight 1275 gm. Route i.t.

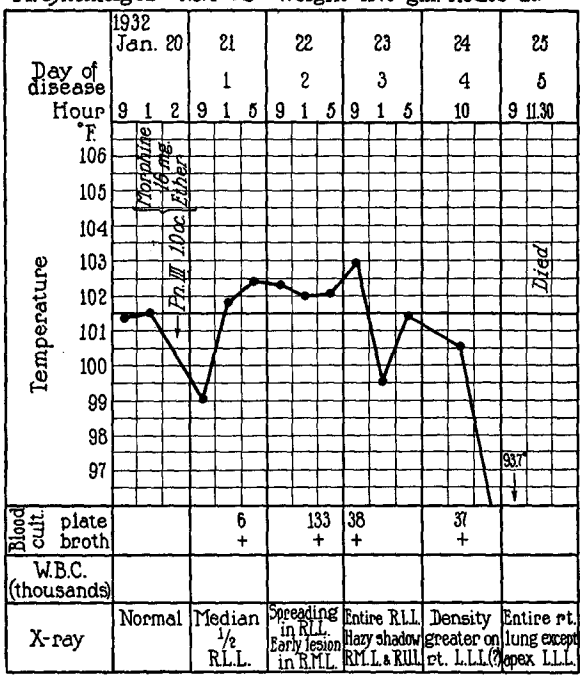

CHART 6. Experimental pneumonia with a relatively mild septicemia terminating fatally.

M. cynomolgos No. 9-0 ♂ Weight 1950 gm. Route i.b.

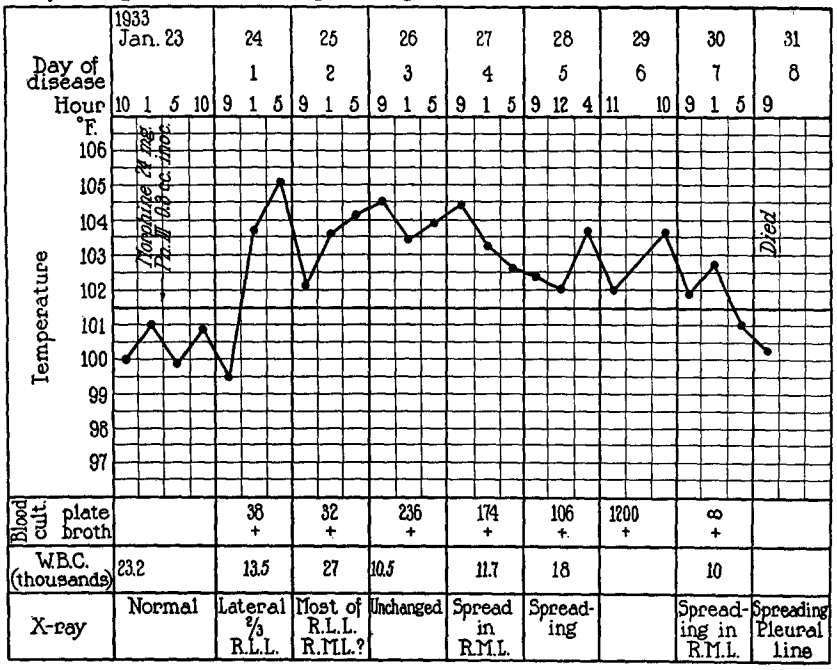

CHART 7. Experimental pneumonia showing a persistent spread with a moderately severe septicemia followed by a terminal heavy septicemia.

upper lobe was found at autopsy. Fibrinopurulent pleurisy and pericarditis were present.

Group C. Lobar Pneumonia with Septicemia (250–2000 Colonies per Cc.)

The animals included in this group present a more severe form of the disease than those of the preceding group. Of 12 animals, 3 recovered, a mortality of 75 per cent.

The height of the septicemia in the 3 recovered animals during the first 3 days was 700, 468, 366 colonies per 1 cc. of blood, respectively, while in the fatal cases the highest was 1812 colonies per 1 cc. The average duration of the disease in the recovered cases was 6 days, in the fatal 4.6 days. The average weight of the recovered animals was 2120 gm.; that of the animals which died was 2280 gm. The inoculum of Type III Pneumococcus in recovered animals was 0.2, 2.0, 0.5 cc., respectively, with an average of 0.9 cc.; in fatal cases the average was 0.6 cc., with a range from 0.05 cc. to 1.0 cc. In 2 of the recovered cases only one lobe was involved, in the other, two lobes. In 2 of the fatal cases one lobe was involved, 2 had two lobes affected, and in 5 there was involvement of three or more lobes. In 6 of the 9 fatal cases, Pneumococcus III was obtained from pericardial or pleural fluid at autopsy.

