tum is zero. If at any time $v_{2\theta} \equiv 0$ then at all times later $v_{2\theta} \equiv 0$. Let us assume then that $v_{2\theta} \equiv 0$ at all times.

Eliminate $j_\theta B_z$ from the two equations (3) and (5). We then get

$$\rho\left(\frac{\partial \boldsymbol{v}_2}{\partial t} + \boldsymbol{v}_2 \cdot \nabla \boldsymbol{v}_2\right)_r = \frac{en}{c} E_r - (\nabla \cdot p_1)_r \tag{7}$$

Study of this equation shows that E_r which must only make $v_{2r} = v_{1r}$ and $(\nabla \cdot p_2)_r$ which from its definition can only depend on the r distribution of $\boldsymbol{v}_{2r}$, n, and the local temperature will be independent of the magnitude of the magnetic field impressed at the wall of the tube. A change in $\boldsymbol{B}_0$ will cause a change in $(\nabla \cdot p_1)$ which will just be balanced by the change in $j_\theta B_z$. The containment time of the plasma will be independent of $\boldsymbol{B}_0$ and will be the same as for $\boldsymbol{B}_0 \equiv 0$.

Conclusion and Applications.—The two "collision-free" transport equations of a plasma do not have mutual interaction terms equal to zero although the plasma may be dilute enough to make actual "collisions" a rare possibility. These interaction terms make it impossible to contain a high-temperature plasma in a simply connected container kept at a low temperature.

These results are more nearly consistent with the findings of Lehnert.[3]

They also are entirely consistent with the numerous results obtained with the Ionic Centrifuge[4] with the end plates at negative voltage and the cylinder floating.

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*GENETIC CONTROL OF THYMUS LYMPHOID DIFFERENTIATION**

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As our knowledge of the functional and pathological aspects of lymphoid systems in their central role in immunity and leukemia increases, the lack of understanding of the primary differentiative mechanism leading to the formation of such systems becomes limiting. Thus we find that theories of antibody formation as well as of leukemia etiology hinge ultimately on hypothetical differentiative mechanisms which are neither established from lymphoid systems nor generally valid for any differentiating system as yet analyzed in multicellular organisms.

We have recently reported that the embryonic mouse thymus, isolated as an epithelial rudiment prior to lymphoid differentiation, can develop into a lymphoid system upon isolation in tissue culture[1] as well as after transplantation to the anterior chamber of adult mouse eyes.[2] The present paper concerns itself entirely with grafts grown for seven days in the anterior eye chamber, and takes into consideration the genetic constitution of donor and host tissues. The experiments

