Sex Ratios of Newborns: Associated with Prepartum and Postpartum Schizophrenia

Abstract. *From a review of the records of schizophrenic women whose psychotic symptoms were associated with pregnancy, it was found that those who had developed a psychosis within 1 month of conception delivered only live female infants. A predominance of males was born to 13 women who became psychotic during the first month after delivery. These observations are interpreted as consistent with a theory that schizophrenia is associated with plasma factors which interact with the fetus and provide the basis for a higher fetal mortality.*

Shearer *et al.* (*1*) reported that only female infants were born to women who had conceived within 1 month before or after an acute schizophrenic episode ($P < .001$). The authors concluded that their data suggest that there is in schizophrenia a serum factor specifically toxic to the Y chromosome either in sperm or in fertilized ova, but that later stages of gestation are not affected.

Charts of female patients at Manhattan State Hospital New York City were reviewed, and all fully documented pregnancies, associated with a sudden onset of psychotic symptoms but without complicating maternal neurological or medical illness, were selected. The first appearance of psychotic symptoms was used as the criterion for onset of illness. The chart diagnosis of schizophrenia was required and was confirmed by the presence of at least three of the following: hallucinations, delusions (of persecution or grandeur), catatonic motor symptoms, disordered affectivity (flattening, inappropriateness, unrelatedness), and thought disorder.

Fifty-four pregnancies met the criteria. All conceptions had occurred out of hospital, and three-quarters had occurred before the mother became mentally ill. Twenty conceptions had occurred during or shortly after treatment with a neuroleptic drug. There were 49 full-term births, 20 males and 29 females. I related the date of conception and sex of each offspring to the time of onset of the mother's schizophrenic episode (Table 1). Of 13 women who became psychotic within 1 month of conception, two were receiving neuroleptic drugs throughout gestation; all of their offspring were female. Of 13 women who became psychotic within 2 months after parturition, 2 delivered females and 11 delivered males.

There were five spontaneous abortions, at the onset of the mother's schizophrenia. Two occurred within the 1st month; one occurred during the first trimester, and two during the second trimester. The sex of the aborted fetuses was not recorded.

Among the defective offspring, there were four stillbirths, all male. Two newborns who died within the first 4 days after birth were males. Of six offspring with birth defects (deafness, mutism, cerebral palsy, blindness, and mental retardation) five were male. Only one, a second twin in a difficult labor, was a female.

These data, substantiating those of Shearer *et al.*, indicate that the male embryo and fetus are affected by the sudden development of the mother's prepartum schizophrenia. Absence of male live births when conception and psychotic onset coincide, and the predominance of birth defects in males, suggests that when the mother becomes psychotic within 1 month of conception the male embryo is destroyed, resulting in either a missed or an overt spontaneous abortion. When the mother becomes psychotic during the 2nd or 3rd month of pregnancy the male fetus either develops abnormally or dies slowly. Reports concerning the relation between the offspring's sex and the development of postpartum psychoses are unclear. Most investigators have combined separate diagnostic groups when considering what effects the sex of the offspring has on the mother (*2, 3*), or have reported no relation between the sex of the offspring and mother's reaction after delivery (*4–7*). These studies generally lack adequate diagnostic criteria, and no direct correlation between the sex of off-

Table 1. Schizophrenic symptoms, conception, and live births.

Time of onset of schizophrenia (months)	Offspring		χ^2 (1 d.f.)	$P <$
	Male	Female		
	Before conception			
> 10	2	2	0.3	N.S.
7 to 9	0	1		
4 to 6	2	2	6.2	N.S.
2 to 3	2	0		N.S.
	Before childbirth			
± 1	0	2	2.0	.001
2 to 3	2*	4	0.7	N.S.
4 to 6	1	0		N.S.
7 to 9	0	0	2.0	
	After childbirth			
0 to 1	10†	1	0.3	.01
1 to 3	1	13	13.0	
7 to 12	0	4	0.7	N.S.

* Mother of one male offspring developed toxemia of pregnancy before 24th week of gestation; infant born prematurely. † An 11th male offspring died 4 days postpartum (no autopsy).

Table 2. Case reports of postpartum psychoses and sex of offspring (only completely documented cases are included). Numbers in parentheses are references; $\chi^2 = 28.6$; $P < .001$.