Charts illustrating the variations in the course of infection in this group are presented.

Monkey 1-27 (Chart 8) is an instance in which recovery occurred following a severe form of the disease. The pneumonia spread during the first 3 days, with the septicemia reaching its height (366 colonies per cc.) at that time. On the 4th day resolution began, and the blood was sterile on the 5th day. The leukocyte count varied inversely with the septicemia.

Monkey 6-1 (Chart 9) represents the type of case in which a progressively spreading lesion with increasing septicemia terminated fatally on the 5th day. The white blood count fell steadily. At autopsy, complete consolidation of the right lower and middle lobes and of the left middle lobe was found.

Monkey 9-6 (Chart 10) is an example of the course of the disease in an animal in which, with a spreading pneumonic lesion, septicemia is absent at first, then mounts rapidly to a fatal outcome on the 5th day. The leukocytes were maintained at a good level throughout. A pneumothorax, apparently spontaneous, occurred on the uninvolved side on the 4th day. The chart also records the depressant effect of a preliminary injection of morphine on the temperature of the animal. Autopsy revealed a left-sided pneumothorax with partial collapse of the lung. On the right side, consolidation was complete in the upper and middle lobes

M. cynomolgos No. 1-27 ♂ Weight 1700 gm. Route i.b.

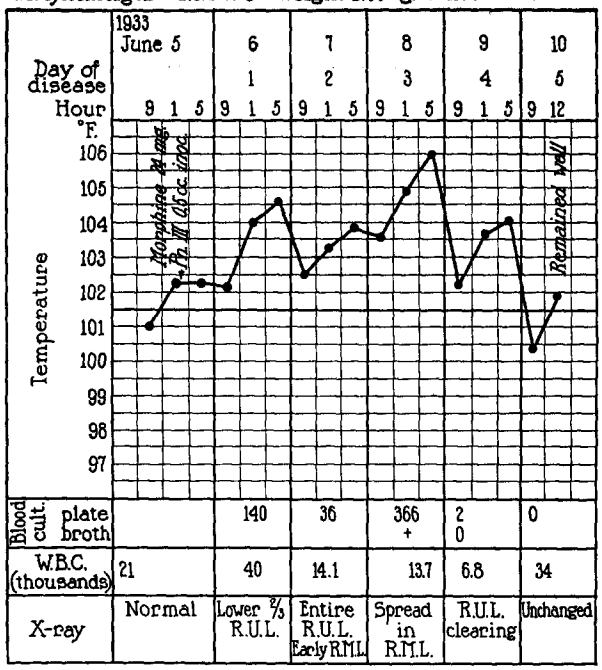

CHART 8. Experimental pneumonia with a moderately severe septicemia followed by recovery.

M. cynomolgos No. 6-1 ♂ Weight 2625 gm. Route i.b.

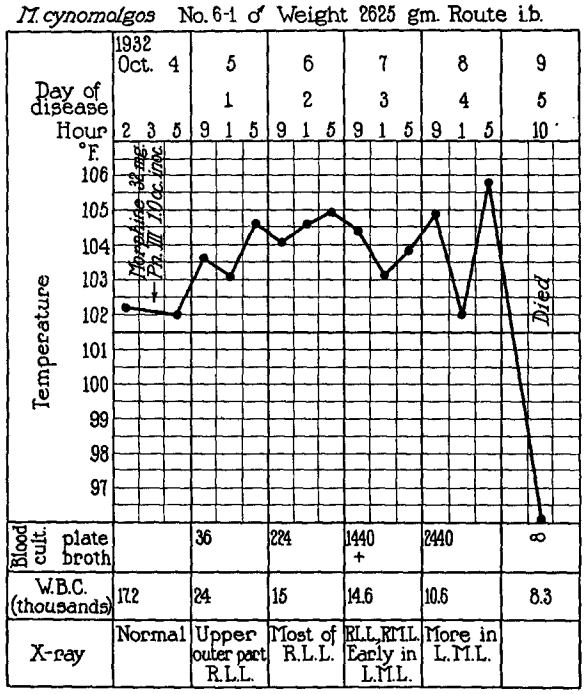

CHART 9. Monkey 6-1 represents the type of case with a spreading lesion and increasing septicemia terminating fatally.