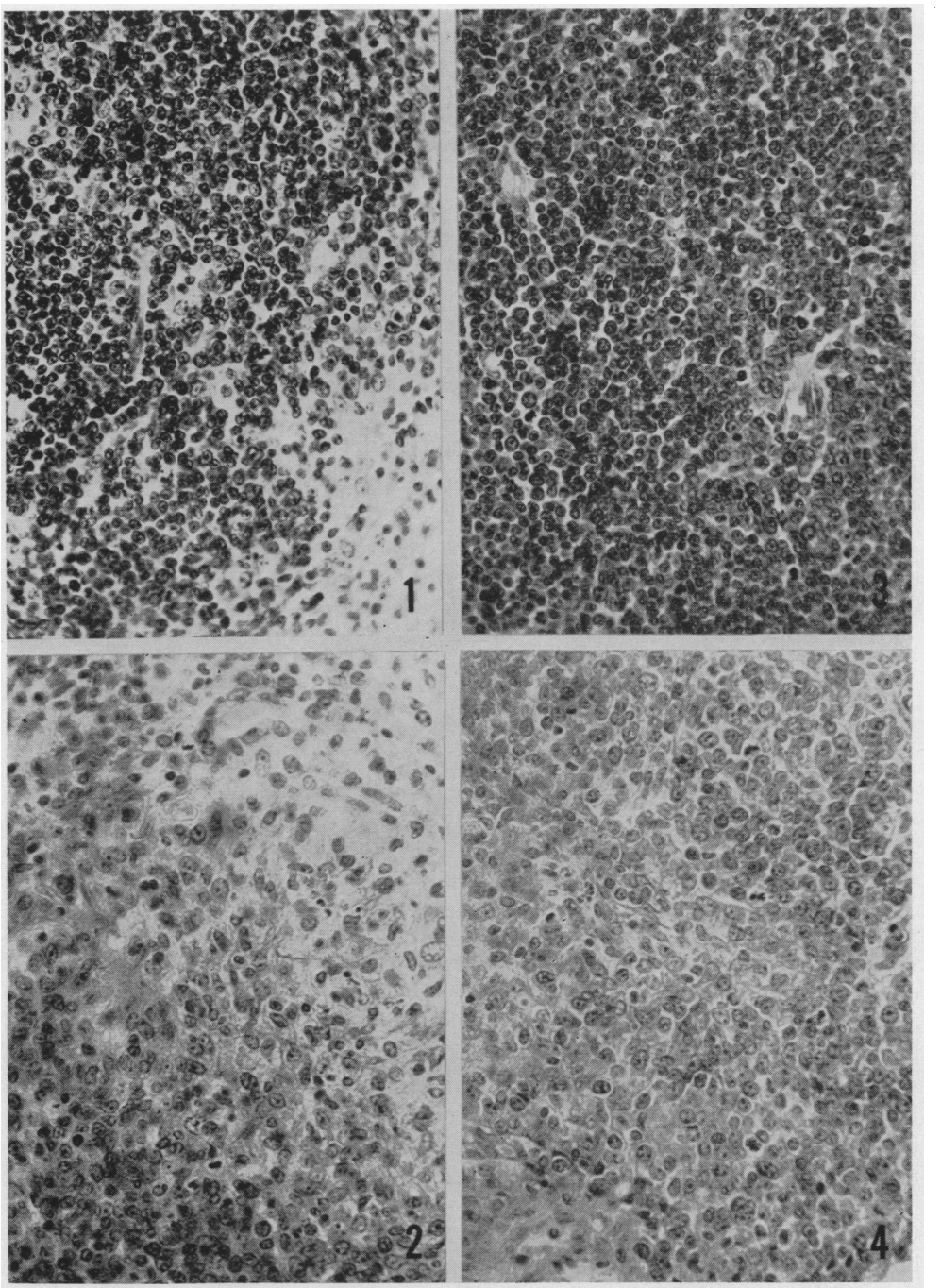
demonstrate that in contrast to other embryonic systems the developmental direction of the thymus can be profoundly and rapidly influenced, typical lymphoid differentiation depending on donor-host compatibility.

The unique nature of the results is interpreted as manifestation of a release from tissue-level control mechanisms normally associated with differentiation in multicellular organisms. The operational feasibility of both directive and selective influences in lymphoid differentiation is discussed. Finally, a hypothesis is developed which states that the thymus represents the primary rudiment of the mammalian immunological system.

Materials and Methods.—Mice of strains C_3H, Bagg albino C, and AKR/Lw were used. Embryonic age was determined by observation of vaginal plugs. Thymus rudiments were obtained from 12-day embryos of C_3H, C, and F_1 (C ♀ × C_3H ♂) matings, and from 13-day (12-day equivalent) embryos of AKR matings, lung rudiments from the same embryos serving as source of control material when required. With a few exceptions in transplants to AKR mice, recipients were adult male mice of 2–5 months' age. Normally, each mouse received only one graft, but in experiments in which lung and thymus morphogenesis were compared, both eyes were utilized, one receiving lung, the other receiving thymus. Grafts were made into nembutal-anaesthetized animals in standard fashion,[3] recovered after seven days, fixed in Bouin's, sectioned at 5–7 μ, and stained with hematoxylin and eosin.

