with additional $CaCl_2$ and thromboplastin. The theoretical level (100%) is present at the start, and the fall to 95% in 2½ hours and 75% in 4 hours is again of a minor order, quite unlike the dramatic prothrombin disappearance reported in the Iowa experiments.[6]

Discussion. It is concluded that thrombin and (citrated) prothrombin can co-exist with no more destruction of either than can readily be attributed to the natural instability of both preparations. Thrombin itself is neither an activator nor a destroyer of prothrombin. The lytic factor is an independent entity which, from previously reported data,[5] we believe to be an enzyme factor, probably serum tryptase.

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Influence of Sulfathiazole Therapy on Plasma Lipids in Pneumonia.*

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Previous investigations[1, 2] by the author have shown that during the febrile periods of acute infections such as pneumonia, there is a definite fall in the values for total and ester cholesterol, total fatty acids and phospholipids. The iodine numbers of the total fatty acids and of the phospholipid fatty acids also are lowered.

Further studies[3, 4] have revealed the interesting fact that the early administration of specific serum for pneumonia in children leads to a critical drop in the fever with rapid recovery which prevents the development of any significant changes in the levels of the plasma lipids. On the other hand, chemotherapy with sulfapyridine also causes a fall in the fever with improvement in the patient's condition but with little or no influence on the lipids of the serum which continue to undergo changes similar to those found in untreated cases of pneumonia. This latter observation raises the question as to whether

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1 Stoesser, A. V., and McQuarrie, Irvine, *Am. J. Dis. Child.*, 1935, **49**, 658.

2 Stoesser, A. V., *Am. J. Dis. Child.*, 1938, **56**, 1215.

3 Stoesser, A. V., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 168.

4 Stoesser, A. V., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 201.

the response to all forms of chemotherapy is the same. Sulfathiazole, the thiazole analogue of sulfapyridine, was therefore investigated.

Six children ranging in age from 6 to 13 years were selected. All of the subjects were ill with pneumonia due to the pneumococcus. They received 0.3 g per kg of body weight per day of sulfathiazole for the first 48 hours after admission to the hospital and 0.15 g thereafter. The drug was administered orally every 4 hours, 6 times per day. It was well tolerated by all of the children. The first sample of blood for lipid determinations was obtained just before the sulfathiazole was started. At this time each child had been ill from one to 2 days and the fever was high, ranging between 39.5 and 40.4°C. The second sample was collected about 24 hours after critical drop in temperature to normal. The third and fourth blood samples were obtained on the fourth and seventh days of convalescence respectively. The sulfathiazole was discontinued on the morning of the fourth day of normal temperature just after the third sample had been drawn. Bloor's methods[5, 6, 7] were used to determine the total, ester, and free cholesterol values. The microgravimetric technic of Wilson and Hansen[8, 9] was employed in studying the other serum lipids. The Rosenmund-Kuhnhenn method as described by Yasuda[10] was used to determine the iodine absorption of the serum fatty acids.

The results are summarized in Table I.

The pneumonic infections in the 6 children were similar in nature. The cholesterol values were already a little lower than normal before sulfathiazole was started. The lowest level was reached in case 3. Following the administration of the drug, 4 of the subjects experienced a precipitous drop in the temperature to normal in 24 hours. In cases 2 and 3 the temperature did not reach the normal level until 48 hours after the onset of the drug therapy. After one day of no fever, the second blood sample was collected and the cholesterol esters were found to have risen to within the normal range in all except case 3. The roentgenograms revealed beginning resolution in 4 cases. On the fourth day of convalescence it was almost complete in all subjects. There was little change in the cholesterol values. By the seventh day, the roentgenograms showed complete resolution. The total cholesterol and esters were normal.

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5 Bloor, W. R., *J. Biol. Chem.*, 1916, **24**, 227.

6 Bloor, W. R., and Knudson, Arthur, *J. Biol. Chem.*, 1916, **27**, 107.

7 Bloor, W. R., personal communication to the author.

8 Wilson, W. R., and Hansen, A. E., *J. Biol. Chem.*, 1936, **112**, 457.

9 Hansen, A. E., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 376.

10 Yasuda, M., *J. Biol. Chem.*, 1931-32, **94**, 401.

TABLE I.
Plasma Lipids of Pneumonia Before, During and After Administration of Sulfathiazole.

Case No.	Total cholesterol				Cholesterol esters				Free cholesterol			
	Mg per 100 cc serum											
	A	B	C	D	A	B	C	D	A	B	C	D
1	153	234	229	253	107	158	167	211	46	76	62	42
2	189	231	283	294	140	145	201	211	49	86	82	83
3	143	169	167	192	83	86	100	107	60	83	67	85
4	192	189	219	208	108	105	141	143	84	84	78	65
5	176	252	276	297	104	176	204	208	72	76	72	89
6	173	227	208	204	110	152	120	130	63	75	88	74
Avg	171	217	230	241	108	138	156	168	62	80	75	73

	Total fatty acids, mg %				Iodine No. of total fatty acids				Phospholipids, mg %				Iodine No. of phospholipid fatty acids			
	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D
1	285	419	380	415	102	102	107	108	92	122	113	130	111	105	108	109
2	352	426	424	465	108	105	106	106	93	99	130	147	117	115	113	115
3	268	283	284	366	96	104	98	93	104	92	91	120	101	112	107	106
4	375	368	353	334	101	103	112	112	136	139	119	119	110	111	118	116
5	406	627	645	631	96	94	96	90	130	164	165	160	106	109	113	104
6	325	405	420	433	101	103	99	97	109	130	125	125	112	110	112	106
Avg	335	421	417	440	100	101	103	101	111	124	123	133	109	110	112	109

A—Blood sample collected before sulfathiazole was started.
B— " " " after 24 hours of normal temperature.
C— " " " on 4th day of convalescent period.
D— " " " " 7th " " " "

The total fatty acids and the phospholipids were depressed before the administration of sulfathiazole. The total fatty acids rose rapidly following the critical fall in temperature induced by the drug; the phospholipids returned to normal more slowly. The iodine numbers of the total fatty acids and of the phospholipid fatty acids underwent little change. The response to sulfathiazole was similar to that of specific serum therapy. This observation is significant for it may associate the fall and rise of plasma lipids with the appearance of immune bodies. In serum therapy the administration of antibodies produces a crisis and the serum lipids rise rapidly to within the normal range. In sulfathiazole and sulfapyridine therapy a critical drop in temperature occurs but only with the former drug is there a concomitant return to normal of the plasma lipids and Kneeland[11] has shown that a greater stimulation of the immune mechanism exists in the patient treated with sulfathiazole.

[11] Kneeland, Yale, and Mulliken, Barbara, *J. Clin. Invest.*, 1940, **19**, 735.