Immunologically Competent Anesthesiologists

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Lymphocyte cultures were prepared from blood of six anesthesiologists and six male graduate students with no history of recent exposure to anesthetics. Stimulation of lymphocytes by phytohemagglutinin (PHA) was assessed by determining uptake of the DNA precursor, thymidine, 72 hours following the addition of PHA. The results indicated that lymphocytes from these anesthesiologists were normally reactive to PHA. No support was provided for the hypothesis that occupational exposure to anesthetics causes immunosuppression among anesthetists. (Key words: Phytohemagglutinin; Lymphocytes; Immune response; Anesthesiologists.)

A 20-YEAR retrospective study of the causes of death of anesthesiologists in the United States and Canada disclosed that these specialists had a death rate from malignant diseases of the lymphatic and reticuloendothelial tissues higher than that in a corresponding control population. The capacity of lymphocytes of patients with Hodgkin’s disease to respond to phytohemagglutinin (PHA) is markedly depressed. The interpretation of this finding was that these patients had diminished immunologic responsiveness, similar to that of patients with leukemia. Since several studies suggest that general anesthetics in sufficient doses may be immunosuppressant, it becomes appropriate to ask whether anesthesiologists exposed to trace amounts of anesthetic gases in the operating room might be somewhat immunosuppressed and thus run a higher risk of the development of lymphoid malignancies. The present study was designed to test this question.

Methods

Six male, healthy members of the faculty of the Northwestern University Department of Anesthesia served as lymphocyte donors. Each administered anesthesia daily at one of the teaching hospitals, and is exposed to anesthetic gases in a fashion thought to be representative of practicing anesthesiologists in general. On the day of donation, the anesthesiologist had no breakfast, and at 7 AM, 200 ml of whole blood were withdrawn from an antecubital vein.

All subsequent procedures were also done using sterilized materials and aseptic technique. Forty milliliter samples of blood were added to 55-ml plastic tubes containing 12 ml of a 4 per cent dextran solution (mol wt 200,000), 300 mg heat-sterilized carbonyl iron, and 0.4 ml heparin solution (500 U.S.P. units/ml in 0.85 per cent NaCl without preservative). These tubes were capped and mixed at 37 C for an hour in a rotational mixer. The samples were then divided among 20-ml siliconized glass tubes. The blood was sedimented in an upright position for 45 to 60 minutes at 37 C. The plasma was aspirated and pooled in a 55-ml plastic tube. A large magnet was applied to the side of this tube to attract the iron-containing phagocytes, and with the magnet applied, the contents of the tubes were decanted into another tube, which was then centrifuged for 10 minutes at 500 X g at 2 C. The supernatant was aspirated. To the remaining sedimented cells were added 10 to 15 ml of minimum essential Eagle’s medium (MEM) containing 50,000 units penicillin G, 50 mg streptomycin, and 50 mg glutamine/100 ml MEM. This mixture was agitated gently, the magnet reapplied, and the contents of the tube decanted into another tube. A total cell and differential count of a sample of this was made using phase-contrast hemocytometry. The leukocyte separation with
this method resulted in only one neutrophil per 100 to 200 lymphocytes in the final preparation. Knowing the cell count, the appropriate dilution was made with cell-free autologous plasma to achieve a resultant suspension of 10^6 lymphocytes/ml.

One-milliliter samples of this mixture were added to tissue culture tubes containing 2 ml of MEM (containing the antibiotics as outlined above) and 0.05 ml of reconstituted PHA-M (Difco), all experiments using PHA from the same lot. From each donor, 24 cultures were prepared with PHA added, and four to ten without. Cultures were maintained at 37°C in a tissue culture incubator containing 5 per cent CO_2 in humidified air for a period of 72 hours. At that time, 2 μCi of tritiated thymidine (HT, 5.0 Ci/mM) were added. Three hours later, the cultures were harvested and prepared for liquid scintillation counting as described previously.

An identical procedure was followed for six healthy, paid volunteer donors taking no medications. Each was a male graduate student in either the dental or the medical school at Northwestern University, and the procedure for blood donation was explained by the author and a written consent for venipuncture obtained. Each of these donors was also asked not to have breakfast until after the donation, which in all cases was at 7 AM. The cell preparation and the remainder of the procedure was identical to that for the anesthesiologists. All samples were counted for 10 minutes in a Nuclear-Chicago Mark I scintillation counter, and these counts corrected for quench by the channels-ratio method, using a 137Ba external standard. Counting efficiency ranged from 34 to 38 per cent, and results were expressed as disintegrations per minute (dpm).