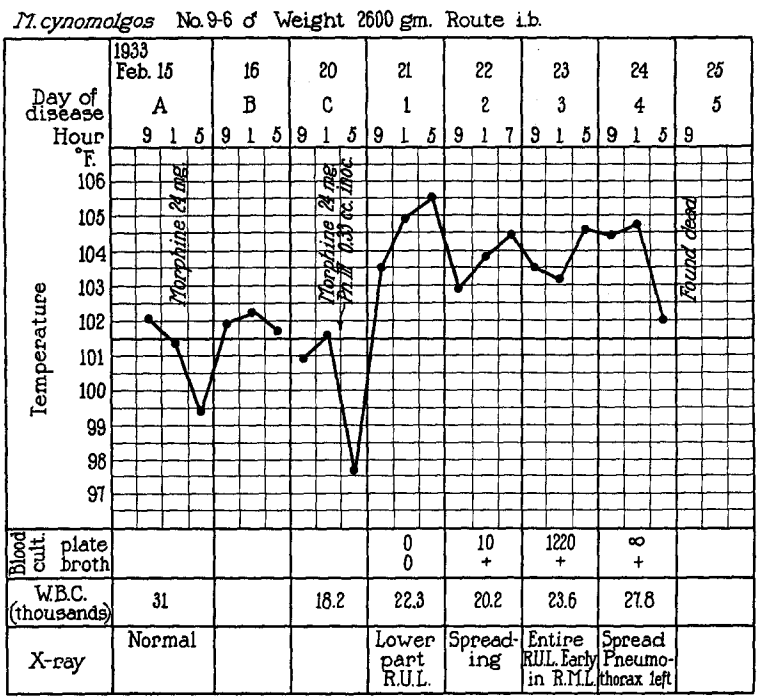

CHART 10. Experimental pneumonia with negative blood culture at first, followed by a rapidly mounting septicemia. Note depressant effect of preliminary injection of morphine on temperature.

and present in one-third of the lower lobe. Fibrinopurulent pleurisy was also present. Roentgenograms taken during the course of the disease are shown in Figs. 7 to 11.

Group D. Lobar Pneumonia with Septicemia (More than 2000 Colonies per Cc.)

In this group of 16 monkeys, there were no recoveries. The infection in these animals was characterized by the frequent early involvement of more than one lobe, sometimes diffuse, a rapidly mounting septicemia, exhaustion of leukocyte response, and early death.

The average weight of the animals was 1670 gm.; the average infecting dose was 0.79 cc., with a maximum of 1.5 cc. and a minimum of 0.3 cc. In 2 monkeys, only one lobe was involved; in 6, two lobes were affected, while in the remaining 9 animals three or more lobes were involved. In 6 instances, empyema, peri-

carditis, or both, were present. The average duration of the disease was 2.8 days. In several instances at autopsy, in addition to Type III Pneumococcus, Gram-negative bacteria of the *B. coli* or *B. lactis aerogenes* group were found. These organisms were considered terminal invaders. It is of interest to note that in several instances they were present in the throat cultures of the same animals before infection.