Results.—As previously reported, when an F_1 (C × C_3H) thymus rudiment is transplanted into F_1 (C × C_3H) host eye, the rudiment develops rapidly into a lymphoid structure, and within one week becomes histologically similar to the thymus of a newborn animal.[2, 4] Preliminary studies on the sequence of events show that after two days the graft is well established and growing, that after four days it is clearly shifting in a lymphoid direction, and that in the next three days rapid growth and lymphopoiesis occur. The timing parallels the differentiation of thymus *in situ*, where lymphocytes appear in 15- to 16-day embryos, and reach *ca.* 12 million in the newborn (19-day) mouse.[5] While there is considerable variation in the size attained by implants, the histological differentiation seen seven days after transplantation is characteristic and consistent. The graft is almost exclusively lymphoid, with a few scattered epithelial foci and dispersed stromal material.

The initial rationale in the transplantation experiments to be reported (Table 1 and Figs. 1–4) was that in view of the known role of the thymus in AKR-strain leukemia[6] an effect of AKR environment on the differentiation of thymus rudiments from nonleukemic strains might be expected. F_1 (C × C_3H) rudiments were transplanted into AKR mouse eyes, grafts into F_1 (C × C_3H) mice serving as controls; grafts were recovered after one week. Control grafts behaved in a typical manner. Grafts implanted into AKR eyes had become established and well vascularized and had grown considerably, although somewhat less than control grafts. The histological appearance of the grafts was, however, strikingly different from the control grafts. In place of the expected lymphoid differentiation, these grafts had grown into a large, somewhat disorganized mass of epithelial and fibrous material interspersed with vesicles and some debris. The total amount of lymphoid material varied from little to none, and where found, it seemed restricted to the areas furthest removed from the host-donor tissue interfaces; furthermore, such lymphoid areas



12-DAY EMBRYONIC THYMUS RUDIMENTS GROWN FOR 7 DAYS IN THE ANTERIOR EYE CHAMBER OF ADULT MALE MICE.

FIG. 1.—C_3H thymus rudiment in F_1 (C × C_3H) host eye.
FIG. 2.—F_1 (C × C_3H) thymus rudiment in AKR host eye.
FIG. 3.—AKR thymus rudiment in F_1 (AKR × C_3H) host eye.
FIG. 4.—C_3H_a thymus rudiment in C host eye.

appeared to be undergoing regression or alteration.

The experiments were repeated, using lung rudiments as control tissue. F_1 (C × C_3H) lung tissue growing in AKR mice was indistinguishable from similar tissue growing in F_1 (C × C_3H) mice. On the other hand, F_1 (C × C_3H) thymus growing in AKR mice again showed the predominantly nonlymphoid direction of differentiation.

Reciprocal experiments were now performed, in which AKR thymus rudiments were transplanted into AKR and F_1 (C × C_3H) hosts, lung tissue again serving as control. The results were comparable. AKR lung tissue grew well in both types of hosts, and no distinction was seen between the two groups. On the other hand, while AKR thymus rudiments developed into typical lymphoid grafts when transplanted into isologous AKR hosts, they developed into characteristic non-lymphoid type grafts when grown in F_1 (C × C_3H) hosts.

At this point it was felt that the transplantation effect might well be independent of the leukemic properties of the AKR strain, so that a large number of graft combinations were made using C_3H, C, AKR, F_1 (C × C_3H) and F_1 (C_3H × AKR) mice. The results, summarized in Table I, were consistent. In all situations in-

TABLE 1

LYMPHOID DIFFERENTIATION AS A FUNCTION OF DONOR-HOST COMPATIBILITY

	Predominant Differentiation			
	Lymphoid		Non-lymphoid	
Donor Strain	Host strain	Number	Host strain	Number
C_3H	C_3H	5/5	C	10/12
	F_1 (C × C_3H)	11/11		
C	C	4/4	C_3H	10/10
	F_1 (C × C_3H)	5/5		
F_1(C × C_3H)	F_1 (C × C_3H)	100+/100+ [a]	C	4/4
			C_3H	6/7
			AKR	37/41 [b]
AKR	AKR	8/8 [c]	F_1 (C × C_3H)	6/8
	F_1 (C_3H × AKR)	9/9		

