to the severe symptoms noted in tularemia.

Nevertheless, impairment of normal energy yielding reactions seems to be a critical factor influencing the course of infection. An analogy to this is provided by Gilfillan *et al.* (4,5) who studied the adverse influence of *Salmonella pullorum* on liver enzymes of the tricarboxylic acid cycle in baby chicks. They, likewise, concluded that many of the symptoms of the infection were referable to disturbances in this particular metabolic pathway.

Although these comparisons are made between 2 unrelated hosts and 2 unrelated bacterial species, there appears to be an underlying similarity in fundamental pathology in each instance. Gilfillan and his collaborators(5) have suggested the possible role of endotoxins in producing the abnormalities they observed. The work of Berry *et al.*(6) substantiates this concept. They demonstrated that mice poisoned with endotoxin of *Salmonella typhimurium* were depleted of nearly all carbohydrate. However, poisoned mice given a protective dose of cortisone maintained carbohydrate levels 2 to 3 times as great as that of the poisoned controls. Quite possibly, similar effects may be produced in rats by action of an endotoxin of *P. tularensis* which has been demonstrated and characterized by Ormsbee and Larsen(7) and which appears to be related to those of other gram-negative bacteria.

An evaluation of the effects of specific endotoxins on host metabolism would be most desirable in studies of tularemic infection.

Summary. Aconitase and fumarase activity in liver tissue of tularemic rats was demonstrated to be reduced by more than 33% below normal values at height of infection. Administration of cortisone in a concentration of 5 mg per rat per day during infection supported aconitase activity at nearly normal levels for 48 hours but failed to do so beyond that time. Liver fumarase activity of rats treated with cortisone was maintained at only slightly higher levels than observed for the controls. The data presented suggest extensive adrenal involvement in tularemic rats which can be alleviated only partially and temporarily by daily administration of cortisone.

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Connective Tissue V. Comparison of Synthesis and Turnover of Collagen and Elastin in Tissues of Rat at Several Ages.* (26329)

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Previous work from this laboratory has shown that collagen of several tissues of rat increased with age while elastin content remained relatively constant(1). Since there are variations in rates of synthesis and turnover of collagen in several tissues of growing rats(2), it becomes important to study the synthesis and turnover of collagen and elastin in tissues of rats as a function of age.

Methods. Female rats, Wistar strain, 5 weeks, 8 months and 2 years of age, respectively, were injected intraperitoneally with saline containing uniformly labeled C^{14}-lysine (7.8 μc per 100 g body weight). Groups of 3-6 rats were sacrificed at 1, 3, 10, 20, 30 and 40 days, respectively, after injection.

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TABLE I. Synthesis and Turnover of Proteins of Aorta of Female Rat.

(Figures are expressed as relative specific activity ± stand. dev. Assuming maximum specific activity as 100, the specific activity of the remaining days is expressed as % of maximum specific activity.)

Proteins	Age	No.	1 day	3 day	10 day	20 day	30 day	40 day
Nonscleroprotein	5 wk	1–3*	100 ± 39 (222)†	73 ± 10	43 ± 5		20	10
	8 mo	4–5	100 ± 18 (154)	89 ± 4	53 ± 5	30 ± 5	29 ± 1	22 ± 3
	2 yr	4	100 ± 49 (259)	56 ± 8	40 ± 7	27 ± 5	22 ± 4	18 ± 3
Soluble collagen	5 wk	1–3*	100 ± 15 (140)	61 ± 25	40 ± 11		17	9
	8 mo	4–5	91 ± 9	100 ± 17 (77)	24 ± 6	31 ± 11	21 ± 1	24 ± 3
	2 yr	4	100 ± 13 (198)	43 ± 3	27 ± 3	24 ± 6	13 ± 4	16 ± 1
Insol. "	5 wk	1–3*	71 ± 12	93 ± 30	100 ± 12 (41)		78	54
	8 mo	4–5	100 ± 61 (18)	78 ± 44	57 ± 6	57 ± 6	57 ± 11	57 ± 17
	2 yr	4	64 ± 21	100 ± 7 (14)	50 ± 7	29 ± 21	32 ± 7	43 ± 28
Elastin	5 wk	1–3*	57 ± 12	70 ± 27	67 ± 9		100 (33)	70
	8 mo	4–5	75 ± 10	25 ± 15	100 ± 50 (4)	100 ± 25	50 ± 35	100 ± 75
	2 yr	4	25 ± 0	38 ± 50	30 ± 50	25 ± 50	50 ± 50	100 ± 50 (2)

* Combined sample from 2-3 rats.