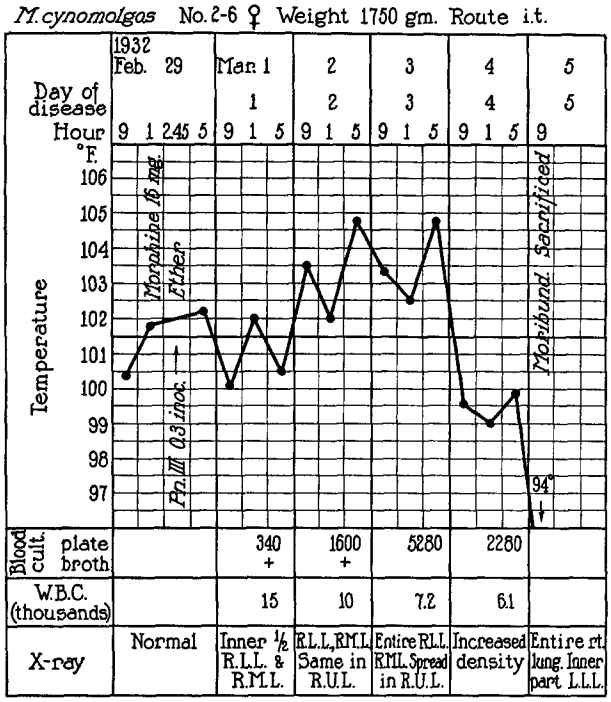

CHART 11. Experimental pneumonia with severe septicemia the first 3 days of disease.

The charts of representative cases are presented.

Monkey 2-6 (Chart 11) is an example of a consistently spreading pneumonia with a septicemia of 5280 colonies per 1 cc. of blood on the 3rd day. There was a progressive depression of the leukocytes. The animal was sacrificed when moribund on the 5th day. Consolidation of the entire right lung, as well as of the lower part of the left lower lobe, was found.

Monkey 7-3 (Chart 12) represents the rapidly fatal type of disease with empyema and extreme septicemia. In this instance there was almost a complete

exhaustion of the leukocytes on the 2nd day, when death occurred. The temperature was subnormal throughout. At autopsy, 6 cc. of seropurulent fluid was found in the right pleural cavity. The entire right lower lobe was consolidated; the right middle lobe was collapsed and covered with gelatinous exudate; the right upper lobe was markedly congested.

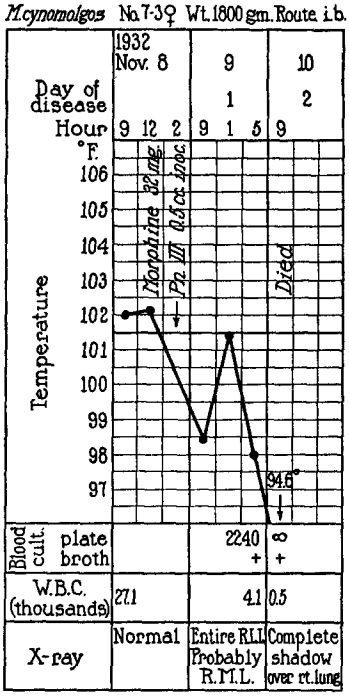

CHART 12. Experimental pneumonia representing the rapidly fatal type of disease with empyema and extreme septicemia.

DISCUSSION

In the present group of 68 monkeys, in which intrapulmonary infection was established by the intratracheal or intrabronchial inoculation of Type III Pneumococcus, a disease closely resembling lobar pneumonia in man was produced. In 50 per cent of the animals, the disease terminated fatally. There was usually an initial pneumonic consolidation of one lobe, or part of one lobe, which then spread to involve a greater pulmonary area. An initial rise of the circulating white blood cells was commonly followed by a decrease at the height

of the disease. The temperature was elevated during the disease, and usually fell with a critical drop at the time of recovery. Invasion of the blood by Type III Pneumococcus occurred in 70 per cent of the cases.

The severity of the disease varied with individual animals. Of 20 monkeys in which pneumonia was unaccompanied by septicemia, all recovered, many of them after a brief course during which comparatively little extension of the primary lesion occurred. On the other hand, no recoveries occurred in 16 monkeys in which the pulmonary infection was associated with extreme septicemia. In these instances, subnormal temperature, marked depression of the leukocytes, and rapidly mounting septicemia were followed by early death; at times there was diffuse pulmonary involvement. Empyema and pericarditis were noted frequently.

In the intermediate groups in which pneumonia was accompanied by moderate or heavy septicemia, the disease ran a more uniform course, with a duration of 4.5 to 6 days. In animals in which the septicemia was moderate (1–250) during the first 3 days, the mortality rate was 45 per cent; with heavy septicemia (250–2000) accompanying pneumonia, the mortality rate reached 75 per cent.

Although a number of factors are involved, the degree of septicemia accompanying the pneumonia appears to be the most useful clinical index of the ultimate outcome of the disease in the individual case. With septicemia, more progressive extension of pneumonia is observed, the depression of leukocytic response is more marked, and the general illness of the animal is usually more pronounced. In contrast to Type III pneumococcus pneumonia in man, the septicemia which accompanies experimental lobar pneumonia in monkeys is of a higher order, and spontaneous recovery may occur after a degree of septicemia rarely encountered even in fatal cases in man. Nevertheless, in the marked inconstancy of the clinical picture, experimental pneumonia of the monkey resembles Type III pneumococcus pneumonia in the human being.

