increased. Normal animals and those with a distensible LPA anastomosis (groups 1, 4, and 5) never developed a pressure gradient and had significantly lower mean pressures in the central pulmonary artery after RPA occlusion (Table 1).

Vascular resistance in all transplanted and nontransplanted lungs distal to any LPA narrowing was similar. In all cases, vascular resistance distal to the indistensible LPA decreased normally when flow to the left lung increased after RPA ligation (Table 2).

Thus, much of the fixed resistance noted in standard lung autotransplants can be attributed to the indistensible arterial anastomosis rather than to altered innervation. Denervation does not influence the capacity of the small pulmonary vessels to dilate in response to increased flows. Our results indicate that this form of pulmonary vasodilatation is largely a passive or mechanical phenomenon (*3*, *4*) which cannot occur without the normal distensibility of the large pulmonary arteries.

All animals in groups 2 and 3 died within 48 hours of operation. All the normal animals (group 1) and five animals in each group with a transplant and a distensible LPA anastomosis (groups 4 and 5) survived for more than 7 days after operation. The transplanted lung therefore did assume total pulmonary function while its vasculature carried the entire pulmonary blood flow.

Many (*1*, *2*, *5*) although not all (*6*) investigators have observed that transplanted lungs have a high vascular resistance. Ischemic injury to the pulmonary microvasculature, which is preventable (*7*), may be manifested by an elevated resistance. Obstruction to pulmonary venous drainage at the left atrial anastomosis may be a cause, but it too is preventable (*6*, *8*). The denervation inevitably accompanying transplantation has been thought the major cause of the high fixed vascular resistance observed in transplanted lungs (*1*, *2*, *9*). This belief was sustained by a report that division of all the connective tissue about the left pulmonary hilum, a procedure presumably denervating the left lung, prevented the vascular bed of that lung from dilating after RPA ligation (*2*). However, the electromagnetic flow-meter probes positioned about the LPA in those experiments (*2*) could have acted like the band in our experiments (group 2) and prevented LPA dilatation. The fixed vascular resistance of the left lung (*2*) also could have been produced by an indistensible LPA rather than by denervation. Our results indicate that the indistensible standard arterial anastomosis is responsible for the fixed resistance in grafted lungs and show that transplanted (denervated) lungs with normally distensible arteries and arterial anastomoses may have normal vascular resistance with the ability to vasodilate with increased flow.

Our findings regarding the regulatory mechanisms of the pulmonary vasculature (*4*, *10*) emphasize the importance of passive factors, especially the increase in cross-sectional area of the large pulmonary arteries, in the vasodilatation accompanying increased flow (*3*, *4*). Innervation is not necessary for this type of vasodilatation, and denervation of a lung does not produce a fixed high vascular resistance in that organ. Circulation in a denervated lung of an otherwise intact animal can now be studied without the necessity of measuring the flow to each lung.

Since transplanted lungs can vasodilate and carry the bulk of the pulmonary blood flow without damage and at tolerable pressures in the pulmonary artery, therapeutic lung transplantation may be considered in patients with severe pulmonary vascular disease. Total functional dependence may now be placed immediately on the grafted lung, and the efficacy of immunosuppressive programs and lung preservation techniques to be used in pulmonary transplantation can be evaluated better.

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Lactate Dehydrogenase Electrophoretic Variant in a New Guinea Highland Population

Abstract. *Six examples of a variation in the LDH-A subunit have been detected in 408 samples from three exogamous clans in the New Guinea Highlands. The New Guinea variant is similar to the Memphis-4 variant. Origin of the New Guinea variant could not be traced by genealogy but it seems likely to have persisted for several generations.*

Since Boyer and his colleagues (*1*) described the first genetically controlled variant of human lactate dehydrogenase (LDH; E.C.1.1.1.27) several further electrophoretic variants involving changes in either the A or B subunits have been reported. Vesell (*2*) has reviewed the evidence on the distribution of these variants: for 2103 whites in the United States and Europe, three A and one homozygous B; in 1585 U.S. Negroes, nine A and two B; in 223 black Africans, one A and one B; in 245 Turkish Cypriots, two A variants. In addition, an A variant has been described from Brazil. No LDH variants were found in studies of 100 Papuans, 238 Micronesians, 79 Xavante Indians in Brazil, and 284 American Indians. It appears that there is a higher chance of mutations in the A subunit being detected (16 A : 4 B) and that there is a greater frequency of LDH variants among U.S. Negroes and black Africans (0.72 percent) than among whites (0.19 percent). The number of persons studied in other ethnic groups is too small to permit useful comparison.

We have screened 408 samples from a Melanesian population in the New Guinea Highlands for LDH variants. Six persons showed identical variations in the LDH isozyme pattern after starch-gel electrophoresis of red-cell hemolyzates. For electrophoresis the bridge buffer we used was 0.2*M* phosphate–citric acid, *p*H 7.0, and gels were prepared from a 1 : 20 dilution of the same buffer

[12 percent hydrolyzed starch by weight to volume (Connaught)]. The gels were placed between metal cooling plates in which water was circulated at about 15°C, and a gradient of 2 volt/cm along the gel was applied for 16 to 18 hours. After electrophoresis, the horizontally sliced gels were incubated for 1 hour at 37°C with a reaction mixture containing 0.1 ml of 70 percent, weight to volume, sodium lactate, 10.0 mg of nicotinamide adenine dinucleotide, 10.0 mg of tetrazolium salt MTT [3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl tetrazolium bromide], and 10.0 mg of phenazine methosulfate per 100 ml of 0.1 tris-HCl buffer, *p*H 8.2.

