MITOGEN-INDUCED LYMPHOCYTE TRANSFORMATION
AFTER GENERAL ANAESTHESIA

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SUMMARY
The effect of three different types of general anaesthesia on mitogen-induced transformation of human peripheral lymphocytes was studied. The mitogens used were phytohaemagglutinin and concanavalin A. A single anaesthesia had no clear effect on human peripheral lymphocytes.

There is evidence that general anaesthesia interferes with the immune response in man (Bruce and Wingard, 1971). It may affect postoperative infections, anaphylaxis, response to organ transplantation and tumour growth. It has been speculated that there is a relationship between this immunosuppression and the development of postoperative hepatitis (Bruce and Wingard, 1971). Anaesthetists appear to have a higher death rate from malignancy of the lymphoid and reticuloendothelial tissues than many other doctors (Bruce et al., 1968). An increased incidence of still birth, abortion and foetal malformation among women anaesthetists is reported (Askrog and Harvald, 1970; Cohen, Bellville and Brown, 1971; Knill-Jones et al., 1972).

In a recent study we found that halothane anaesthesia is able to suppress the function of T-lymphocytes in the chicken. It had no clear effect on humoral antibody response to a thymus-dependent or a thymus-independent antigen (Viljanen et al., 1973). The present work was intended to clarify the effects of three different types of general anaesthesia on human lymphocytes with special reference to the effect of halothane. The mitogenic response of lymphocytes before and after anaesthesia was studied with two different mitogens, phytohaemagglutinin (PHA) and concanavalin A (con A).

PATIENTS AND METHODS
The study was conducted on 38 patients, all of whom received the same premedication: atropine, pethidine and promethazine. A control blood sample was collected just before induction of anaesthesia.

Group I (thiopentone anaesthesia) consisted of 12 healthy females who were undergoing legal abortion. Their ages ranged from 16 to 44 years (mean 26.5 years). Dilatation and curettage were performed. For anaesthesia, thiopentone 500–600 mg was given intravenously. Methylergonovine 0.2 mg was given intravenously after the operation. No other drugs were used. Blood was sampled for experimental cultures 15–60 min (mean 39.5 min) after induction.

Group II (balanced anaesthesia without halothane) consisted of 15 patients. Their ages ranged from 20 to 41 years (mean 28.8 years). Nine of these patients were undergoing legal abortion which was performed by abdominal hysterotomy. Four patients underwent surgery for a retroverted uterus. Two patients had oophorectomy because of dermoid cysts and ovarian endometriosis. Anaesthesia was induced with thiopentone (250–350 mg i.v.) and maintained with 70% nitrous oxide in oxygen. The semi-open system with a Manley respirator was used. Muscle relaxation was achieved with an infusion of suxamethonium in 5% glucose, except in 4 patients who received pancuronium (6–9 mg i.v.). During the operation pethidine (35–90 mg i.v.) was given if required. After hysterotomy 0.2 mg methylergonovine i.v. was given. Blood samples for experimental cultures were taken 20–70 min (mean 39.6 min) after induction.

Group III (balanced anaesthesia with halothane) consisted of 11 patients; 7 female and 4 male. Their ages were between 8 and 73 years (mean 40.2 years). A variety of general surgical operations was performed. Anaesthesia was induced with thiopentone (200–375 mg i.v.) and maintained with halothane 1% v/v in 70% nitrous oxide in oxygen.
A semi-open system with a Manley respirator was used. Muscle relaxation was achieved with suxamethonium (50–80 mg i.v.) followed by pancuronium (4–6 mg i.v.) in 5 patients and alloferin (10–22.5 mg i.v.) in 7 cases. Pethidine (25–50 mg i.v.) was given as required. All the patients had a 5% glucose infusion. Blood was sampled just before the end of operation, 15–100 min after induction (mean 49.8 min). The response to Con A was determined in only 9 patients in this group.

For the studies of the mitogenic response buffy coat cells from peripheral blood were used. Lymphocytes thus obtained were cultured for 72 hours in 5% CO2 in humidified air at a density of 10^6 cells/ml/tube in medium RPMI 1640 (Grand Island Biological Co.) with 100 units/ml of penicillin and 100 μg/ml streptomycin. Fresh human AB plasma (10%) was used to supplement the culture medium. PHA M (Difco, Detroit, Michigan) was used in a concentration of 50 μl/ml/culture and Con A (Pharmacia, Uppsala, Sweden) in a concentration of 50 μg/ml/culture. All cultures were made in triplicate. To determine the mitogenic response, 0.5 μCi of 5-iododeoxyuridine-125I (specific activity 0.5–1 mCi/mg) (New England Nuclear, Frankfurt, Germany) was added to each culture for the final 18 hours of incubation (Asantila and Toivanen, 1974). The stimulation index for each sample was obtained by dividing the mean incorporation (counts per minute) of 5-iododeoxyuridine-125I in the experimental cultures with the mean incorporation in the control cultures.

Statistical analyses were made by computer using Pearson’s product moment correlation.

RESULTS
In figure 1 the PHA-induced lymphocyte transformation index with each experimental lymphocyte sample is expressed as a percentage of the transformation index of control lymphocytes. This result is recorded as the “comparative transformation rate” (St Hill, Finn and Denye, 1973). Figure 2 shows the results with Con A stimulation. There were no significant differences between the control and experimental groups or between PHA and Con A responses. The duration of anesthesia had no effect on the mitogenic response.

DISCUSSION
Knowledge about the effect of a single anesthesia on the immune response in man is relatively limited (Bruce and Wingard, 1971). Our results indicate that these three types of anesthesia have no clear effect on the mitogenic response of human peripheral lymphocytes. Nor is there a relationship between the duration of anesthesia and the mitogenic response. Halothane does not seem to have a special effect in this respect. The difference between these findings and our previous animal results with halothane may be attributable to the multiple halo-
Lymphocyte transformation after general anaesthesia

In our previous work six anaesthetics, each lasting for 1 hour, were given before lymphocyte culturing. Perhaps a single anaesthesia cannot cause depression of lymphocyte function measurable by these methods. Park et al. (1971) have reported that, after all forms of surgery requiring general anaesthesia, the peripheral blood lymphocytes lose immunocompetence. There are, however, clear differences between their patients and ours. Their patients had very severe diseases which per se are capable of impairing lymphocyte function. Our patients were almost totally healthy. A second difference is the longer follow-up time in the study by Park et al. (1971). In addition, in our study we washed lymphocytes free from autologous plasma in order to avoid halothane contamination. Normal responses to mitogens have been reported with the lymphocytes of anaesthetists exposed to chronic inhalation of various anaesthetics (Bruce, 1972). However, we think that possible immunosuppression caused by chronic exposure to anaesthetics cannot be completely excluded.

References


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Syllabus 1974-75

1974

Thursday, November 28 (Dundee)

“The Differentiation of the Normoblast”, Professor J. D. Robertson.

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Thursday, April 10 (Stracathro)

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Thursday, May 8 (Aberdeen)

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