[a] Standard control used in numerous experiments in addition to the ones reported in this paper.[2, 4]
[b] Includes 14 severely leukemic mice.
[c] Includes four severely leukemic mice.

volving the implantation of inbred-line thymus into its own strain (three types) or into an F_1 hybrid of that strain (three types) typical lymphoid differentiation ensued. No readily recognizable differences in growth or histological differentiation between implants into the strain of origin and implants into F_1 hybrids were observed. In all situations involving the implantation of thymus from one inbred line into a different inbred line (three types) lymphoid differentiation generally failed to ensue. In transplants of an F_1 hybrid into either of the parental strains nonlymphoid differentiation was predominant.

Finally, two preliminary experiments may be reported. In the first, F_1 (C × C_3H) tissue was grafted into AKR mice, F_1 (C × C_3H) mice serving as control hosts; grafts were recovered after two, four, and seven days. Differences between the two groups were apparent after four days in 3 out of 4 cases. In a second experiment, F_1 (C × C_3H) tissue was grafted into 2-week-old C_3H mice (in four cases). In this instance the grafts grew well, became lymphoid, and were indistinguishable from control grafts.

Discussion.—The anterior chamber of the eye has been considered refractory to

early immunological phenomena as evidenced by the ready maintenance and growth for two or more weeks of highly heterologous combinations such as human or mouse tissues in rat eye or chick tissues in mouse eye.[3, 4, 7] Yet in the present experiments the results parallel those that would be expected on the basis of transplantation compatability, lymphoid differentiation being restricted to a compatible host-donor relationship. On the other hand, the rapidity of the effect would be unusual even for adult tissues grown in immunologically active transplantation sites. Furthermore, the response is limited to the lymphoid elements; for growth and vacularization of the implant is not prevented, and there is no general graft rejection.

Whether the process involved in the results is actually immunological, i.e., a specific host response to donor tissue which is lymphocyte inhibiting in effect, is open to conjecture. Experimentally, the same results would be expected if specific lymphocyte-promoting substances, subject to genetic control, were required for lymphoid differentiation. Tissue culture experiments aimed at distinguishing between these possibilities are in progress.

In view of the contrast between the results obtained with thymus transplants and those obtained with other systems it becomes essential to examine critically the properties and functions of the developing thymus lymphoid system. One striking feature of thymus differentiation is the loss of tissue cohesion concomitant with the appearance of lymphoid cells. Whereas reticular, stromal, and epithelial cells are firmly bound to the thymus tissue architecture, the lymphoid series of cells is essentially nonadhesive. Since cellular adhesion is normally an adjunct of embryonic systems, and since intercellular materials are becoming increasingly implicated as controlling elements in differentiative events,[8–10] the change in adhesion accompanying lymphoid differentiation may represent a key factor in our results. Loss of adhesiveness may signify that the normal developmental-control mechanisms are bypassed or play a relatively minor role, and that different control mechanisms can under these conditions become operative or manifest. This rationale suggests that certain other systems such as germ-cell differentiation, would behave in a similar fashion; transplantation experiments to test this point are contemplated.

Although the functions of specific cells in the lymphoid series are not clear, it seems likely that the lymphoid system plays a leading role in immune phenomena. Recent theories of antibody-forming mechanisms[11] have tended to emphasize selection or directed differentiation of certain cells in response to antigen (or antibody). In this connection the present results and preceding discussion seem significant. The transplantation results indicate that the thymus lymphoid differentiating system is subject to genetically-determined external controls. In addition to the directive (or permissive) nature of the host environment, selective models can be designed, e.g., a situation in which cells from two strains are mixed prior to transplantation; the significance of such models remains to be determined. The rationale that the present results are related to loss of tissue cohesion is attractive in this connection, for it permits the application of principles developed for unicellular organisms for this system in distinction to other multicellular differentiating systems.

