orchidism (III, B). However, vitamin deficiency was indicated by the increase in body weight toward normal in those rats injected with biotin (III, C).

Exp. IV. The usual association of cryptorchidism with hypophyseal malfunction suggested that this gland might be involved, particularly in relation to the secretion of gonadotrophin. A decrease in pituitary stimulation, as opposed to a reduction in responsiveness of the tissues, might be expected to result from such a dietary deficiency. Ten animals were placed on the severe S-7 biotin-deficient diet at weaning and given chorionic gonadotrophin intraperitoneally (50 units twice weekly) beginning at weaning. In all 10 rats the testes descended within 10 to 12 days (IV, C). The positive response to gonadotrophin was temporary, however, and within a week the testes began to reascend. While the gonadotrophin thus appeared to counteract or mask the cryptorchidism, therapeutic attempts with testosterone propionate (500 μg twice weekly) proved ineffective (IV, B). Laboratory Chow controls showed the same testicular development (IV, D) as did rats fed chow while receiving chorionic gonadotrophin (IV, E).

Exp. V. The effect of slow starvation with a reduced quantity of complete diet was tested by feeding Laboratory Chow in amounts up to one-half the normal intake While not unequivocal, these results indicate that testicular development may be retarded in semi-starved rats, smaller gonads descending 1-2 weeks after those of controls and then with signs of reduced spermatogenesis (V, A,B). Supplements of gonadotrophin administered along with this semi-starvation diet partially remedied the incipient cryptorchidism.

Some rats from each experimental group, while under nembutal anesthesia, were investigated for contractility of the cremaster musculature. Isotonic contractions recorded kymographically from the tip, the body, or from an excised strip of cremaster muscle showed no characteristic differences in the control and experimental animals other than those due to size of the animals. Weak responses in rats which had undergone severe dietary restriction and inanition indicated that lesser, rather than greater, contractility of the cremaster muscle occurred.

These results are interpreted to indicate that the cryptorchidism is brought on by a type of pseudo-hypophysectomy resulting from general inanition and is not specifically induced by biotin deficiency(9). Biotin lack may intensify the condition, but is not the sole cause of the cryptorchidism, nor is biotin therapy effective in remedying the situation.

§ 9-A ration of Wilson *et al.*(8): vitamin test casein 10, egg white 20, corn starch 28.5, Crisco 20, corn oil (Mazola) 4, cod liver oil (Squibb) 2, powdered brewer's yeast 8, salt mixture U.S.P. XII_2 7, Sulfaguanidine .5 (g) Egg white supplied by Henningsen Lamesa, Inc.; sulfaguanidine contributed by Lederle Laboratories.

9. Mulinos, M. G., and Pomerantz, L., *J. Nutrition,* 1940, v19, 493.

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An Attempt to Transmit Rheumatoid Arthritis to Humans. (19062)

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The etiology of rheumatoid arthritis remains an enigma. The suppressive effects of cortisone on the manifestations of the disease throw no light on its primary cause. Because of this, and because of the many features of the disease which suggest an infectious etiology, such as fever, leucocytosis, increased sedimentation rate, weight loss and the signs of joint inflammation, a return to the search for infection seems indicated. This search however, must be at the level of the ultramicroscopic organisms since many years of intensive research have excluded a bacterial cause. The recent isolation of pleuropneumonia-like organisms in Reiter's Syndrome, which closely resembles rheumatoid arthritis

(1,2) and the beneficial effects of antibiotics in certain cases of rheumatoid arthritis(3), strengthen the hypothesis of an infectious cause. Gordon suggests that there may be a group of "rheumatic" viruses having specific affinity for connective tissue structures. He observed elementary bodies in rheumatic tissues, and drew attention to the highly specific affinity of viruses for particular tissues such as the dermatotrophic smallpox virus and the neurotrophic poliomyelitis virus(4).

The following study was undertaken to explore the possibility of virus etiology. Since viruses (such as the virus of infectious hepatitis) may be species-specific, an attempt at direct human passage was the method chosen.

Procedure. Five subjects exhibiting the classical features of active rheumatoid arthritis and having effusions into joints or bursae were selected as donors. Under sterile conditions with local procaine anesthesia approximately 10 cc of fluid was aspirated from the involved joint or bursa of each donor. A sample of this fluid was submitted to routine bacteriologic study and was in all instances sterile. The fluid was collected in sterile rubber stoppered vials and stored at −20°C until an appropriate recipient was available. The group of recipients consisted of 10 males and 7 females, aged from 42 to 87 years, the average age being 61.2 years. They were chosen because their prognosis for life beyond several weeks was considered hopeless. Their illnesses were as follows: Six cases of various kinds of metastatic carcinoma, one case of myelogenous leukemia, 4 cases of malignant hypertension, one case of severe recurrent embolism of cardiac origin, 2 cases of severe arteriosclerotic gangrene, one case of renal failure with uremia and 2 cases of terminal hypertensive heart disease. Under sterile conditions, and local anesthesia with procaine, 1.0 cc of the joint fluid obtained from the donor subject was injected directly into one of the knee joints of the recipient subject. The injected joint was examined at one to 3 day intervals for evidence of local disease, and the patient was observed for evidence of systemic infection or reaction. The post-injection periods of observation ranged from 2 days to 92 days, the average period of observation being 28.7 days. Two of the patients were observed for 92 days and 85 days respectively, and 8 patients were observed for periods of longer than one month's duration.

Results and discussion. In 3 instances transient mild local warmth was noted in the injected joint of the recipient subjects. This occurred within 24 to 48 hours after injection and was of only 24 to 36 hours duration. There was no associated swelling or discomfort and it was felt that this simply represented a local irritant or foreign body type of reaction. In no case was there any real articular or systemic manifestation suggesting any form of arthritis.

Four cases of the series were subjected to post-mortem examination. In none of these was there any histologic evidence of articular or periarticular inflammatory changes which could indicate transmitted infection.

The negative findings by the method as above described do not by any means exclude the possibility of a virus etiology of rheumatoid arthritis, for the following reasons: 1. An element of natural or acquired immunity cannot be excluded since most of the recipient subjects were in the older age group. 2. An associated stress factor may be necessary for the precipitation of active clinical disease, the virus or other causative agent remaining dormant unless this occurs. 3. Because of the long latent periods characteristic of certain viruses, notably that of serum hepatitis, the periods of observation in this study may be too short for the disease to develop.

Conclusions. In no instance was there clinical or pathological evidence for transmission of active rheumatoid arthritis from one human to another by the direct passage method of study as described.

1. Dienes, L., Ropes, M. W., Smith, W. D., Madoff, S., and Bauer, W., *New Eng. J. Med.*, 1948, v238, 509, 563.

2. Dienes, L., Berg, R. L., and Weinberger, H. J., *Ann. Rheum. Dis.*, 1948, v7, 259.

3. Brown, Thos. M. P., Wichelhausen, Ruth H., Merchant, Wm. R., and Robinson, Lucille B., *Am. J. Med. Sci.*, 1951, v222, 618.

4. Gordon, M., *Lancet*, 1948, v1, 697, 740.

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