may be involved in immediate hypersensitivity responses[13]. Until now, CRP-like proteins have not been found in the ova or spermatozoa of any species. The presence of such a protein in lumpsucker gametes once again raises the question of the function, if any, of CRP in vertebrates. Agglutinins for some cells and in particular for erythrocytes, have been found in extracts of the ova of a number of lower vertebrates and invertebrates[14,15]. These agglutinins have been called 'protectins'[16], since they may act to protect the eggs from invasion by pathogens. Whether the lumpsucker CRP-like protein we have described is protective in any way for the fish gametes is at present unknown. The occurrence of the protein however, in both eggs and sperm adds further interest to the speculation and predictions of the biological role of CRP in vertebrates.

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Immunosuppressive Effect of a Mouse Placenta Fraction on H-2 Incompatible Split Heart Allografts[1]

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Summary. A soluble placenta fraction from mice (A.CA) mated with H-2 histoincompatible males (A/Sn) significantly prolonged the survival of heterotopic A/Sn heart transplants in A.CA recipients. No prolongation of A/Sn heart graft survival was obtained with the corresponding A.CA placenta fraction after A.CA × A.CA mating.

Pregnancy represents an exception to the rule of allograft rejection[3]. An intriguing biological question is how the fetus, possessing paternal histocompatibility antigens, is protected from the expected immunological destruction. Ample evidence of immune stimulation is found in the mother in the form of hypertrophy of regional lymph nodes and the production of sensitized lymphocytes and antibodies to fetal histocompatibility antigens[4]. There is, however, also substantial data in support of a partial impairment of the mother's immune response, particularly the cell-mediated, during pregnancy[5–8]. The mechanisms responsible for this impairment are poorly understood[4,9]. Most likely several mechanisms are responsible for the fetal exemption from the consequences of the immune response. The theory that uterus represents an immunologically privileged site has been rejected[4] and there are no special features of the maternal immune system that makes it tolerant to fetal tissue. There is, however, growing evidence that mucoproteins in the glycocalyx on trophoblasts can mask transplantation antigens and possibly interfere with the effect of sensitized lymphocytes[10,11]. Furthermore, trophoblasts have been shown to inhibit the spreading of macrophages in vitro[12]. Finally, maternal antibodies or antigen-antibody complexes may exert a blocking effect on the cell-mediated immune response[4] and various gestational hormones[11,13–16], and certain α-globulins[17] in maternal plasma have been reported to have immunosuppressive effect. We report here a significant immunosuppressive effect of a soluble mouse placenta fraction on the survival of split mouse heart grafts transplanted over a strong histoincompatibility (H-2^a→ H-2^t) barrier.

Materials and methods. A technique for heterotopic grafting of split allogeneic mouse hearts earlier described[18] was used. A.CA mice served as recipients and A/Sn baby mice (24–48 h age) as donors in the present study. The electrical activity of the transplants was monitored with a Tektronic 410 cardioscope. Placenta was excised from A.CA mice on days 16–18 after mating, homogenized in cold, sterile 0.25 *M* sucrose solution and ultrasonicated with a Branson B-12 sonifier equipped with a microtip. 5 ml samples were treated in glass tubes submerged in ice under constant stirring. Six 30 sec pulses of sonic energy (20 kHz 50 watt) were applied at 30 sec intervals. A.CA recipients were given 0.3 ml of this placenta homogenate i.p. on every 2nd day after transplantation, starting on day 0.

The placenta homogenate was centrifuged further at 20,000 *g* for 20 min at +4°C. The pellet was resuspended in 5 ml 0.25 *M* sucrose solution, the sonication procedure was repeated and after centrifugation as above the 2 supernatants were pooled and concentrated 6× by ultrafiltration. The final pellet was resuspended in 2.5 ml 0.25 *M* sucrose solution with the aid of gentle sonication.