† Figures in parentheses are actual SA (cpm/mg of protein) observed.

TABLE II. Synthesis and Turnover of Proteins of Uterus of Female Rat.

(Figures are expressed as relative specific activity ± stand. dev. Assuming maximum specific activity as 100, the specific activity of the remaining days is expressed as % of maximum specific activity.)

Proteins	Age	No.	1 day	3 day	10 day	20 day	30 day	40 day
Nonscleroprotein	5 wk	1–3*	100 ± 30 (328)†	82 ± 30	31 ± 2		6	4 ± 1
	8 mo	4–5	100 ± 6 (386)	86 ± 30	27 ± 6	10 ± 2	7 ± 2	5 ± 1
	2 yr	4	100 ± 9 (560)	66 ± 1	25 ± 0	10 ± 1	7 ± 1	5 ± 1
Soluble collagen	5 wk	1–3*	100 ± 45 (220)	99 ± 34	34 ± 3		11 ± 5	4 ± 2
	8 mo	4–5	100 ± 8 (262)	94 ± 20	24 ± 9	12 ± 3	8 ± 0	6 ± 0
	2 yr	4	100 ± 18 (330)	64 ± 13	26 ± 5	15 ± 9	9 ± 1	8 ± 2
Insol. "	5 wk	1–3*	56 ± 22	100 ± 67 (101)	88 ± 21		30	19 ± 4
	8 mo	4–5	34 ± 8	100 ± 52 (77)	33 ± 13	38 ± 14	35 ± 4	21 ± 6
	2 yr	4	43 ± 28	100 ± 46 (35)	86 ± 28	100 ± 32	76 ± 20	40 ±14

* † See legend, Table I.

TABLE III. Synthesis and Turnover of Proteins of Tendon of Female Rat.
(Figures are expressed as relative specific activity ± stand. dev. Assuming maximum specific activity as 100, the specific activity of the remaining days is expressed as % of maximum specific activity.)

Proteins	Age	No.	1 day	3 day	10 day	20 day	30 day	40 day
Nonscleroprotein	5 wk	3–5	69 ± 9	100 ± 10 (163)†	56 ± 14		20 ± 2	13 ± 2
	8 mo	4–5	100 ± 14 (135)	95 ± 8	52 ± 7	27 ± 7	21 ± 2	18 ± 6
	2 yr	4	100 ± 46 (347)	46 ± 8	22 ± 2	19 ± 1	13 ± 9	9 ± 1
Soluble collagen	5 wk	3–5	48 ± 4	100 ± 18 (77)	66 ± 18		34 ± 4	20 ± 5
	8 mo	4–5	18 ± 8	92 ± 38	100 ± 39 (13)	77 ± 15	54 ± 15	77 ± 30
	2 yr	4	90 ± 30	100 ± 60 (10)	70 ± 80	50 ± 50	30 ± 20	40 ± 10
Insol. "	5 wk	3–5	17 ± 6	58 ± 14	75 ± 17		100 ± 6 (36)	44 ± 6
	8 mo	4–5	0	40 ± 40	40 ± 40	100 ± 40 (2.5)	40 ± 40	100
	2 yr	4	0	0	0	0	0	0

† Figures in parentheses are actual SA (cpm/mg of protein) observed.

Tissues from aorta, tendon, uterus and skin were fractionated into nonscleroprotein (NSP), soluble collagen (SC), insoluble collagen (IC) and elastin (E) as described before(2). Methods employed in chemical determinations and radioisotopic procedures have been previously detailed(2).

Results. Rates of synthesis and turnover of protein moieties in aorta, uterus, tendon and skin at different ages are compared in Tables I, II, III and IV.

With age, there was no difference in the synthesis and turnover of NSP in uterus, tendon and skin, while the turnover rate of NSP in aorta was slower at 8 months and 2 years, respectively, than at 5 weeks.

In all tissues studies, the turnover rates of SC were slower at 8 months and 2 years, respectively, than at 5 weeks. The maximum specific activity (SA) of SC in tendon was significantly higher in rats 5 weeks old than in those 8 months and 2 years old, respectively.

