Letters to the Editor

Sir

Pregnancy & Neoplasm are two outstanding examples of natural tolerance to homograft. Our accidental observation in the year 1977 that (1) *intra amniotic instillation of 2 ml Tetanus Toxoid causes abortion* has been confirmed again and again in 688 cases so far in fixed single dose schedule, while 2 ml of intra amniotic instillation of normal saline in thiomersol base failed to evoke such response i.e. abortion, in 72 cases. (2) I also observed that *1 cc of B.C.G. if injected intra amniotically,* induces dissolution of the foetus and auto absorption of the foetus takes place. After 10 such BCG experimentations the ethical subcommittee attached to IPGMER advised me not to proceed with BCG experimentations for future theoretical possibilities of Choriocarcinoma. (3) while Bovine Serum Albumin (n = 12) triple antigen also causes abortion (n = 14). We actually concentrated on the problem of abortion with intra amniotic instillation of Tetanus toxoid *for midtrimester only*, though even at 8 weeks - 12 weeks there are abortions, but the possibility of incomplete abortion is very high – justifying the use of prostaglandin/oxytocin support for proper evacuation. (4) Safety studies (FDP, Fibrinogen, Platelet etc.) for coagulation profile has reaffirmed our faith on this method of abortion when comparing with other midtrimester abortion agents like hypertonic saline, prostaglandin, ethicredin lactate.

Since 1985 we have been injecting this agent as an outpatient protocol to mothers who were admitted for hysterectomy and ligation, with advice to get admitted when the pain starts, and subsequently Laparoscopic ligation/minilap was undertaken with consent of the patient (n = 194); however certain problems remained to be solved. (*a*) Induction abortion interval varied from 86 hours to 28 days (99%). Intrafoetal injection (suggestion by Prof. Klopper) and increasing the doses of Tetanus Toxoid up to 6 cc or repeating the doses weekly (suggestion by Prof. S. Nardi and Prof. Silverstein) failed to standardise the induction abortion interval (n = 74).

I may summarize the advantage of this method of abortion for midtrimester, by mentioning (*b*) Cheapest method for midtrimester abortion costing about 10 American cent per patient (the price of Tetanus Toxoid). (*c*) Safety profile and subsequent pregnancy potential is extremely good. (*d*) Abortion is spontaneous and complete (92%). Eight per cent of patients required postaglandin/oxytocin/DE support.

METHODS FOR AVOIDING THE PROBLEM

Injection under ultrasound guidance at the OPD - advice the patient to go home and to report to the hospital when the pain or bleeding starts.

Other methods like addition of foetotoxic/immunomodulators Like Vitamin A,

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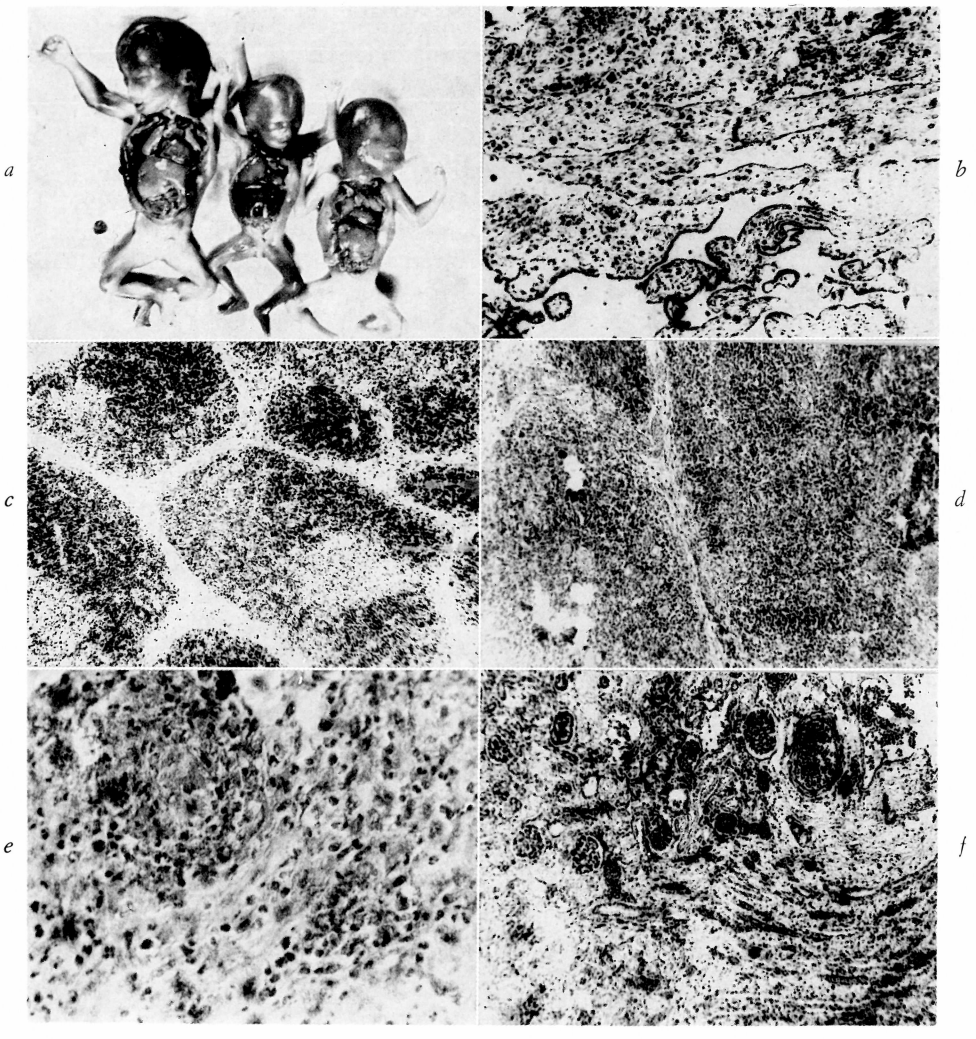

