estrogen. This is to be assumed from the fact that during this early period the very high levels reached by the RNA/DNA ratio of the uterus characteristic of these early months are reached only during the stimulated stages of the estrous cycle. The RNA/DNA values for the unstimulated stages of the cycle remain constant at about .70 to .80 throughout the entire period studied here (from 2½ to 14 months). The correlation obtained here between the increase in the amount of RNA per cell (the RNA/DNA ratio) and the percentage increase in protein nitrogen during the stimulated stages is merely further confirmation of the increase of cellular RNA at times of protein synthesis which has been noted previously by many other investigators in other types of biologic materials. That there might be a correlation between cellular RNA and water content might be expected from our general recognition of the fact that increase in water content of a tissue generally occurs during active growth(17,18). However, such a correlation between the RNA/DNA ratio and water content has not been demonstrated specifically previously.

Summary. Changes in the total DNA, protein nitrogen, the RNA/DNA ratio and water content have been studied in the uteri of mice of strain 129 from 1 to 14 months of age. RNA/DNA (an estimate of relative RNA per cell) at the stimulated stages of the estrous cycle is maximal at the time of maximal uterine growth, between 2½ and 5 months of age. The RNA/DNA of the uterus at the stimulated stages is higher than at diestrus at all ages. However, the differences between the diestrous values and that reached by the ratio at the stimulated stages slowly decreases with age. The cellular RNA content is significantly correlated with the water content of the uterus under the conditions studied here and is also positively correlated with the amount of protein nitrogen synthesized.

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Inactivation of Histamine by Lung Tissue from Histamine-Sensitive and Histamine-Resistant Mice.* (20725)

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Mice are naturally resistant to histamine. Inoculation with *H. pertussis* vaccine greatly increases the sensitivity of these animals to histamine(1,2), to bacterial vaccines(2), and to anaphylactic shock(2,3). It appeared possible that *H. pertussis* vaccine might sensitize mice to the lethal effects of histamine by altering the ability of the animals to inactivate

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this agent. The tissues of most animals contain an enzyme histaminase which will detoxify histamine. Mouse lung is a rich source of this enzyme(4).

Materials and methods. Adult male white mice weighing 16 to 23 g were employed. A group of mice was injected with 0.2, 0.1, and 0.1 ml of *H. pertussis* vaccine† on each of 3 successive days. Six days after the last injection, 4 of the pertussis-inoculated mice and 4 uninoculated animals were challenged intraperitoneally with 50 mg/kg of histamine dihydrochloride. If all pertussis-inoculated mice died and all control mice survived, the remaining pertussis-injected animals were considered to be histamine-sensitive. The LD50 of histamine dihydrochloride in pertussis-inoculated mice was found to be 4.7 mg/kg; in uninoculated mice, 570 mg/kg. The histamine-inactivating power of mouse lung was determined by the method of Rose, Karady, and Browne(5), with certain modifications. The lungs of 5 histamine-sensitive or 5 histamine-resistant mice were pooled, weighed and ground. The ground tissue was placed in an Erlenmeyer flask and made up to a volume of 25 ml with a phosphate buffer solution of pH 7.2. One thousand μg of histamine was added per g of lung tissue. The weights of the pooled tissues varied from 0.6 to 1.19 g. After the addition of 5 drops of toluene, the mixture was incubated at 37°C for 16 hours. At the end of the incubation period, the sample was heated at 90°C for 3 minutes, filtered, and diluted with buffer; the histamine remaining was assayed by measuring the fall in blood pressure of an atropinized cat under barbiturate anesthesia. Cats were anesthetized by intraperitoneal injections of 30 mg/kg of sodium pentobarbital. Atropinization was accomplished with hourly subcutaneous injections of 1 mg/kg of atropine sulfate and the effectiveness of atropinization was checked every 30 minutes by the failure of 2 μg of acetylcholine injected intravenously to cause a drop in blood pressure. The fall in diastolic blood pressure due to histamine was recorded at the carotid artery by means of a Statham Transducer in conjunction with a Brush strain analyzer (Model B1-310) and oscillograph (Model B1-202). Intravenous doses of a standard histamine solution were alternated with doses of the unknown and the error of each assay was deducted from the data of the experiment itself by the method of Vos(6). The experimental error varied from 2 to 22%.

† The pertussis vaccine employed (50 billion organisms/ml) was supplied through the courtesy of Dr. W. F. Verwey, Sharpe & Dohme Inc., West Point, Pa.