In aorta, SA of IC was significantly higher at 5 weeks than at 8 months and 2 years. At the 2 latter ages, it decreased to approximately half in 10 days with little decay thereafter, and at 5 weeks reached a similar level at the end of 40 days. In uterus no apparent difference occurred in the maximum SA of IC at any age. However, the decay of IC was slowest at 2 years of age.

In tendon, the SA of IC was highest at 5 weeks of age. Synthesis was barely detectable at 8 months and not measurable in the 2 years old animal. The decay of IC in tendon was measurable only at 5 weeks.

In skin, the SA of IC was higher at 5 weeks of age than at 8 months and the SA of IC was higher at 8 months than at 2 years. Appreciable decay of IC in skin was observed only at 5 weeks.

The SA of elastin in aorta was significantly higher at 5 weeks than at 8 months or 2 years. A detectable decay of elastin in the aorta occurred only in 5-week-old rats.

Discussion. With the exception of the uterus, IC and elastin were synthesized at significantly higher rates at 5 weeks of age than at 8 months or 2 years, and the IC of tendon and skin showed a higher SA at 8 months than at 2 years.

These data indicated that the concentration of newly formed collagen in the several tissues studied and of newly formed elastin in the aorta were highest at an early age. The turnover rates of collagen in tendon, skin and aorta are relatively slow; these results

TABLE IV. Synthesis and Turnover of Proteins of Skin of Female Rat.
(Figures are expressed as relative specific activity ± stand. dev. Assuming maximum specific activity as 100, the specific activity of the remaining days is expressed as % of maximum specific activity.)

Proteins	Age	No.	1 day	3 day	10 day	20 day	30 day	40 day
Nonscleroprotein	5 wk	3–6	100 ± 17 (221)†	87 ± 8	41 ± 9		10 ± 1	7 ± 1
	8 mo	4–5	100 ± 16 (220)	87 ± 15	30 ± 11	19 ± 4	13 ± 1	10 ± 2
	2 yr	4	100 ± 32 (334)	61 ± 10	34 ± 6	19 ± 2	9 ± 3	8 ± 3
Soluble collagen	5 wk	3–6	100 ± 8 (160)	80 ± 17	40 ± 11		10 ± 1	9 ± 2
	8 mo	4–5	100 ± 26 (73)	96 ± 22	43 ± 11	34 ± 6	18 ± 3	16 ± 3
	2 yr	4	100 ± 38 (102)	47 ± 12	26 ± 5	20 ± 5	17 ± 4	15 ± 5
Insol. "	5 wk	3–6	51 ± 10	100 ± 26 (61)	84 ± 16		41 ± 11	41 ± 3
	8 mo	4–5	42 ± 17	58 ± 25	67 ± 33	100 ± 25 (12)	67 ± 8	83 ±21
	2 yr	4	25 ± 25	63 ± 37	43 ± 25	95 ± 25	100 ± 75 (4)	50 ±50

† See legend, Table III.

are in accord with Neuberger's work on the collagen of rat tendon(3). The highest SA for collagen was found in uterus, for which decay values were also highest and were observed even in old age. In aorta, in the older age groups, there was a turnover of collagen during the first 10 days following administration of C^{14}-lysine, after which no further loss of material was observed. This may indicate at least 2 distinct insoluble collagen components. Such nonhomogeneity of collagen has been reported for various soluble collagens(4,5,6,7,8). The elastin of aorta did not decay in activity in the older age groups, a finding which agrees well with the data of Slack(9).

Summary. 1. Synthesis and turnover of collagen and elastin was studied in rats of 5 weeks, 8 months and 2 years of age, respectively, by observing incorporation and removal of uniformly labeled C^{14}-lysine. 2. Synthesis of collagen and elastin was more rapid in the tissues of young rats (5 weeks) than in those of older animals. In tendon, no detectable synthesis of IC was found at 2 years of age. 3. The uterus was the only organ examined, which showed appreciable synthesis and turnover of collagen in older animals. 4. The turnover rate of collagen in relation to other proteins was low in all animals even in those 5 weeks old. No turnover was observed in the insoluble collagen of tendon and skin at 8 months and 2 years of age, respectively.

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