Under the conditions of the present study, it has been impossible to predict in advance the probable course of experimentally induced pneumonia in the individual monkey. The summary of experience has been that the greatest variable is the individual resistance of the

animal, which is probably the resultant of many interrelated factors. Attempts were made, therefore, to analyze the different measurable variables and, if possible, to correlate them with the differences observed in the course and outcome of the disease in different animals.

The virulence of the particular strain of Type III Pneumococcus used throughout these experiments was, so far as could be determined, relatively constant. This is shown by the fact that when tested in rabbits, after an interval of 9 months, its original virulence for that species was unchanged.

In a number of instances, studies were made of the pneumococcidal power of the blood of monkeys before infection, but the results were uniformly negative. Similarly, skin tests with pneumococcus nucleoprotein revealed no suggestion of previous sensitization, since the tests elicited no reaction in the normal animals. These observations afforded no evidence of preceding immunization such as has been emphasized by Wadsworth (9) and Stillman (10).

A survey of the original white bood counts, the counts done on the 1st day after infection or averaged during the first 3 days of the disease, presented no evident relationship between the height of the early counts and the course or outcome of the pneumonia. There was, nevertheless, a distinct tendency for the number of circulating leukocytes to fall during the height of the disease and to rise with recovery. Less constant was the tendency for the leukocytes to rise when empyema or pericarditis occurred, even though these cases always terminated fatally. A similar lack of correlation between the white blood counts and the outcome of experimental pneumonia was also observed by Blake and Cecil (1) in their study.

As regards the influence of the size of the infecting dose of organisms upon the character of the resulting disease, it may be stated that the mortality rate was higher in the animals which received the largest doses of culture. There was, however, marked variation in the severity of the disease in individual animals regardless of the amount of culture inoculated. Furthermore, the extent of pulmonary involvement and the height of the septicemia following infection with the large doses of organisms was no greater than that frequently seen in animals receiving the small doses. The same facts are demonstrated when the dose is computed on the basis of body weight.

There appears, therefore, to be no clear relationship between the size of the infecting dose and the outcome of the experimental pneumonia.

General atmospheric conditions apparently play a rôle in the resistance of the animals to infection. In general, during the winter the type of infection produced with small doses of organisms was similar to that obtained in the warm weather with larger doses of organisms. The individual variation was noteworthy at all times, however.

The severity of the depressant action of ether or morphine, indicated by stupor and subnormal depression of body temperature, differed considerably in different animals. There was apparently a tendency for monkeys in which the depressant effect was most marked to be the sicker. Furthermore, the inhalation of ether is known at times to produce in experimental animals a hemorrhagic edema of the lungs. Temporary lowering of the physiological resistance of an experimental animal, so as to allow bacteria introduced into the respiratory tract to gain a foothold, has been described following chilling, alcohol, morphine, fatigue, and deficient diets. In the present study, it is not unlikely that differences in the effect of morphine or ether upon different animals may have had a definite influence upon the severity of the disease in these animals.

Localization of the infecting material should undoubtedly have a distinct influence upon the course of the disease. In the great majority of animals which recovered spontaneously, only one or two lobes were involved, whereas with more widespread involvement a high percentage of fatalities occurred (Chart 1). With the intratracheal method, in which ether anesthesia was used, there is a somewhat greater tendency for the infecting material to be distributed more widely than when the intrabronchial method is employed. Reference to Table II, however, reveals similar forms of disease produced by both methods. With the intratracheal route, the early consolidation was most frequently noted by X-ray in the median portion of the involved lobe, whence it spread to involve the entire lobe; with the intrabronchial method, by which the infecting material is placed farther out in the bronchial tree, the original consolidation was first seen in a more lateral position in the lobe, spreading medially. In either case, the lesion may progress to involve one or more lobes completely, or the process may be limited to part of a lobe.