The pattern of the New Guinea variant LDH was compared with that of the Memphis-4 variant. Under the conditions of electrophoresis the two variants had identical mobilities (Fig. 1); in both cases the banding pattern is consistent with a mutation in the LDH-A subunit. The slower bands of isozymes 2 and 3 in the New Guinea variant are weaker than the corresponding bands of the Memphis-4 variant. This may be due to differential loss of activity in the mutant subunit, which has affected the New Guinea samples to a greater extent than in the case of the Memphis-4 sample because of the unavoidable delay in examining the material from the Highlands. An alternate explanation is that the New Guinea mutant, though having identical electrophoretic properties with Memphis-4, is intrinsically less stable. Study of fresh samples may distinguish between these alternatives.

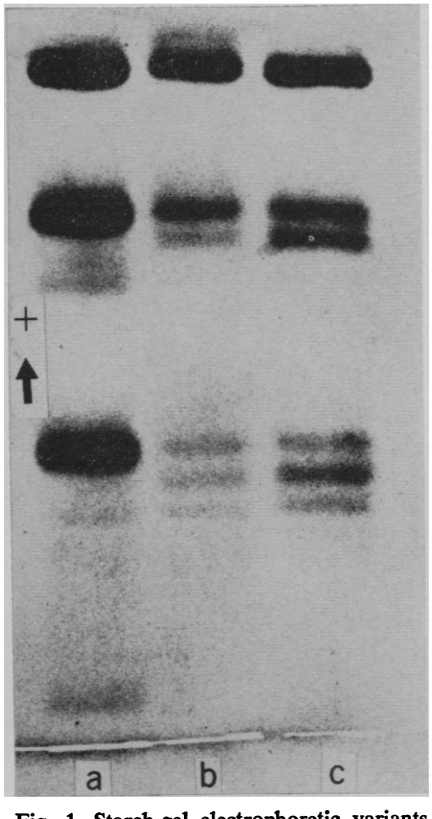

Fig. 1. Starch-gel electrophoretic variants of LDH. (a) Normal, (b) New Guinea variant, and (c) Memphis-4 variant. Bridge buffer: 0.2*M* phosphate–critic acid, *p*H 7.0; gel buffer 1:20 dilution of bridge buffer.

The original Memphis-4 variant (*3*) was detected in three generations of a Caucasian family in the United States. A similar variant, possibly identical, has also been described in two families in Lancashire, England (*4*). There was a total of 15 sibships containing at least one affected member in the two English families and the ratio of affected to total sibs did not differ significantly from 0.5, indicating no measurable selective effect against either the normal or affected phenotype. Although these families resided in the same geographical area a search of parish records covering five generations revealed no relationship between them. The possibility of a more remote connection, however, still exists.

The New Guinea individuals showing the LDH variant are members of three exogamous clans which, in turn, are part of a single clan cluster of Enga-speaking people living in the Lagaip subdistrict of the Western Highlands of New Guinea, 160 km northwest of Mt. Hagen. The clans are traditionally believed to have a common ancestry and although our records do not permit the construction of a genealogical tree relating all the affected persons to one another, it is likely that they are derived from a common source. Moreover, the variant LDH types have probably persisted in this area for several generations.

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Punishment by Response-Contingent Withdrawal of an Imprinted Stimulus

Abstract. *Newly hatched ducklings were exposed to a moving, imprinted stimulus; if they followed it, the stimulus was withdrawn briefly. The tendency to follow gradually declined during punishment periods, but it returned to pre-punishment amounts when punishment terminated. This finding attests to the efficacy of withdrawal of reinforcement as a technique for behavioral control.*

Previous research indicates that, in the immature duckling, presentation of an imprinted stimulus can serve as an effective reinforcement for the development and maintenance of a variety of responses. If, for example, presentation of the stimulus is contingent upon a key peck, the tendency to emit this behavior undergoes a marked increase in probability (*1*); similarly, if stimulus presentation is contingent upon a distress call, the frequency of these calls increases (*2*). Both findings imply that, like the presentation of other stimuli that serve as reinforcement (food, water, warmth, and so forth), presentation of an imprinted stimulus can increase the probability of the overt behavior at the moment of stimulus presentation.

In the present investigation we raised the corollary: Can an imprinted stimulus also function in a complementary fashion to reduce the probability of the behavior at the moment of stimulus withdrawal? Since immature ducklings are frequently observed to follow a moving imprinted stimulus, we arranged to withdraw the stimulus briefly whenever the duckling began to follow it.

Specification of the effects of this procedure is important for several reasons. (i) Punishment is often defined as either response-contingent presentation of an aversive stimulus or response-contingent withdrawal of a reinforcing stimulus; and although the former procedure has been studied extensively (*3*), the latter has rarely been investigated (*4–6*). The procedure used here provided an opportunity for examining further punishment via withdrawal of reinforcement. (ii) The accumulated evidence (*7*) indicates that the immature duckling's reactions to an imprinted stimulus are largely examples of filial-type behavior. By investigating punishment via withdrawal of an imprinted stimulus, the present research provided an opportunity to examine an important but seldom explored source of behav-