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Reports of Scientific Meetings

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Symposium on the Allergic Risk in Anesthesia

Adverse drug reactions occurring during anesthesia and operation are of growing concern. The continuous introduction of new drugs into the armamentarium of the anesthetist makes the problem increasingly evident. The diagnosis and prevention of these reactions require close collaboration between the allergist, the anesthesiologist, and the pharmacologist. The antigenicity of these drugs in terms of significant side effects must be investigated before their clinical use.

With this in mind, the Departments of Anesthesia (Prof. J. M. Picard, Prof. M. C. Laxenaire); Allergy and Clinical Immunology (Prof. J. P. Grilliat, Dr. D. Moneret-Vautrin); and Pharmacology (Prof. M. Lamarche) in Nancy organized a tripartite symposium on the risks of allergic reactions during anesthesia. Experts in these fields from France and many other countries gathered to discuss this topic.

Of considerable interest was the report of a national French survey of serious drug reactions. Most of the reactions were considered related to massive, nonspecific release of histamine. However, some were true anaphylactic reactions, confirmed by immunologic tests such as the Shelley test (indirect basophil degranulation test), and the lymphocyte transformation test (LTT). Pentobarbital and succinylcholine were reported to be the two drugs most frequently responsible for these adverse reactions.

In another interesting study, Dr. Sigiel (Nancy) investigated the variation in histamine levels in whole blood in relation to types of anesthesia. She presented data indicating that most crucial was the technique of anesthesia, including the route and speed of administration. However, no correlation could be established between the change in whole-blood histamine level and the clinical signs. Decreased levels of histamine were found twice as often in individuals who had abnormal release of histamine, determined by intradermal testing with compound 48/80 (a polyamine that nonspecifically and non-immunologically displaces histamine). It was suggested that the cutaneous receptors for histamine in these individuals have an increased affinity for histamine, *i.e.*, more was fixed than was released. On the other hand, Professor Doenicke (Munich) found that levels of histamine in plasmas of normal controls increased as much as 350 per cent (normal = 0.69 ± 0.26 ng/ml) after use of propanidid, thiopental, methohexital, or alphadione (Althesin). No increase was found when Etomidate (ethyl-1- (2-methylbenzyl) imidazole-5-carboxylate) was used as an induction agent. Increases in histamine levels were tolerated without symptoms until a threshold of 3 ng/ml was reached, after which clinical signs appeared.

Professor Girard (Geneva) used several tests to define postoperative changes in the immune system. First, he observed depression of *in-vivo* delayed hypersensitivity to *Candida* antigen, *Trichophyton*, tuberculin, and mumps vaccine using intradermal cutaneous tests. The reactions became and stayed negative within ten days postoperatively and usually normalized within three weeks. This is much longer than the corresponding period for the *in-vitro* lymphocyte transformation test. He also found that postoperative lymphopenia involved primarily the thymus-derived lymphocyte population. This finding was confirmed by the depressed PHA (phytohemagglutinin) transformation of lymphocytes. Professor Nicholas (Nancy) found that an increase in serum IgE occurred one to five days postoperatively in atopic patients. No change was found in nonatopic patients.

Dr. Moneret-Vautrin (Nancy) attempted to delineate factors that might help to identify patients with increased risk of allergic drug reaction during local and general anesthesia. She reported that patients who have histories of allergy did not appear to have an increased frequency of adverse reactions to drugs, but in the event a reaction occurred, it was more severe. A history of drug reac-

tion also increased the frequency and the severity of a second reaction. However, previous exposure to the same anesthetic drug appeared to increase the risk only when the exposures were frequent and close.

Spasmophilia was a problem of special interest to the Nancy group. The syndrome was found in 80 per cent of patients who had serious drug reactions, versus only 10 per cent in the normal population. Spasmophilia may be described as a state of hyperexcitability of the neurons often accompanying fatigue and anxiety. In many cases a dysfunction of magnesium metabolism and increased secretion of catecholamines are also involved. The relationship between spasmophilia and allergy remains vague, and may be related to an anomaly of membrane receptors (Professor Duc, Nancy). The greatest risk for drug reactions was associated with the simultaneous occurrence of two or three factors. The Nancy group also presented evidence that it was unreliable to test patients with either *in-vivo* (intradermal and compound 48/80) or *in-vitro* (basophil degranulation) tests when they had recently sustained severe drug reactions. Due to a refractory period of histamine release, reliable testing had to be deferred until six weeks later.

The lack of correlation between the lymphocyte transformation test, cutaneous tests, and allergy was demonstrated by reports from both Dr. Mathieu, (Boston) and Dr. Walton (London). The use of the LTT test in the diagnosis of so-called "halothane hepatitis" was seriously questioned by the data from these two laboratories. In addition, the Boston group presented evidence of immunologic changes reported for viral hepatitis A or B.

The meetings proved very fruitful for the three partcipating groups, and promoted very stimulating discussions. The need for continued interdisciplinary collaboration was reasserted. The proceedings of this symposium will be published in a special issue of *Annales d'Anesthesie Française.*

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Neuromuscular Blockade

SUCCINYLCHOLINE AND TRAIN-OF-FOUR The use of train-of-four stimulation to evaluate neuromuscular block produced by succinylcholine during N_2O-O_2 anesthesia in man is described. The first phase is associated with minimal train-of-four fade, while the second is accompanied by marked fade. The second phase appears to resemble block produced by *d*-tubocurarine and probably corresponds to phase II (dual block). The second phase was observed to have an abrupt onset beginning after the administration of 3–5 mg/kg succinylcholine. The initial phase was associated with infusion of 1–3 mg/kg of the drug. The beginning of the second phase appeared to coincide with the development of tachyphylaxis. The author concludes that phase II does not have a gradual onset as has been suggested, and that it may be related to tachyphylaxis. *(Lee C: Dose relationships of phase II, tachyphylaxis and train-of-four fade in suxamethonium induced dual block in man. Br J Anaesth 47: 841–845, 1975.)*