CHANGES IN PERIPHERAL BLOOD LEUCOCYTES FOLLOWING I.V.
ANAESTHESIA AND SURGERY

Sir,—Observations of leucocytosis following anaesthesia and surgery are certainly not new. Current interest is, for the most part, centred around possible depression of cellular immune response by the various anaesthetic agents on the cancer patient treated by surgery. The high incidence of apparently “anaphylactoid” or hypersensitivity-type adverse responses to the newer i.v. anaesthetic agents is also creating an interest in the mechanism of immunological recognition (or memory) to i.v. drugs in general.

It is important to differentiate the three major factors influencing leucocytosis. These are: (a) the effect of the concentration of the i.v. agent on the chemotaxis of cells, (b) stimulation by the i.v. agents of intermediary humoral factors, such as complement and prostaglandins, which cause cell migration, and (c) the role of tissue trauma. These factors are defined both by the time sequence in which they occur and by the type of leucocytes involved. Chemotactic effects occur from the point of induction and in vivo are probably restricted in time by the pharmokinetics of the drug. These are possibly of only a few minutes’ duration unless a continuous infusion procedure is being employed. This phase is well documented in vitro by Boyden chamber experiments (Moudgil et al., 1977). The trauma factor probably develops about 2 h after anaesthesia and surgery, and is characterized by a massive influx of polymorphs into the circulation, an effect which may last for several days (Ryhänen, 1977). The intermediate humoral effect, lasting about 20–60 min, is the least understood and may even be dismissed as insignificant. This is the point, however, at which immunological phenomena appear to be initiated. We have chosen to study this particular aspect and, in view of some misunderstanding of our published observations (Watkins et al., 1976), would like to summarize the situation.

White cell counts, increasing by about 25% of the pre-induction values 5–10 min after induction, are observed in approximately 60% of all patients receiving Althesin, propanidid or methohexitone for the first time. Such changes on first exposure to a drug cannot be associated with immunological recognition (memory). Our studies indicate a degree of complement C3 activation in these patients which explains also the analogous plasma histamine release curves observed by Lorenz (1975). Although we have not yet established statistical significance of the leucocyte changes with these three anaesthetic drugs, the new hypnotic, etomidate, produced highly significant changes (P < 0.001). A second exposure to these drugs appears to induce a degree of immune recognition in at least 5% of all patients. This is characterized by more pronounced C3 activation, a marked decrease in polymorph counts and either static, or a slight increase in, lymphocytes numbers. These reactions are essentially subclinical, but a similar pattern of leucocytosis to Althesin has been observed in an animal model by our associates. Here, the second exposure to Althesin resulted not only in a dramatic decrease in peripheral polymorphs but also in severe clinical anaphylaxis. We were recently fortunate in obtaining leucocyte data in a patient who exhibited a severe anaphylactic response to thiopentone (table 1).

The data, although far from complete, indicate the almost constant behaviour of the lymphocytes in contrast to the polymorphs which decreased dramatically initially (1 h) followed, 6 h later (as the trauma response occurs), by an equally dramatic increase.

We would suggest that the difference between subclinical response and full clinical responsiveness is essentially one of magnitude. Patients showing clinical responsiveness may do so either by a direct activation of their complement system or as a result of immunological hypersensitivity. The responding patient is likely to be genetically predisposed in a specific manner, but there is little reason to believe that patients with specific atopy are at high risk with any i.v. anaesthetic agent. Finally, it is worth noting that induction of anaesthesia with inhalation anaesthetics does not appear to produce a variation in the peripheral leucocyte count.

J. WATKINS
A. M. WARD
T. N. APPLEYARD
Sheffield

REFERENCES

AYRE’S T-PIECE AND POLLUTION

Sir,—The advantages of administering anaesthesia by means of an Ayre’s T-piece (or Y-piece) in infants and small children are well recognized. However, the use of this system for controlled respiration by intermittent occlusion of the open end of the expiratory limb with a finger tip produces considerable pollution. This problem has been solved by simple modification of the system: the rather stiff polyethylene tubing used for the expiratory limb has been replaced by a length of soft silicone rubber tubing (wall thickness 1 mm). Controlled respiration is accomplished easily by intermittent compression of the expiratory limb. Exhaust gas is scavenged through a wide-bore corrugated rubber tubing (air flow 25–30 litre/min) by introducing the end of the expiratory limb a few centimetres into the open end of the corrugated tubing. The system seems to work satisfactorily in clinical practice. The resistance and flow requirements of the system and the efficacy of the gas scavenging are currently under investigation.

NIELS VALENTIN
Hvidovre, Denmark

<table>
<thead>
<tr>
<th>Time after injection</th>
<th>Total white cell count</th>
<th>Polymorphs and monocytes</th>
<th>Lymphocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 min</td>
<td>8.0</td>
<td>3.4</td>
<td>4.1</td>
</tr>
<tr>
<td>1 h</td>
<td>5.0</td>
<td>1.4</td>
<td>3.4</td>
</tr>
<tr>
<td>6 h</td>
<td>18.5</td>
<td>13.9</td>
<td>4.6</td>
</tr>
</tbody>
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Correspondence

Changes in peripheral blood leucocytes following i.v. anaesthesia and surgery are certainly not new. Current interest is, for the most part, centred around possible depression of cellular immune response by the various anaesthetic agents on the cancer patient treated by surgery. The high incidence of apparently “anaphylactoid” or hypersensitivity-type adverse responses to the newer i.v. anaesthetic agents is also creating an interest in the mechanism of immunological recognition (or memory) to i.v. drugs in general.