TABLE I. Inactivation of Histamine by Lung Tissue from Histamine-Sensitive and Histamine-Resistant Mice.

	Histamine-resistant mice		Histamine sensitive mice	
	Exp. No.	Histamine destroyed per g tissue in 16 hr* (μg)	Exp. No.	Histamine destroyed per g tissue in 16 hr† (μg)
T§	1	512.5	3	181.3
C§		0‡		0
T	2	582.0	4	154.7
C		0		0
T	6	503.4	5	191.0
C		0		0
T	7	522.0	9	183.3
C		0		0
T	8	571.6	10	164.4
C		0		0

* Mean ± S.E. 538.9 ± 16.2. Statistically significant ($p = <.01$) when compared with values for histamine-sensitive mice.

† Mean ± S.E. 174.9 ± 7.6.

‡ Destruction of histamine less than 5% was considered negligible.

§ T = test; C = control.

As controls, the minced lungs of 5 histamine-sensitive or 5 histamine-resistant mice were heated for 3 minutes at 90°C prior to their incubation with histamine. The control samples were then treated exactly as the test mixtures. In the case of the controls, at least 96% of the added histamine was always recovered. Unheated tissues from uninoculated mice destroyed 55 ± 3% of the added histamine; whereas, unheated tissue from pertussis-inoculated animals destroyed only 17 ± 2% of the added histamine. In all, a total of 10 experiments were carried out in which 100 mice were employed.

Results and discussion. The data in Table I indicates that lung tissue from uninoculated mice inactivated 538.9 ± 16.2 mg histamine/g tissue, as compared with 174.9 ± 7.6 mg for pertussis-inoculated mice. The difference between these values is highly signifi-

cant ($p = <.01$). These observations suggest that mice inoculated with pertussis vaccine become sensitive to the lethal effects of histamine by virtue of the reduced ability of their tissues to inactivate this amine.

H. pertussis vaccine may have a toxic effect on the enzyme, presumably histaminase, which destroys histamine. This vaccine may also exert its effect indirectly by damaging the adrenal gland. The tissues of an adrenalectomized animal have a reduced histaminase activity(7). In their sensitivity to histamine, to bacterial vaccines and to anaphylaxis, pertussis inoculated mice are very similar to adrenalectomized animals(2).

Summary. Lung tissue from pertussis-inoculated, histamine-sensitive mice has a reduced ability to destroy histamine as compared with lung tissue from uninoculated, histamine-resistant animals.

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Influence of Hypophysectomy and Growth Hormone on Cartilage Sulfate Metabolism.* (20726)

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The biochemical effects of growth hormone on cartilage are virtually unknown, yet the proliferative response of epiphyseal cartilage to growth hormone is one of the most impressive biological affects of this endocrine substance when administered to immature hypophysectomized rats. The recent demonstrations(1,2) of the uptake of radioactive sulfate by cartilage and its incorporation into chondroitin sulfate suggested that this process might be profitably explored as to its endocrine control. Toward this end, the effects of hypophysectomy and growth hormone injection on the uptake of radioactive sulfate have been examined relative to the normal animal and are here described.

Methods. A tracer dose of S^{35} labeled inorganic sulfate containing 1.5×10^7 counts per minute in a 0.1 ml of saline was injected into the saphenous vein of ether anaesthetized rats. Blood samples were removed after 13, 19 and 25 hours of equilibration and the heparinized plasma was separated by centrifugation. Plasma samples were deproteinized with an equal volume of 10% trichloracetic acid and the inorganic sulfate precipitated with an ethanolic solution of benzidine(3). The twice ethanol-washed precipitate of benzidine sulfate was then determined colorimetrically with β-napthoquinone sulfonate(4). An aliquot of the dissolved benzidine sulfate solution was plated on a copper planchet and radioactivity estimated at virtual infinite thinness. For the determination of the specific activity of cartilage sulfate (inorganic and esterified), samples of rib cartilage were dissected free of adherent tissues and 40-50 mg were digested with 3 ml 4 N HCl for 2 hours in a boiling water bath after which the samples were evaporated to dryness. Solution of the residue in 5 ml of water was almost complete and any undissolved carbonized residue was removed by centrifugation and discarded. The pH of the solution was between 2.0-2.5. The sulfate was precipitated with ethanolic benzidine, filtered on paper and air-dried. The radioactivity of the benzidine sulfate precipi-

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