markedly affected by changes in the level of thyroid hormones than was the rate of incorporation into microsomal protein (*4, 5, 12,* and Table 2).

The stimulation of terminal oxidation by the thyroid hormones could not in itself account for the increase in metabolic rate which follows the injection of triiodothyronine into thyrodectomized rats (*4, 5*). However, since thyroidectomy markedly reduced the growth rate, there are probably many factors which would tend to increase the demand for energy, and hence the rate of oxygen uptake, once the capacity for oxidative phosphorylation was increased by the thyroid hormones. The suggestion made by Tata *et al.* (*5*) that changes in oxidative capacity may simply reflect an adaptation to an increased demand for energy is unlikely, since, in the same study, they also observed that the increases in oxidative activity in the liver preceded the rise in basal metabolic rate. The direct activation effects of thyroxine which have been reported earlier (*6, 13*), and in this paper, also indicate that this adaptive response is improbable. Furthermore, other recent work (*14*) has shown that an increased demand for energy results in a large increase in the activity of the slowest steps of the citric acid cycle with little effect on electron transport capacity. Thus, increased demand for energy produces effects just the opposite of those produced by triiodothyronine.

The stimulation of the electron transport phosphorylation system is probably only one of many effects of the thyroid hormones on metabolism. However, such an action may be an essential prelude to any stimulation of a process requiring energy, such as protein synthesis (*12*). Clearly, any rise in the metabolic rate can only result from an increase in the rate of utilization of energy (*15*).

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Tolerance between Host and Donor Tissue in Birds

Abstract. *Two methods were used to develop tolerance in the host toward donor cells. In the first method chicken embryos were joined by the parabiotic union of the chorioallantoic membranes after 9 days of incubation. The second method consisted of the use of embryonic transplants of limb buds from donor embryo to host embryo. These transplants were made after 96 hours of incubation with chicken embryos. Other species used were incubated to comparable development. Both methods were successful in the development of tolerance. However, the degree of tolerance attained varied within each method.*

One of the limiting barriers faced by skilled surgeons today is the fact that, in general, tissue transplants from one human to another eventually disintegrate and slough away. Certain exceptions to this general rule exist. Cartilage and tissue from the cornea of the eye can be transplanted from donor to host and are both tolerated and nourished. Transplants between members of a pair of identical twins usually give successful "takes."

Beyond these exceptions it appears that tolerance between host and donor tissue must be developed in some manner before transplants develop into successful takes and as such can be retained by the host. Our work with birds has been concerned with the development of this tolerance to a point where the host will accept, tolerate, and nourish the tissue of the donor. To explain the necessity for such a conditioning process, let us examine the situation which develops when tissue transplants are made between unrelated animals which have undergone no conditioning.

Every animal carries certain genes called histocompatibility genes. These have the power to direct the formation of certain structures on the surface of cells called antigens. For each histocompatibility gene a specific antigen develops. If these antigens are transferred on cells to a host animal whose cells do not already carry the same antigen, they very shortly stimulate the antibody system of the host to produce antibodies. These antibodies function in neutralizing the foreign antigens. Once this is fully accomplished, the function of the donor cells becomes impaired and they start to disintegrate. In a short time the transplanted donor tissue is completely eliminated.

Aside from the use of drugs or x-rays, which temporarily inhibit the action of the antibody system, there seems to be only one means by which the antibody barrier can be bridged. In the embryonic and neonatal animal the antibody system is very passive. Some serologists suggest that this is the period during which the antibody system becomes acquainted with the individual's own antigens and accepts them as its own. As a result they will not be attacked by the antibody system when it becomes more active. At any rate we do know that if foreign antigens on donor cells are introduced into the organization of the host during the passive state of the antibody system, it will at times accept them as the host's own antigens. Sometimes this tolerance is lasting; sometimes it is relatively short-lived.

It is well known that the fetal membranes of dizygotic cattle twins (two-egg twins) will often become anastomosed, and the embryonic blood streams of the twins will mix. It has been shown (*1*) that each twin retains for a long time blood cells whose origin traces to the other twin. Furthermore, after birth such twins will accept skin from each other (*2*). This is in contrast to full siblings of separate birth, which normally reject each other's skin.