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Immunosuppressive effect of A.CA placenta fractions in A.CA recipients of split A/Sn heart transplants

Treatment	No. of transplants	Mean survival and range (days)
None	8	11.3 (9–13)
Placenta homogenate[a] (A.CA × A/Sn)	8	13.5 (10–20)
Placenta pellet[b] (A.CA × A/Sn)	6	11.0 (10–12)
Placenta supernatant[a] (A.CA × A/Sn)	6	13.0 (11–15)
Placenta supernatant concentrated[a] (A.CA × A/Sn)	9	15.3 (13–17)
Placenta supernatant concentrated[a] (A.CA × A.CA)	5	11.5 (10–12)
Serum from pregnant A.CA (A.CA × A/Sn[c])	11	10.3 (7–13)
Amniotic fluid from pregnant A.CA (A.CA × A/Sn[d])	9	11.4 (9–14)

[a] 0.3 ml given i.p. on every 2nd day after transplantation starting on day 0. [b] 0.15 ml given i.p. on every 2nd day after transplantation starting on day 0. [c] 0.15 ml of serum given i.p. on days 0, 6 and 9 after transplantation. [d] 0.15 ml of amniotic fluid given i.p. on days 0, 6 and 12 after transplantation.

A.CA recipients received 0.15 ml of the resuspended pellet or 0.3 ml of the concentrated supernatants (24 mg protein/ml) i.p. on every 2nd day after transplantation, starting on day 0.

Results and discussion. Placenta supernatant, particularly after concentration, significantly ($t_{(16)} = 5.51^{XXX}$) prolonged the survival of strongly H-2 incompatible split A/Sn heart transplants (Table). In contrast, neither placenta supernatant (24 mg protein/ml) from A.CA females mated with A.CA males, nor amniotic fluid (12 mg protein/ml) or serum from A.CA females mated with A/Sn males, had any significant immunosuppressive effect.

The negative results with amniotic fluid and placenta supernatants from females of the A.CA × A.CA mating speak against α-fetoprotein[19] as the major immunosuppressive factor. Neither do the latter results support the idea that placental glycoprotein hormones[11,13–16] are responsible for the effect. Other possible factors which could explain the immunosuppressive effect are maternal serum-derived α-globulins[17] or antibodies[4]. The fact that only placenta supernatant from A.CA mice mated with A/Sn males had distinct immunosuppressive effect is compatible with an effect mediated by antibodies or antigen-antibody complexes; but further experiments are necessary in order to identify the active principle.

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Effect of an Antiandrogen on the Lymphoid System*

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Summary. A side-effect of the administration of cyproterone acetate, an antiandrogenic steroid, to newborn, juvenile or adult male mice (in doses comparable to those used clinically) was found in a marked reduction of the white pulp of the spleen and reduced weight or even absence of the thymus.

The antiandrogenic steroid, cyproterone acetate (6-chloro-17-hydroxy-1α,2α-methylene-pregna-4,6-dien-3,20 dione acetate, Androcur, Schering AG, Berlin) is being used in human medicine when the production of endogenous testosterone is to be inhibited (sexual de viations such as hypersexuality, benign prostatic hyperplasia, prostatic cancer)[1–5].

We used cyproterone acetate (CA) in some experimental studies aimed at specifically inhibiting certain cellular antigens of which the expression turned out to be to some extent androgen-dependent[6,7]. CA was given s.c. to newborn, juvenile or adult male mice for 4 or 6 weeks or only as a single dose (Table). The long-term dosage was calculated (on body weight basis) from the doses reported to be administered per os in man. That their biological effect may be equivalent seems to be indicated by a similar picture of spermatogenesis which was not completely disturbed, only the production of sperm being markedly inhibited.

The body weight was reduced only in the groups where the treatment was started in newborn or juvenile males. Spermatogenesis was inhibited in all groups and testes weight reduced in most of them. A reduced spleen weight was found only when the treatment was started neonatally, but the microstructure of the organ was affected in all groups; there was always an increased granulopoiesis and erythropoiesis in the red pulp, whereas the white pulp was reduced and occasionally almost completely lacking. In the thymus, the change concerned weight and mostly also morphology irrespective of the age at which the treatment was started and the dose administered. The organ was sometimes hard to detect, even histologically. The striking reduction of size was in some cases accompanied by so drastic a depletion of lymphocytes that the cortex and medulla were virtually indistinguishable. Also frequently observed was dilatation of blood vessels in the medulla. Following a single administration of CA, particularly in the higher dose range, the normal structure of the thymus was sometimes reversed in that the medulla contained more lymphocytes than the depleted