egg-borne transmission or by intrauterine infection, but NIV probably is transmitted to the reciprocal hybrid with BALB/c mothers by C3H-A^{vy}fB sperm or seminal fluid, since BALB/c is not infected with NIV.

The occurrence of mammary tumors in the parent females used to produce the reciprocal hybrids can be seen in Table 3. The incidence of mammary tumors (82 percent) for C3H-A^{vy}fB females is typical for the strain, and the incidence (8.7 percent) for the BALB/c female parents is not significantly different from the incidence (20 percent) for strain BALB/c.

The classification of mammary tumors occurring in the reciprocal hybrids is shown in Table 2. Most of the tumors were adenocarcinoma type A or B and adenoacanthoma; this finding compares well with the results obtained for strain C3H-A^{vy}fB. However, there were 15 type C mammary tumors. Tumors of this type have been seen before in hybrids where one of the parents was of strain BALB/c and in old females of strains without the MTV.

Hepatoma, multiple in many cases, was the other principal neoplasm occurring in strain C3H-A^{vy}fB and in the reciprocal hybrid females (Tables 1 and 3). Cholangiomas (*9*), an interesting lesion, also occurred in these animals with the A^{vy} gene. Thus far cholangiomas have been found only in the livers of animals with multiple hepatomas.

The results from reciprocal hybridizations and experiments with foster nurses demonstrate that the factor responsible for the very high incidence of mammary tumors in C3H-A^{vy}fB mice is not maternally transmitted but is passed equally well by either parent. Since the hybrids were allowed to have a set number of litters or were maintained as virgins, the hormonal stimulation of the gland was reasonably equivalent in the reciprocal groups; however, the higher incidence in the breeders than in the virgins was a significant hormonal effect. Two other factors, however, must be considered. The A^{vy} gene and the NIV are transmitted equally to the F_1 offspring by the C3H-A^{vy}fB parent, and both apparently play an important role in the development of mammary tumors in these mice. It is, therefore, of interest to ascertain whether the C3H-A^{vy}fB strain harbors a variant of NIV with a high tumorigenic capacity, or whether the effect of the A^{vy} gene is to enhance the usually poor oncogenic ability of NIV and thus to promote a high incidence of mammary tumors, or whether A^{vy} acting in some other way causes the high incidence.

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Sex Ratio of Newborns: Preponderance of Males in Toxemia of Pregnancy

Abstract. *The ratio of males to females in 1061 babies born to mothers with toxemia of pregnancy is 1.24. The ratio increases as the severity of the disease increases, being 1.71 in cases in which the urinary output of protein is equal to or greater than 3 grams per 24 hours. Histoincompatibility of the fetus and mother, including incompatibility due to an antigen (or antigens) dependent on the Y chromosome, is suggested to function in the pathogenesis of pregnancy toxemia.*

Incompatibility of fetus and mother as a cause of toxemia of pregnancy was first suggested by Dienst in 1905 (*1*). His findings, based on ABO groups in the mother and fetus, were supported by some others (*2*). Later studies, however, suggest that the distributions of different combinations of ABO and Rh groups in the fetus and mother are similar in toxemic and normal pregnancies (*3*). Nevertheless, the possible role of other antigens, at that time unknown, was considered by some geneticists as early as 1946 (*4*). We now report that the ratio of males to females in babies born to toxemic mothers is significantly increased; we suggest that this indicates the importance of feto-maternal histoincompatibility in the pathogenesis of toxemia of pregnancy.

Table 1. Ratio of males to females in 1061 newborn babies (including 18 sets of twins and one set of triplets) of mothers with toxemia of pregnancy and of 8257 control babies. The controls were healthy babies born to healthy mothers during the same period and in the same hospital as babies of toxemic mothers. The difference between the sex ratio of babies born to toxemic mothers and that of controls is significant ($\chi^2 = 7.97$; $P < .01$).

Group	Newborns (No.)		Ratio of males to females
	Males	Females	
Toxemia	588	473	1.24
Control	4196	4061	1.03

Data were collected from records taken in the Department of Obstetrics and Gynecology, University of Turku, from 1961 to 1969. All babies, both premature and full-term, born to toxemic patients, including those with the mild preeclamptic form, were considered. The criteria of Dieckmann (*5*) were used to establish the diagnosis of toxemia.

Mothers with toxemia of pregnancy have boys significantly more often than

Table 2. Ratio of males to females in 1061 babies born to mothers with toxemia of pregnancy. The degree of the maternal disease was determined from the urinary protein output (UPO) or the diastolic blood pressure (DBP).

