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PROTEIN FERTILITY FACTOR AND CONGENITAL DEVELOPMENTAL DEFECTS

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No general agreement yet exists on a name for protein fertility factor [7]. An organ-specific placental α_2-globulin was first identified in 1976 in extracts of human placenta [1]. Later this globulin was discovered in organs of the reproductive system of both women and men [3, 5, 6] and its biosynthesis was shown to depend on hormonal contraceptive preparations [4]. On comparative immunodiffusion analysis the placental α_2-globulin was found to be similar to PP-14 [9], α-uterine protein [12], and progestin-endometrial protein [8]. The molecular weight of all these proteins lies within the range 25-50 kD, since the protein can exist in two forms or can form complexes with other serum or placental proteins [2, 5-8, 10, 12]. Since this α_2-globulin is synthesized not only by decidual cells and cells of the uterine mucosa in the secretory phase of the menstrual cycle, but also in the seminal vesicles of men [5, 11], we decided to propose a new name for this protein: "protein fertility factor" (PFF).

This paper gives the results of a semiquantitative analysis of PFF in human seminal fluid in order to reveal the connection between the PFF level in the sperm and birth of children with congenital developmental defects.

EXPERIMENTAL METHOD

Antiserum against PFF was obtained by immunization of rabbits with semipurified preparations of PFF isolated from extracts of abortion material or from amniotic fluid [1, 6]. Amniotic fluid, diluted to obtain the clearest precipitation line, was used as the standard antigen for immunodiffusion analysis. The antisera were additionally exhausted with dry plasma and with extracts of normal human organs. The sensitivity of the test system was about 2 mg/liter. The results of assay of PFF in the groups compared were subjected to statistical analysis by Student's test. Clinical observations were made on couples attending the Out-Patient Department in Ivanovo for genetic counseling. The men collected the sperm after coitus interruptus or by masturbation and sent it to the laboratory in glass bottles. The bottles were kept in the freezing compartment of domestic refrigerators and kept there until required for analysis. In all cases the karyotype of the husband and wife was determined, and no abnormality was found. Altogether 35 married couples with viable offspring (without any gross morphological developmental defects) and 18 couples who had given birth to children with various severe developmental defects, incompatible with life, were investigated.

EXPERIMENTAL RESULTS

The content of PFF in sperm obtained from men with normal children varied within quite wide limits — from 16 to 256 mg/liter (mean 45.9 mg/liter). Normally the PFF concentration in the sperm varied as a rule from 16 to 64 mg/liter. However, in 12 of the 18 men whose

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TABLE 1. PFF Level in Sperm of Husbands and Physical State of Newborn Infants

Diagnosis	Number of observations	PFF concentration in sperm, mg/liter			
		2—8	16—32	64—128	256
Without visible developmental defects (healthy)	35	0	27	7	1
Anencephaly	4	2	2	0	0
Hydrocephalus	5	4	1	0	0
Spina bifida	3	2	0	1	0
Multiple severe developmental defects	6	4	2	0	0
Total	53	12	31	8	1

Legend. Level of significance calculated by Student's test: normal (N) 35, M = 45.9, m = 7.6; severe developmental defects: N = 18, M = 15.0, m = 3.6; t = 3.68; $p < 0.01$.

wives had given birth to children with severe developmental defects, the PFF level varied from 2 to 8 mg/liter. However, the PFF level in the sperm of six of the 18 men was within normal limits. On average for this group of husbands the PFF level was 15 mg/liter. Consequently, a relatively low PFF level in the father's sperm coincided in almost 67% of cases with the birth of a nonviable offspring (Table 1). The significance of the difference between groups of men with normal and low PFF levels in their sperm can be regarded as perfectly safe ($p < 0.01$). It goes without saying that during investigation of the married couples no special tests were carried out for the establishment of paternity, because this was not among the aims of the study.

Results indicate the probability of significant correlation between the PFF concentration in the father's sperm and his ability to produce a normal child. However, the molecular mechanism of the participation of PFF in the process of conception and in the formation of severe developmental defects remains completely unstudied. It would be interesting to investigate the ability of the spermatozoa to bind PFF molecules specifically and to retain them in the female genital tract until contact had been made with the female sex cell. The problem we have raised here may perhaps give a fresh impetus for research in this direction.

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