The use of starch as a protective medium for the bacteria, as suggested by Terrell, Robertson, and Coggeshall (8), has been found to be unnecessary for the production of lobar pneumonia in the Java monkey. In 8 animals inoculated by the intrabronchial route with broth cultures of Type III Pneumococcus alone, the results were quite similar to those obtained when starch was employed. In these instances, again, distinct variations in the course of the disease in individual monkeys was noted.

The features mentioned are those which are considered to play a rôle in influencing the course of the experimental pneumonia due to Type III Pneumococcus after it has been established. A discussion of the pathogenesis and pathology will appear in a subsequent communication.

The results of the present study furnish evidence that, with Type III Pneumococcus, pneumonia of lobar distribution comparable in its clinical features to human lobar pneumonia can be produced in monkeys. The course of the disease is variable, and under existing conditions the result in individual animals is not predictable in the early stages of the disease.

SUMMARY

It has been possible by the intratracheal or intrabronchial inoculation of Type III Pneumococcus to produce in monkeys of the *M. cynomolgos* species an experimental pneumonia which in its clinical aspects closely resembles pneumococcus lobar pneumonia in man. The experimental disease is characterized by the development of a well localized pulmonary lesion of lobar distribution which tends to spread, the frequent occurrence of septicemia, a sustained fever, and the termination of the infection after a variable interval, in recovery or death of the animal. Wide variations in the severity of the disease in different monkeys have been noted. These variations appear to be due primarily to differences in the resistance of individual animals. The height of the septicemia accompanying the experimental pneumonia has been found to be the most valuable objective index of the probable outcome of the disease. Other factors which may influence the course and outcome of the disease are discussed.

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EXPLANATION OF PLATES

PLATE 45

The intrabronchial method of inoculation demonstrated by the injection of lipiodol.

FIGS. 1 to 3. Roentgenograms of monkey's lung showing catheter in upper bronchus of right lower lobe and the different stages in the injection of 0.5 cc. of lipiodol.

FIG. 4. Lateral view of same animal.

FIG. 5. Roentgenogram of monkey's chest after the injection of 0.5 cc. of lipiodol into both the left lower lobe and the lower part of the right upper lobe.

FIG. 6. Same as Fig. 5, with animal in lateral position.

PLATE 46

Roentgenograms taken during the course of experimental pneumonia in Monkey 9-6, which terminated fatally.

FIG. 7. Control. Before infection (Feb. 10).

FIG. 8. 1st day after infection (Feb. 21), showing early consolidation in the right upper lobe.

FIG. 9. 2nd day (Feb. 22), showing spread of pneumonia in the upper part of the right upper lobe.

FIG. 10. 3rd day (Feb. 23), showing complete involvement of the right upper lobe and probably extension into the right middle lobe.

FIG. 11. 4th day (Feb. 24), showing a left pneumothorax together with a well marked involvement of the right upper and middle lobes (Chart 10).

