THYMUS-TREATED RATS CONTRASTED WITH CONTROLS

	Controls	F_1	F_2	F_3	F_4
Average birth weight in gms	4.6	5.0	5.2	5.7	5.7
Ears opened (days)	2½–4	2	1–2	1	1
Teeth erupted (days)	9–10	4.7	1–2	1	1
Hair appeared (days)	14–17	10–14	4–6	4–5	3
Eyes opened (days)	14–17	12–15	4–6	4–5	3
Testes descended (days)	35–40	15–29	5–9	4–6	4–5
Vagina opened (days)	60–70	35–45	23–31	21–25	18–19

Weight curves of rats under the influence of thymus extract reveal a markedly accruing acceleration in the third, fourth and fifth generations. This is shown in the accompanying figure in which C represents the controls, F_1 the second generation, F_2 the third, F_3 the fourth and F_4 the fifth generation under the effects of excess of thymus. The shaded areas represent the growth curve of more than 2,000 Wistar rats between October 7, 1933, and January 30, 1934. A study of these curves indicates that treated animals of the third, fourth and fifth generations at all times from the fourth to the fortieth day weighed more than double the control rats and at all times up to thirty days of age outweighed the rats of the Wistar Institute. Between the third and the twentieth day our fifth generation rats exceeded the Wistar rats in

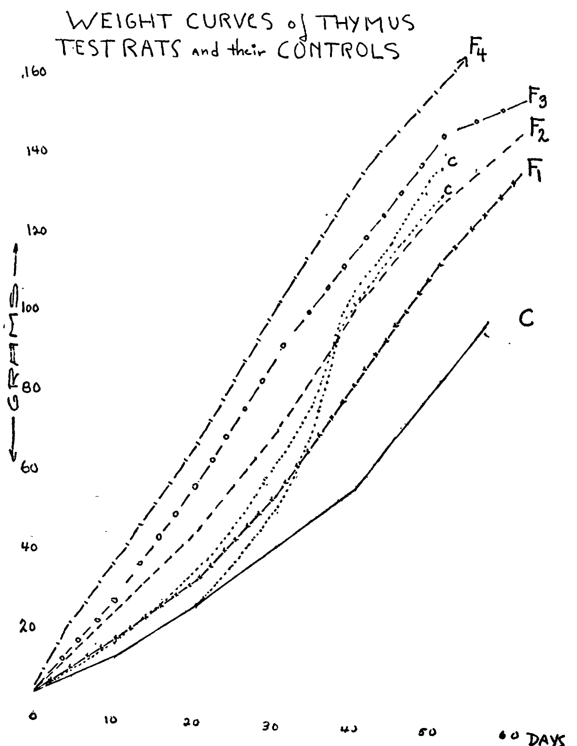

FIG. 1

weight by more than 100 per cent. After the sixtieth day these curves tend to come together, so that eventually the test animals are not perceptibly larger than the controls. Giants do not result. Thymus effects concern primarily early growth and development.

The psychical precocity is as striking as the physical in the thymus-treated strain of rats. Thus fifth generation (F_4) test animals appear almost as capable and alert as normal rats of 16 to 20 days of age. Weaning is possible at 3 days of age. Animals weaned as early as the third day have fared as well or better than their litter mates left with their parents.

The thymus treated animals appear to be healthy, contented and docile. Their actions, asleep or awake, resemble those of normal controls in every way. They do not resent the needle to any great extent, apparently suffering no pain or distress following the injection of thymus extract.

Thymus extract administered to the parents accelerates the rate of growth and development in the young. The normal relation of growth and development to time is disturbed and precocity results. Accruing acceleration in growth and development is encountered in succeeding generations born to thymus-treated parents. The results with the thymus extract have led us to adopt the same procedure in the study of other hormones and glandular products with the idea of amplifying evidence of their effects.

L. G. ROWNTREE
J. H. CLARK
A. M. HANSON

ISOLATION OF THE INFECTIVE PRINCIPLE OF VIRUS DISEASES

A NUMBER of attempts have been made to concentrate the infective principle of virus diseases, particularly of tobacco mosaic. Considerable success has been attained in these efforts and the results are of great interest. If the virus is non-living the isolation of the virus as a definite chemical compound might be anticipated as the end result of such efforts. Without attempting a discussion of the living or non-living character of the causative agents of virus diseases, the following calculations are of interest in relation to the isolation of the infective principle.

Assume the molecular weight of the infective principle to be 100,000; then 100,000 grams of pure infective principle will contain 6.06×10^{23} molecules and one molecule will weigh $10^{-18} \times \frac{1}{6.06}$ grams. Assume the number of infective particles per cubic centimeter of juice to be 1,000,000; then one cubic centimeter of juice will contain $10^{-12} \times \frac{1}{6.06}$ grams of infective material. To secure 0.1 gram of pure infective material, assuming 100 per cent. yield, it would be necessary to begin with $0.1 \div 10^{-12} \times \frac{1}{6.06}$, or 606,000,000 liters of juice.