Sex	Newborns (No.) to mothers with toxemias of					
	UPO (g/24 hour)			DBP (mm-Hg)		
	< 0.1	0.1–2.9	$\geqq 3.0$	< 90	90–109	$\geqq 110$
Males	332	203	53	41	277	273
Females	296	146	31	39	242	192
Ratio of males to females	1.12	1.39	1.71	1.05	1.14	1.42

the control mothers do (Table 1). The ratio of males to females increases with the severity of the toxemia, as determined by the daily urinary excretion of protein or by the diastolic blood pressure (Table 2).

Information with respect to parity and blood groups (ABO and Rh with anti-D) of the mother and the newborn was available for 585 (55 percent) toxemic pregnancies, all of which were full-term (*6*). The ratio of males to females (1.22) in this group, which is not different from that for the entire group of toxemic patients (Table 1), indicates that the increased sex ratio is not related to prematurity. Parity had no effect on the sex ratio, because the ratio was the same in the case of primiparas as in that of multiparas. Distribution of the 16 different combinations of ABO groups and the four combinations of Rh groups within the toxemic group was similar to that within the 6096 controls (*7*).

In 1955, Salzmann reported an increased sex ratio in 287 babies born to toxemic mothers less than 30 years old (*8*). He put forward a theory about the role of male fetal hormones in the pathogenesis of toxemia. Today, the existence of a weak histocompatibility antigen (or antigens) determined by the Y chromosome is well established in the mouse (*9*), and there is considerable evidence for the same phenomenon in man. This evidence is based on the mother's ability to recognize the male fetus, as indicated by the following: (i) the fact that the ratio of males to females in live births decreases with increasing parity, whereas this ratio increases in stillbirths; and (ii) the fact that the number of preceding boys influences both the sex ratio of subsequent children and the intervals between births (*10*). Operation of an antigen (or antigens) dependent on the Y chromosome as a histocompatibility system in man is supported also by our recent data suggesting that the effect of feto-maternal ABO incompatibility and Y-chromosome-linked incompatibility on placental weight is cumulative (*11*).

We believe that it is possible to explain the increased ratio of males to females born to toxemic mothers as an expression of histoincompatibility between mother and fetus. Mothers with toxemia more often have HL-A antibodies (induced by cells from the conceptus) than healthy parturients do (*12*). We propose that toxemia of pregnancy has a partial immunological basis. Like other paternal antigens in all placentas (*13*), the potential Y-chromosome-dependent antigen (or antigens) must be present in the placenta of the male fetus. Histocompatibility antigens may potentiate the immunogenicity of other placental antigens known to be shared by the kidney (*14*), and this immunization may lead to renal lesions and other hallmarks of toxemia.

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Adenosine 3′,5′-Monophosphate in Rat Pineal Gland: Increase Induced by Light

Abstract. *Rats were maintained in alternating periods of 12 hours of light and 12 hours of darkness. The concentration of adenosine 3′,5′-monophosphate in pineal gland was six times higher at the end of the light period than at the end of the period of darkness. This effect of light was abolished in blinded animals.*

The concentration of adenosine 3′,5′-monophosphate (cyclic AMP) (*1*) and the activity of the adenyl cyclase (*2*) are particularly high in the pineal gland when compared with other areas of the brain. Norepinephrine increases pineal adenyl cyclase activity (*3*), and some of the effects of this catecholamine on the pineal gland are mediated through the formation of cyclic AMP (*4*). Because adenyl cyclase activity (*5*) as well as the concentration of norepinephrine in the pineal (*6*) are influenced by light, we investigated whether light also changes the content of cyclic AMP in this gland. Our experiments show that the concentration of cyclic AMP in rat pineal is six times higher after 10 hours of light than after 10 hours of darkness; moreover, the increased content of cyclic AMP induced by light is abolished in blinded rats.

Groups of 16 to 32 male Sprague-Dawley rats (180 to 220 g) were placed in two separate air-conditioned rooms and were kept in alternating photoperiods of 12 hours of light and 12 hours of darkness for at least 3 weeks. Light sources were white fluorescent lamps (General Electric) yielding 1070 to 1600 lu/m^2. A small blackened corridor separated the two rooms. Ten hours after exposure to light or darkness, the rats were decapitated and the pineal glands were removed and frozen within 30 seconds. For the rats in darkness, these operations were carried out with the aid of a lamp with a General Electric red soft bulb (BAS, 25 watts, 120 volts).

Cyclic AMP was determined by a method described by Ebadi *et al.* (*7*). Briefly, the frozen pineals were homogenized in a Duall glass tissue grinder with 300 μl of $ZnSO_4$ (0.3M) containing 1×10^{-18} mole of cyclic [^{3}H]AMP (2.35 c/mmole) to monitor recovery. The homogenates were frozen and thawed several times to release the bound cyclic AMP. A portion (20 μl)