The experiments focus attention on the lack of information concerning thymus function. Since the thymus represents the dominant lymphoid rudiment of the early embryo and since it differentiates during the period of development when the

embryo is most sensitive to external modifications of the immunological system,[12] it seems appropriate to suggest that the thymus represents the major rudiment of the mammalian immunological system.[13] Implicit in this suggestion is the assumption that lymphoid cells which arise in the thymus subsequently become disseminated in a selective fashion. That thymic lymphoid cells originate *in situ* from nonlymphoid cells has been recently demonstrated by transplantation and tissue culture studies;[4] the presence of a lymphocyte circulation has been shown;[14] and the selective nature of thymus cell localizations in other lymphoid regions has been established.[15] The precision of selective settling of thymic lymphoid cells is seen in the regional intra-splenic distribution of thymic cells introduced into lethally irradiated animals;[16] and this conforms well with the demonstrated depression of spleen germinal center activity following thymectomy.[17]

A summary of the points of discussion leads to the presentation of a unified view of thymus function, lymphocyte differentiation, and the development of immune systems. Initially the thymus is subject to typical inductive tissue interactions, but during development the loss of tissue adhesion leads to the establishment of a new set of controlling and directing elements. Cells selected and/or directed toward lymphoid differentiation then develop into thymic lymphoid cells which migrate from the thymus into specific areas of the developing spleen. Here, in their new environment they directly or indirectly become foci for production of antibody-forming cells.

The hypothesis, though speculative, is attractive in being readily amenable to testing. One would predict that embryonic thymectomy would lead to a reduction of the antibody-forming capacity; this experiment can be performed in lower vertebrates. One would expect that heterotypic combinations of embryonic spleen and thymus would lead to complex differentiation not attainable by these rudiments individually. And finally, one would hope that such heterotypic combinations involving the differentiation simultaneously of spleen and thymus in tissue culture would lead to the formation of a system competent to perform immunological reactions *in vitro*.

Summary.—Thymus rudiments from 12-day-old mouse embryos of C, C_3H, and C ♀ × C_3H ♂ matings and from 13-day (12-day equivalent) embryos of AKR matings were grown for 7 days in the anterior eye chamber of adult male C, C_3H, AKR, F_1 (C × C_3H) and F_1 (C_3H × AKR) mice.

In all situations involving the implantation of inbred-line thymus in its own strain or in an F_1 hybrid of that strain, as well as of F_1 hybrid thymus in a similar F_1 hybrid host, typical lymphoid differentiation occurred. In all combinations in which the thymus from one strain was implanted into an unrelated strain or in which thymus from an F_1 hybrid was implanted into either parental strain or into an unrelated strain, lymphoid differentiation was reduced. Instead, grafts developed into disorganized, large masses of fibrous and epithelial material.

It is suggested that the explanation may lie in the loss of tissue adhesion concomitant with lymphoid differentiation, that this constitutes a release from tissue-level control mechanisms normally associated with differentiation, and that this permits different control mechanisms to become operative or manifested.

A hypothesis is developed which states that the thymus may represent the major primordium of the mammalian immunological system.

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† With the technical assistance of William D. Ball and E. Mattie Morin.

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*ACTION OF RADIATION ON MAMMALIAN CELLS, IV. REVERSIBLE MITOTIC LAG IN THE S3 HELA CELL PRODUCED BY LOW DOSES OF X-RAYS**

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In previous studies reproductive death, reversible mitotic lag, and visible chromosomal damage were described in mammalian cells irradiated *in vitro*.[1, 2] Presumptive evidence was presented that chromosomal damage is the underlying lesion responsible for cell killing by radiation. Several laboratories have recently reported life-cycle analyses of cells exposed *in vitro* to high doses of radiation, where the bulk of the cell population has suffered irreversible loss of the capacity to reproduce indefinitely.[3] These studies have yielded divergent results about the stage in the life cycle which is most characteristically damaged by such lethal radiation experience. The randomness of chemical bond breakage produced by ionization makes possible a wide variety of molecular changes when a cell is irradiated. At low doses, however, one may expect a relatively simplified picture of radiation injury, since presumably only the most vulnerable cell functions will