In making such a calculation it should be emphasized that the figures used for the molecular weight of the infective principle and for the number of infective particles per cubic centimeter are assumptions.

Little definite evidence is at hand as to the size of the infective particles in virus diseases. Duggar and Karrer[1] concluded on the basis of filtration experiments that the infective particles of tobacco mosaic approximate those of fresh 1 per cent. hemoglobin solution, which would indicate a diameter of around 30 millimicrons. Waugh and Vinson[2] state that preliminary experiments show the radius of the infective particle of tobacco mosaic in purified preparations to be less than 5 millimicrons. MacClement and Smith[3] recently report diameters of 15 millimicrons for tobacco and yellow mosaic viruses, 40 to 50 millimicrons for aucuba mosaic and 150 millimicrons for *Hyoscyamus* virus. If these figures represent the particle size of the infective agent of tobacco mosaic and the molecular weights usually given for proteins are employed, a molecular weight of the order of 100,000 for the virus of tobacco mosaic does not seem an unreasonable assumption.

The number of infective particles per cubic centimeter is not known and it is probably impossible with the data at hand even to approximate it. Allard[4] inoculated young tobacco plants by puncturing every leaf of any size, usually four or five, in several places with a needle dipped in the infective juice. Diluting the juice 1,000 times with tap water had no effect on its infectiousness; at a dilution of 1 to 10,000 some attenuation was found; and at a dilution of 1 to 1,000,000 infection was rare. Assuming that a successful inoculation represents an infective particle and the amount of juice introduced by the needle prick is 0.0001 cubic centimeter, we might estimate the number of infective particles at 10,000 per cubic centimeter in the juice diluted 10,000 times or at 100,000,000 per cubic centimeter in the undiluted juice. Geoffrey[5] using a glass spatula, rubbed leaves with infected juice. He secured as many as 283 local lesions per leaf with juice diluted 1 to 10,000. Assuming that each lesion represents an infective particle and 0.01 cubic centimeter of juice was used on each leaf, this would mean 283,000,000 particles per cubic centimeter. On the basis of the number of local lesions formed on *N. glutinosa,* Caldwell[6] has calculated the concentration of the virus of aucuba mosaic to be 3×10^7 particles per cubic centimeter.

[1] Duggar and Karrer, *Ann. Missouri Bot. Garden,* 8: 343, 1921.

[2] Waugh and Vinson, *Phytopath.,* 22: 29, 1932.

[3] MacClement and Smith, *Nature,* 130: 129, 1932.

[4] Allard, *Jour. Agr. Res.,* 3: 295, 1915.

[5] Geoffrey, *Ann. App. Biol.,* 18: 494, 1931.

The following table shows how great the number of infective particles must be per cubic centimeter of juice if an infective principle of molecular weight of the order of 100,000 can be isolated from reasonable quantities of juice. Assuming a molecular weight of 100,000, the varying number of infective particles per cubic centimeter in the table given below would require the quantities of juice indicated, to yield one tenth gram of infective material, if no loss of the principle occurs during isolation.

Number of infective particles per cubic centimeter of juice	Quantity of juice necessary to yield 0.1 gm of infective material of molecular weight of 100,000
10^6	606,000,000 liters
10^7	60,600,000
10^8	6,060,000
10^9	606,000
10^{10}	60,600
10^{11}	6,060
10^{12}	606
10^{13}	60
10^{14}	6

From the above table it is evident that if 0.1 gram of infective material of molecular weight of 100,000 exists in 6 liters of juice the number of infective particles would necessarily be 10^{14} per cubic centimeter. This figure is a million times the number indicated by the work discussed above. Highly speculative as the figures on the molecular weight of the virus principle and especially on the number of infective particles per cubic centimeter may be, the figures given in the table are of interest to the general problem of the isolation of the active principle of virus diseases.

William J. Robbins

University of Missouri

[6] Caldwell, *Ann. App. Biol.,* 20: 100, 1933.

BOOKS RECEIVED

Gesell, Arnold. *An Atlas of Infant Behavior.* Vol. I: *Normative Series.* Pp. 523. Vol. II: *Naturalistic Series.* Pp. 527–921. 3,000 photographs. Yale University Press.

Johnson, Gaylord. *The Stars for Children.* Pp. 170. Illustrated. Macmillan. $1.50.

Morton, Dudley J. *Human Anatomy—First Dissection.* Pp. xiii + 265. *Second Dissection.* Pp. viii + 271–541. Illustrated. Columbia University Press.

Plunkett, Charles R. *Elements of Modern Biology.* Pp. viii + 540. 166 figures. Holt.

Thomas, Arthur W. *Colloid Chemistry.* Pp. viii + 512. 143 figures. McGraw-Hill. $4.00.