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NIELS VALENTIN
Hvidovre, Denmark
EBSTEIN'S ANOMALY—ANAESTHETIC PROBLEMS

Sir,—I read the article on Ebstein's anomaly by Dr Bengtsson and his colleagues (1977) with interest and congratulate them on their careful and successful anaesthetic management. However, I do not believe they can draw any conclusion about anaesthesia for these patients on the basis of this one patient, whatever the practical and theoretical problems. At the National Heart Hospital we regularly anaesthetize such patients for correction of the anomaly, as we do other cardiac patients, with no special precautions except our usual care. I am always a little puzzled by and not a little sceptical of claims for certain anaesthetic agents or combinations in the management of patients with specific conditions. Whilst particular problems may require specific measures, I feel sure that with the great majority of high risk patients a careful approach is more important than a favoured technique. Evidence to the contrary requires suitable controlled studies and must show some important differences in morbidity or mortality or both. Such evidence is hardly available. Many years ago, some of us learned a long and authoritative list of absolute contraindications to thiopentone and this included many grave heart conditions. Today, I suspect that porphyria is all that is left of this list!

A. GILSTON
London

REFERENCE


Sir,—Thank you for the opportunity to answer the letter by Dr A. Gilston. Our intention was not to prove the superiority of the chosen technique but merely to describe problems encountered and any possible difficulties arising. We used a standard anaesthetic technique for a hysterectomy in a patient suffering from Ebstein's anomaly and in our experience this is a very unusual situation.

INGE BENGTSSON
RICARDO MAGNO
INGEMAR WICKSTROM
Gothenburg, Sweden

AN UNUSUAL SOLVENT

Sir,—In common with Siebke, Ellertsen and Lind (1976) we, at Sundsvall Hospital, have observed also that when diazepam is dissolved in Cremophor EL it is less painful on injection i.v. However, one anaphylactoid reaction to Cremophor did occur although the amount of solvent given was only 0.5 ml (Gjessing and Tomlin, 1977).

Recently, we have tried a solvent in widespread clinical use, Intralipid 20%. The formulation consists of diazepam 5 mg per ml of Intralipid and was prepared by Vitrum AB.

We have given diazepam in this formulation to 30 patients, who were undergoing the Brunswik operation under spinal anaesthesia. The drug mixture was given always in 0.5-ml increments through a cannula, through which no other substances were infused. We have not observed any patient to experience pain, and on direct questioning no patient admitted to a sensation of pain. There has been no thrombophlebitis. Dardel, Mebius and Mossberg (1976) found an incidence of pain with diazepam in the same formulation of 0.1%.

Sir,—A detail of technique which I have found useful in "one-shot" extradural injections, but have not seen described previously, is as follows. With the patient lying on his side the "loss of resistance to air" method is used to locate the space. However, if a glass syringe with an excentrically placed nozzle is used for the air injection, it may be filled with the precalculated volume of liquid. (This may require the use of a larger syringe.) With the nozzle uppermost, the loss of resistance test may be used and then by rotating the syringe a half-circle the liquid portion may be injected (after attempted aspiration of blood).

This method avoids the inconvenience of connections which may stick, or the needle tip altering position when the syringes are being changed, and automatically wets the dry syringe for a better seal and smoother running.

D. E. JEAL
Durban, South Africa

One curious phenomenon is that, when given in this new solvent, the amount of diazepam necessary to achieve the level of sedation we require during regional block techniques has been almost doubled. The mean dose requirement was 8.6 mg (SD 2.2 mg) of diazepam compared with a mean dose of 4.92 mg (SD 2.41 mg) of diazepam in aqueous solution given to an equal number of patients having the same operation and the same type of regional block. This difference was statistically significant (Student's t = 6.18, P < 0.001). Some interference with the pharmacokinetics of diazepam was noted when diazepam was given with Cremophor EL as the solvent, but not to this extent (Gjessing and Tomlin, 1977).

Diazepam, a fat soluble compound, has a different brain/fat solvent partition coefficient compared with brain/aqueous solvent partition coefficient, and it is possible that more diazepam remains in the fat emulsion particles circulating in the vascular compartment and is available for metabolism in the liver. A similar explanation could account for the threefold increase noted by Jeppsson and Ljungberg (1975) in the LD₅₀ of diazepam when given in the same fat emulsion solvent.

This raises an interesting speculation on the probable doses of other anaesthetic drugs, including Althesin and propanidid, if Intralipid or other fat emulsions are used as their solvents. The use of such solvents may be a future development in view of the problems associated with their current solvents.

JON GJESSING
Sundsvall
PETER J. TOMLIN
Birmingham

REFERENCES


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