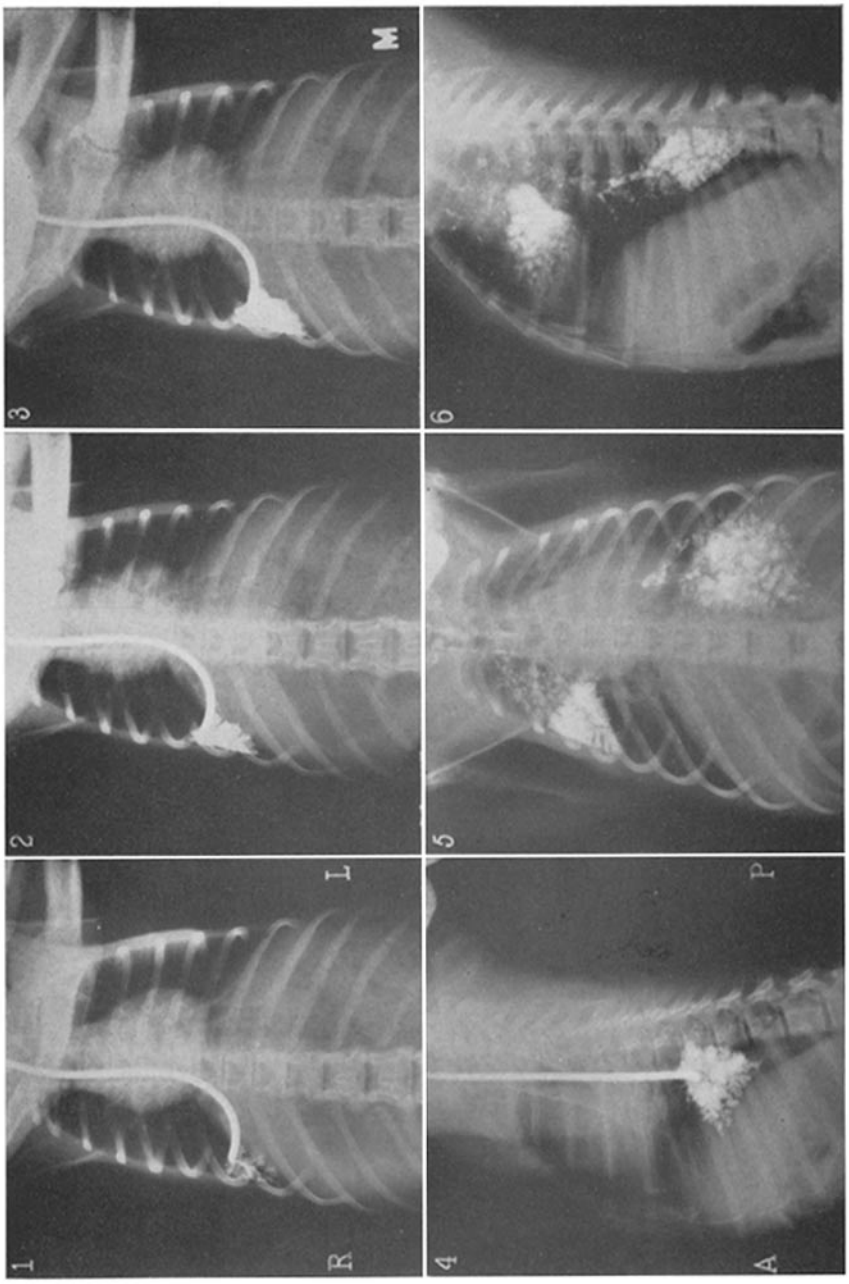
PLATE 47

Roentgenograms of fatal pneumonia in Monkey 5-2.

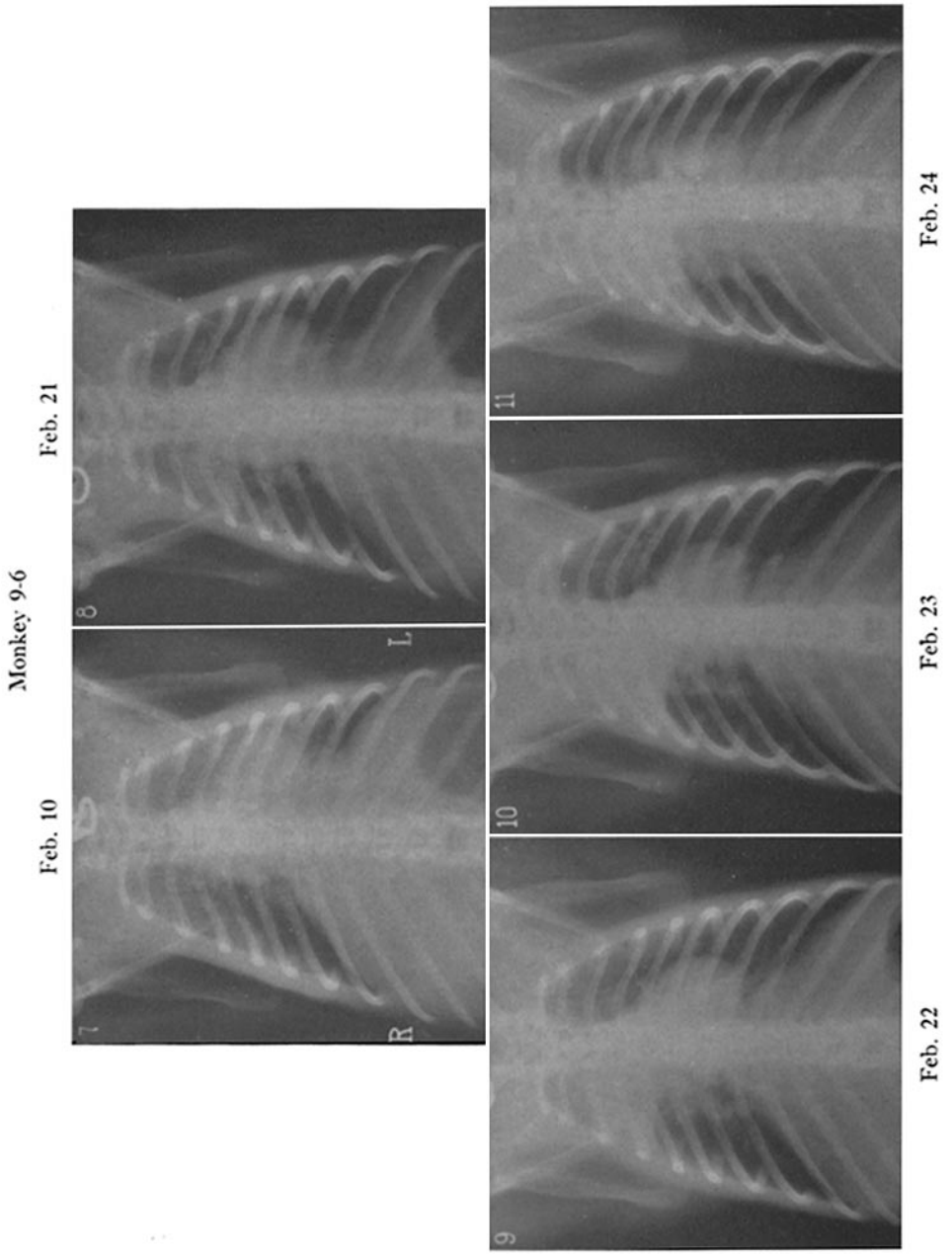
FIG. 12. Control. Before infection (June 8).