In the first phase of the work involved in the development of tolerance between host and donor tissue we employed a method (*3*) which artificially creates a situation in birds analogous to that found in dizygotic cattle twins. After 9 days of incubation, windows are cut in the shells of two eggs, expos-

ing the embryonic membranes. The eggs are rolled together with the windows in alignment, allowing the membranes to make contact. The eggs are sealed together in this position with wax and in a few hours the membranes become anastomosed. Although we can find no fault with the technique used to join the embryos, the hatch of the parabiont chicks is greatly reduced from control eggs which are not joined. Whether the anastomosis of the membranes places some mechanical restriction on the embryos, or whether certain physiological antagonisms develop between the embryos, we cannot say. A considerable number of embryos die soon after secure anastomosis has taken place; others die later in the prenatal period. Nevertheless, approximately 20 percent of the pairs of eggs hatch two chicks. These hatch separately, since they escape from the anastomosed membranes. In most cases they will accept each other's skin. Two mature parabionts with reciprocal transplants are shown in parts 1 and 2 of Fig. 1.

In a separate project conducted here on red blood cell chimeras, it was found by serological tests (*4*) that at maturity one member of a parabiotic pair will retain from 0 to 45 percent of red blood cells which trace their origin to the other parabiont. Usually, the migration of the red blood cells is in one direction only. Thus, for example, one parabiont will retain only 60 percent of the blood cells which originate in itself; the other will retain 100 percent of its own cells. We have no explanation for this behavior. Nevertheless, the parabiont which carries no red blood cells of the partner will readily accept and retain its skin. It may well be that the anastomosis of the embryonic membranes in itself is sufficient to acquaint the antibody system of one member with the antigens of the other, and thus develop tolerance.

In the second phase of the project we used embryonic transplants of limb buds rather than parabiosis to develop tolerance. In previous work conducted here, a leg bud from an embryo of a barred variety of chicken had been successfully transplanted and maintained on the wing bud site of an embryo of the White Leghorn variety (*5*). This operation was carried out after the eggs had been incubated 96 hours. In that case the transplant retained the dark down of the donor when the recipient hatched.