Results

Mean control counts of cultures containing no PHA were 1,632 ± 344 dpm for the anesthesiologists and 1,510 ± 201 dpm for the volunteers. In contrast, PHA-stimulated cultures in the two groups did differ. The mean dpm values of 144 cultures were 254,416 for the anesthesiologists and 164,315 for the volunteers. Table 1 lists the data from each donor. It is clear that the hypothesis that anesthesiologists might show evidence of immunosuppression is not supported by these data. In fact, there was evidence that their lymphocytes were more responsive than normal to the stimulation of PHA, as judged by the incorporation of thymidine into acid-insoluble nucleoprotein.

Discussion

It is evident from these studies that if anesthetic inhalation in the trace amounts found in our operating rooms is immunosuppressant, this must occur only in the rare individual and not as a general rule. None of the volunteer donors had any history of working with, or recent exposure to, anesthetic agents. If their response to PHA is viewed as reasonably representative of the general population, anesthesiologists are quite reactive. Most of the clinical literature dealing with the use of the PHA-lymphocyte response in various disease states indicates that it is depressed as the general immunity of the patient is lowered. Hersh and Oppenheim demonstrated a depression of PHA stimulation in patients given 6-mercapto- purine, methotrexate and prednisolone for chemotherapy. Even salicylates interfere with this test. Against this background of information concerning depression of the response, any enhancement of the response must be of questionable significance at present. Most likely, the results simply indicate that the anesthesiologists studied were normally immunoreactive, using this method to assay this capacity.

A retrospective study of causes of death of anesthesiologists revealed 17 deaths from lymphoid malignancies. Occurring among ap-

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proximately 10,000 anesthesiologists, this represents an incidence of about one in 588. It is obviously impractical to examine 588 practicing anesthesiologists for their immunologic reactivity, so this study does not preclude the possibility that a rare individual may suffer suppression of his immune response as a result of chronic inhalation of traces of anesthetic. Even in patients deliberately immuno-suppressed following organ transplants, the estimated incidence of cancer is 6 to 8 per cent. It is doubtful, therefore, that any correlation between immunosuppression and propensity to lymphoid malignancy can be found by practicable studies of this sort.

Miss Louise Owen gave excellent technical assistance.

References


Drugs and Their Actions

ENDOCRINE FUNCTION AFTER L-DOPA IN PARKINSONISM Nine patients with Parkinson's disease were studied before and during therapy with L-dopa, 6 g/day. The drug caused no significant change in: 1) thyroid function, as indicated by serum thyroxine levels and uptake of T3 resin or radioiodine; 2) adrenal function, as indicated by 24-hour urinary excretion of 17-hydroxy corticosteroids and 17-ketosteroids; 3) pituitary ACTH function, as indicated by increased steroid secretion in response to metapyrone orally (750 mg q 4th x 6); or 4) urinary excretion of gonadotropins. These last findings in man are at variance with those found in animals by others, who were able to demonstrate dopamine effects on gonadotropins. Plasma growth hormone levels were elevated following L-dopa; this response was not altered by glucose given either orally or intravenously. Curiously, L-dopa modified the tolerance to glucose administered orally (but not iv), i.e., the plasma glucose levels, which were unchanged in the first 120 minutes, and plasma insulin response, which was markedly diminished during this time, were both significantly elevated three, four, and five hours after orally-administered glucose. In contrast, after glucose iv, L-dopa did not significantly change glucose decay or plasma insulin levels, nor did tolbutamide influence this lack of response. Data from the control studies suggest that impaired growth-hormone release in response to insulin-induced hypoglycemia and abnormal tolerance to intravenous glucose may be present in Parkinson's disease. (Boyd, A. E., III, Lebovitz, H. E., and Feldman, J. M.: Endocrine Function and Glucose Metabolism in Patients with Parkinson's Disease and Their Alteration by L-Dopa, J. Clin. Endocrinol. Metab. 33: 829-837, 1971.)