FIG. 13. 1st day after infection (June 10), showing early pneumonia in right middle lobe.

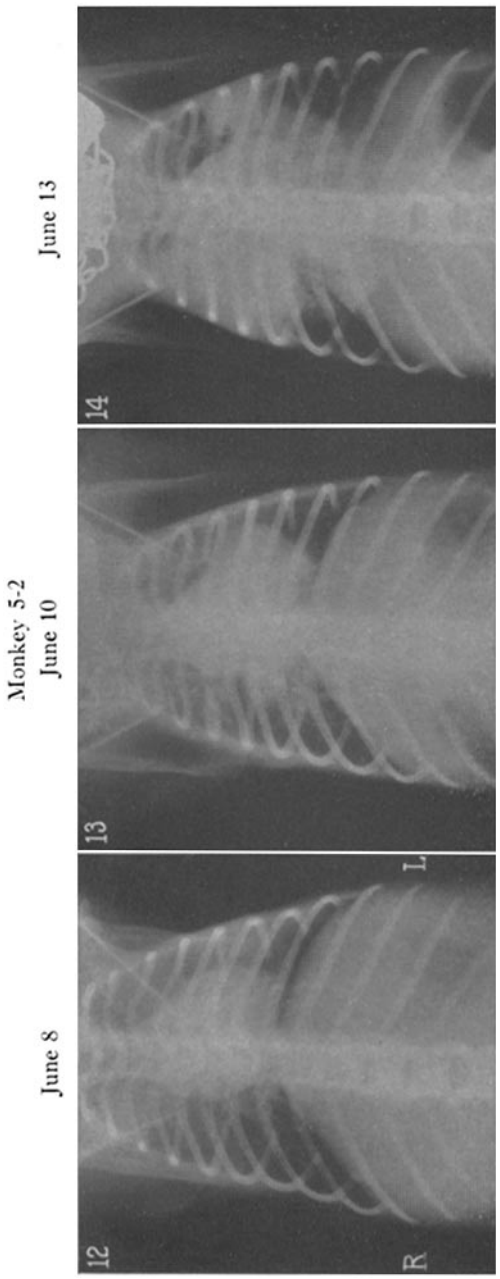
FIG. 14. 4th day (June 13), showing a more diffuse pneumonia involving most of the right middle and upper lobes, the median part of the right lower lobe, and the lower part of the left upper lobe.



(Francis and Terrell: Type III pneumococcus pneumonia. I)



(Francis and Terrell: Type III pneumococcus pneumonia. I)



(Francis and Terrell: Type III pneumococcus pneumonia. I)