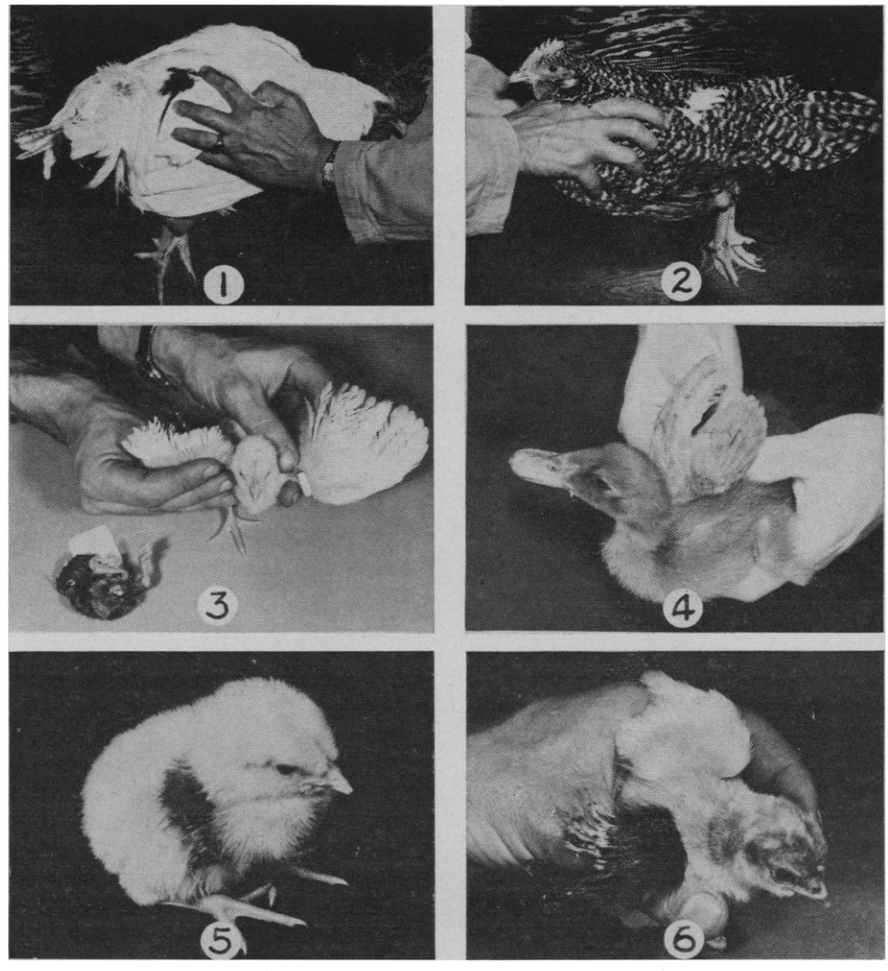

Fig. 1. In *1* and *2* are shown reciprocal skin transplants between chickens which as embryos were joined by parabiosis of the chorioallantoic membranes. All other transplants shown have resulted from embryonic transplants of limb buds: *3*, a wing bud from a barred variety to a white variety in chickens; *4*, a wing bud from a White Leghorn chicken to a Khaki Campbell duck; *5*, a wing bud from a Japanese Quail to a White Leghorn chicken; *6*, a wing bud from a Brown Leghorn chicken to a White Turkey.

In more recent work we have repeated the operation by making transplants between these same varieties of embryos. One of the host chicks which hatched is shown in part 3 of Fig. 1, along with the 19-day donor embryo which failed to hatch. The right wing of the White Leghorn chick is a transplant from the barred donor. Note that in this case the transplant has assumed the color of the host. Furthermore, the chick's own original wing, the left wing, exhibits the phenotype, fast feathering. The transplant exhibits the phenotype, slow feathering. It is interesting to observe that while the transplant took over the host's color phenotype it retained the feathering phenotype of the donor. It is also of interest to note that the transplant developed into a fully functional wing.

After a number of similar transplants had been performed between chicken embryos, it was decided to attempt a similar transfer between species of birds. Because both were available at the time, chicken and duck embryos were used first as experimental material. These birds are of very diverse origin in that they are members of different families, Phasianidae (chickens and pheasants) and Anatidae (ducks and geese). Ducks have longer incubation periods than chickens. Consequently, in order to insure comparable development of the host duck embryo and the donor chicken embryo, the duck eggs were incubated 120 hours and the chicken eggs 96 hours. The first successful transplant was performed by removing a leg bud from a White Leghorn embryo and placing it on the site provided by the removal of the wing bud of a White Pekin em-

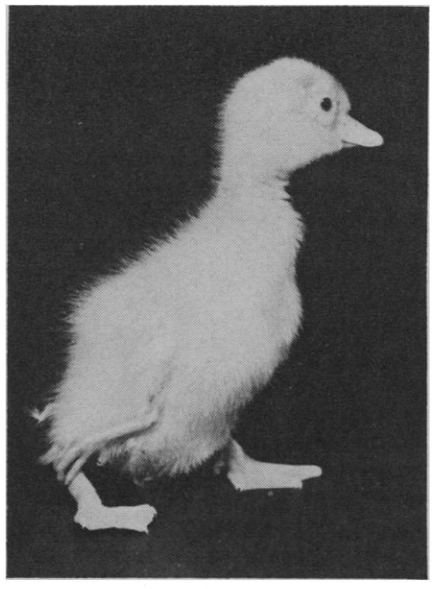

Fig. 2. A White Pekin duckling which as an embryo received a leg bud transplant from a White Leghorn embryo to its wing site. The duckling has now become a mature drake and has retained the transplant.

bryo. The duckling which hatched is shown in Fig. 2. The transplanted leg is rather loosely attached and nonfunctional. Nevertheless, the bird is now a mature male and the transplant is still maintained. In part 4 of Fig. 1, a Khaki Campbell duckling is shown. As an embryo it received a wing bud from a White Leghorn embryo to the site left by the removal of its own wing bud. This transplanted bud became the right wing of the duckling. In this case the color of the host prevailed in the feathers of the transplant but the fast feathering phenotype of the White Leghorn is evident. This wing was reasonably functional. However, when the duckling reached the age of 6 weeks the transplant started to disintegrate and in a short time was completely eliminated as a leathery piece of tissue with attached feathers.