Diagnosis	Case	Offspring		Year
		Male	Female	
Schizophrenic	1	1		1949 (*5*)
Catatonic schizophrenic	1		1	1952 (*6*)
Paranoid schizophrenic	1	1		
Schizophrenic	1	1		1957 (*7*)
Paranoid schizophrenic	1	1 (twins)		
Schizophrenic	1	1		1933 (*12*)
Paranoid schizophrenic	1		1	1964 (*2*)
Schizophrenic	1	1		
Schizophrenic	5	5		1966–8
Schizophrenic	13	11	2	1968

spring and diagnosis of the mother is reported. I studied 26 pregnancies where the mother became psychotic during the 1st month after delivery (Table 2). Twenty-two were associated with delivery of a male and four with delivery of a female. These data suggest a causal relation between the birth of a male child and a postpartum schizophrenia. I believe postpartum schizophrenia to be a release phenomenon, secondary to birth of the male fetus and to the withdrawal from the mother of the male hormonal influence. Successful treatment of postpartum psychoses with progestins (*8*) and androgens (*9*) indicates that this hormonal influence may involve both progesterone and testosterone.

Reports by Keeler *et al.* (*10*), who describe an acute schizophrenic-like episode in a patient after the abrupt withdrawal of Enovid, and by Delay *et al.* (*11*), who report specific endometrial pathology associated with postpartum psychoses, lend validity to these clinical trials and to the concept of a hormonal deficiency in postpartum psychoses.

My data may indicate that the onset of schizophrenia in the mother is an initiating event. If the mother is acutely schizophrenic during the 1st month of her pregnancy, the male fetus succumbs, whereas if the onset of schizophrenia occurs later in the pregnancy, the fetus may physiologically "defend" itself by the production of functionally high hormone levels (progesterone, testosterone) which suppress the disease in the mother, perhaps by (i) preventing the production, or (ii) enhancing the breakdown of a toxic blood factor in the schizophrenic mother. Delivery of a male fetus unmasks the mother's schizophrenia, with an effect similar to that of abrupt withdrawal of a neuroleptic drug.

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Positive Contrast in the Runway Obtained with Delay of Reward

Abstract. *The failure to find positive contrast effects in the runway may be attributed to a ceiling effect that can be overcome with the use of delay of reward. Rats were trained one trial a day in a runway with small, medium, or large reward. When a shift to large reward was combined with delay of reward, shift groups slowed down less than controls.*

Several lines of evidence suggest that the effect of a given magnitude of reward is not a constant but depends on the range of alternative rewards the subject has received (*1*). A typical procedure for demonstrating this effect is to stabilize an animal on one magnitude of reward and then shift it to a different magnitude. Upward shifts that result in the animal's overshooting the level of an appropriate control are called positive contrast. Conversely, downward shifts that result in the animal's undershooting the level of an appropriate control are called negative contrast. Although negative contrast may be more widely found than positive contrast, there is at least one experimental paradigm which regularly produces the positive case (*2*). In the runway, however, there has been a consistent failure to find positive contrast (though the negative case is widely found). We report here a procedure that gives rise to positive contrast in the runway.

The consistent failure to obtain positive contrast effects in the runway when the parameter is the amount of food reward has been attributed to a possible ceiling effect (*3*). If large reward produces the fastest possible speed of running, shifting a group trained on small reward to large reward could not result in a speed greater than that of a control trained continuously on large reward. It has been suggested that the shift be to medium rather than to large reward, which should allow contrast to show itself. This approach has been unsuccessful, however, for reasons that are difficult to assess because the use of medium reward is not a condition that maximizes contrast (*4*).

A different approach involves the introduction of an aversive condition, such as delay of reward, along with the shift in magnitude of reward. Because delay typically results in a slower speed of running, this should assure a submaximum speed and thus allow possible contrast effects to emerge.

The use of an aversive condition to bring out a difference not visible beforehand has been reported in at least one other context (*5*). Two groups of mature rats, one of which had been deprived of food in infancy, were trained with food reward on a position habit in a T-maze; both attained the same asymptotic running speed and percentage of correct choice. However, when shock was introduced on the food side, the food-stressed group slowed down less and continued to choose the food side more than the control. Instead of shock we used delay of reward, which is equally effective in reducing speed of running.

Fifty naive male albino rats (90 days old, Sprague-Dawley strain) were maintained on limited food with free access to water. The rats were divided into three main groups which, after each run in the runway, received one 45-mg Noyes pellet ($N = 20$), four such pellets ($N = 20$), or 22 such pellets ($N = 10$), respectively.

The apparatus was a duplicate of a standard long runway (1.7 m) (*6*). Start, run, goal, and total times were measured by four standard electric timers activated by the interruption of appropriate photocells located 2.5, 33, 108, and 137 cm from the start box; the last photocell was 15 cm inside the goal box.

After 6 days of adaptation to the runway, all subjects were given 41 trials in the runway (one trial a day) by which time running speeds had stabi-