Table 1. — fig. *a*. Haemorrhage in pleuropericardioperitoneal space and softening of the viscera; fig. *b*. Placenta intense congestion, mononuclear invasion and thrombosis on the maternal side; figs. *c, d*. Intense congestion and lymphocytic infiltration of thymus (low and sligh magnification); fig. *e*. Liver; fig. *f*. Kidney in both histological slides, seen through conventional microscope, she congestion and lymphocytic infiltration are intense.

with toxoid injection or Levamisol to mother failed to evoke statistically significant positive response. (5) Now one thing is clear – Intra amniotic instillation of Tetanus Toxoid causes safe midtrimester abortion but why and how i.e. aetiopathogenesis is not clear.

Study of the aborted foetuses before 18 weeks showed autolysis and softening of the foetuses and extensive haemorrhage and congestion at the pleuropericardioperitoneal cavity. Histology also showed extensive haemorrhage and congestion of the viscera – whereas in cases of abortion

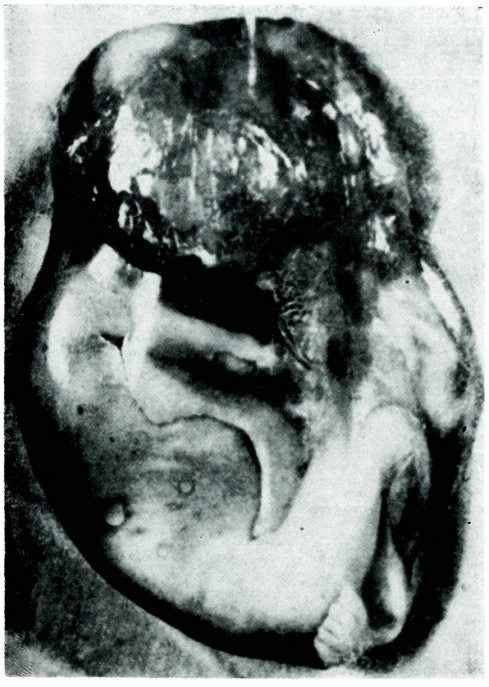

Fig. 1. — This is a 20 weeks live male foetus where the amniotic membrane and placenta came out spontaneously. This is unique method of abortion.

18-20 weeks there is comparatively less haemorrhage and congestion and also the structure of the organ is well maintained. In the case of the maternal side of the placenta there is mononuclear invasion, thrombosis, congestion justifying the possibility of maternal rejection of the conceptus. (6) While 2 cc of Tetanus toxoid injection intra amniotically causes sensitization of the foetal lymphocyte (MIF Study), maternal lymphocytes are not sensitized. Similarly Intramuscular injection of 2 ml Tetanus toxoid causes the mother's lymphocytic sensitization, while foetal thymocyte/lymphocyte are not sensitized. This sensitivity varies with the gestation period and exposure. (7) Matenal intramuscular injection of Tetanus toxoid does not prevent abortion. (8) In case of aborted foetuses there is a significant rise of histamine (160% from gestational control) and hepatic glutamic dehydrogenase (210% more than the control value).

This matter has since then been presented at the IXth World Congress of OB/GYN Tokyo '79, Xth World Congress of Fertility and Sterility, Madrid '80; International Congress of Immunology, Paris '80, International Congress of reproduction, Argentina 1981; Asia Oceanic Congress of OB/GYN of Melburne '82; World Congress of OB/GYN, San Francisco 1982; American Society of Reproductive Immunology Annual Meeting, Durham 1984; World Congress of Pathology '86; World Congress OB / GYN, Montreal 1994; World Congress of Fertility and Sterility, Montpellier France 1995; International Congress of Royal College of OB/GYN, Delhi 1996 apart fom other minor Congresses.

However the problem remains to be solved.

Therefore, I want you assistance on the problems noted below:

a) In a developing foetal system how to standardise the parameters of rejection? – While in adult system we can confirm rejection histologically with Thrombosis, endarterites and mononuclear invasion etc.

b) Whether the foetus is vis a vis rejecting the mother.

c) Whether graft vs host reaction is taking place. – There are some suggestions – foetal paraaortic lymph nodes are increased and also the weight of the foetal liver becomes 4.9-5.4% of the total wieght (normally the weight should be 3.9%).

d) While in some cases there is complete expulsion including the membrane and the amniotic fluid – can you suggest certain studies which can confirm this event as an initiation of normal premature labour (only immunological studies). – Could maternal and foetal lymphocytes

play an essential role in the initiation of the labour process at term?

I am a Gynaecologist and General Surgeon (MBBS 1975), M.D. (OB/GYN), 1980, 2nd Post Graduation in General Surgery (MS in 1983) leaving aside specific training from different institutions in U.S.A., Europe etc. – I do not have a background in animal research, however if it is imperative please give me advice. Meanwhile I have standardised an abortion protocol with a she goat model with intraamniotic antigen under ultrasound guidance and ketamine anaesthesia.

The growth of science has never accepted any barrier of religion, nationality or any other human divisions. Considering your outstanding eminence in this field, *I would be grateful for your suggestions and guidance* so that we can understand the problem in greater detail.

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Sir,

The problem you have presented is quite interesting and could have many implications in our gynecologic activity, especially in birth control.

Personally, I am not an expert in this field but I hope that some colleague will be able to reply to you directly of through our Journal. I invite eveybody to think abont the question and to write their thoughts to me to stimulate research and broaden the general knowledge on this issue with all its many biological and clinical implications.

Prof. A. Onnis