In part 5 of Fig. 1 a White Leghorn chick which as an embryo received a wing bud from a Japanese Quail embryo is shown. This transplant was functional but survived for only 5 weeks. In part 6 of Fig. 1 a turkey poult of a white variety is shown. As an embryo it received a wing bud transplant from a Brown Leghorn embryo. Unfortunately, this poult died at 4 weeks of age but had retained the transplant to that time.

We seem to have little trouble with the retention of transplants between birds of different varieties within domestic chickens (*Gallus domesticus*) where the birds have received early conditioning to the donor antigens either by parabiosis or by embryonic transplants. In the case of transplants between species of birds it is indeed frustrating to see transplants which appear perfect in attachment and condition finally disintegrate and die after a few weeks. One can only speculate as to the reason. Does some slight antibody formation develop even when the antibody system is passive and then become more pronounced as the system becomes more active? This is only one of a number of questions which reasonably might be asked concerning this behavior. However, the fact remains that occasionally transplants to a host from a donor of another species will be tolerated until the host reaches maturity.

A case in point is the now mature Pekin drake shown in Fig. 2, which still retains a White Leghorn transplant. To our knowledge this represents the most diverse tissue ever tolerated for so long a time in a warm-blooded animal. It is true that the cheek pouch lining of the hamster will accept and nourish very diverse tissue (*6*). Here it appears that the lining of the pouch acts as a unidirectional barrier, screening the antigens from the antibody system, yet allowing nutrients to pass through from the host to nourish the donor tissue. In a sense no true tolerance develops. This is indicated by the fact that if some duplicate donor tissue is placed in another location on the body of the hamster, that transplant will be sloughed and that on the pouch lining will be sloughed as well (*7*).

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Unit Responses in the Frog's Tectum to Moving and Nonmoving Visual Stimuli

Abstract. *"Movement-detecting" units that respond little or not at all to illumination without movement, respond well to change in position under stroboscopic light even when relatively large jumps in the visual field occur during a dark pause between two flashes. The threshold angle and angular velocity are different for different classes of units. They are higher for the periphery of the receptive field and increase with decreasing contrast. An inhibitory effect of a large surrounding of the receptive field could be demonstrated in class-2 neurons.*

Various workers (*1*) have described single neurons in the frog's optic nerve which respond to moving visual stimuli but little or not at all to nonmoving stimuli. The present investigation confirms and adds quantitative information on this "movement-detection" and shows it to be actually "change-of-position-detection."

By means of metal-filled micropipettes 1 to 3 μ in diameter (*2*) the spike activity of single axons in the stratum superficiale of the optic tectum was recorded in *Rana pipiens*. The curarized and fixed animals looked through a window at the visual stimuli 24 cm away, carried on a specially constructed perimeter. The stimulus pattern could be moved by a mechanical stage and the movement recorded by means of a potentiometer circuit on one beam of the oscilloscope. The stimuli were large cards bearing spots, stripes, and so forth, illuminated diffusely, or a spot of light 0.2° to 2° in diameter, provided by an assembly of bulb, lenses, and shutter mounted on the perimeter. By the use of stimulating patterns comparable to those of Maturana *et al.* (see *1*) the four classes of units of these authors could be confirmed, as well as some other types not discussed here which were probably tectofugal fibers. The more quantitative stimulation technique gave additional information about these classes.

Class-1 responses (called by Maturana *et al.* "sustained edge detection") are obtained immediately below the tectal surface and are strongest to moving dark spots on a white background. Neurons of this class show no response to diffuse uniform illumination