

the possibility of a special subset of patients on parenteral nutrition, *i.e.*, those receiving drugs with low therapeutic indices and drugs subject to extensive hepatic metabolism. Based on their clinical responses, these patients may require adjustment in drug dosages.

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New Problem Leaks Out

To the Editor:—The complications and problems associated with the use of the Swan-Ganz catheter are numerous and well documented.¹⁻⁵ Recently, however, we encountered a problem not previously described in the literature. A dog was cannulated via the femoral approach for a routine high-frequency jet ventilation study. A #7 Fr. Edwards flow-directed thermodilution catheter was inserted following cutdown and positioned in the pulmonary artery according to waveform. Cardiovascular data were collected repeatedly without difficulty until 2 h later, when there was difficulty obtaining the pulmonary artery occlusion pressure. On two occasions, 1.0 ml of air was injected into the inflation port but not returned. Because it was suspected that the balloon had ruptured, it was immediately replaced. However, when the catheter was examined, no apparent rupture of the balloon could be seen. Next, the balloon was tested by rapid inflation with 1.0 ml of air, resulting in uniform and sustained inflation; whereas slow inflation confirmed the presence of a small leak. To localize this site, the catheter slowly was inflated under water, and bubbles were seen escaping from the distal weld between balloon and catheter surface. Rapid inflation had resulted in tamponade of the faulty joint with no appreciable leak.

It is recommended that Swan-Ganz® catheters be inflated slowly and with the minimum of air to avoid

possible rupture.^{6,*} This case serves to illustrate one inherent problem associated with Swan-Ganz® use, even when following recommended procedures. Rapid inflation of balloon-tipped catheters cannot be justified, because of increased risk of balloon rupture with resultant air embolism, pulmonary artery damage, or failure to detect preexisting balloon rupture.

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* Product Insert: Flow-directed thermodilution catheters. American Edwards Laboratories, Santa Ana, California.

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Multiple Comparison Procedures in the Analysis of Designed Experiments

To the Editor:—An editorial¹ and recent correspondence² discussed problems in the analyses of experimental data from more than two groups reported in the medical literature. It was pointed out that use of multiple *t* tests (or Fisher's unmodified LSD test), in which the Type 1 error (alpha, or the probability of false-positive results) is controlled at some fixed value, commonly 0.05, for each comparison leads to a Type 1 error greater than alpha for the set of tests as a whole.¹ Thus, the probability can be quite high that some of the differences found to be significant actually arose by chance. On the other hand, use of multiple comparison procedures, such as Tukey's test or Scheffe's test, designed to control Type 1 error for the set of comparisons as a whole, results in increased Type 2 error (beta, or probability of false negatives).² These articles will be most useful to readers who must interpret published results of research; however, little practical guidance has been given to the researcher who must choose an analysis suited to his particular data.

The relative merits of the two approaches to Type 1 error have been described clearly,^{1,2} but nothing has been said about the type of questions being asked by the researcher or the aims of his study. These latter considerations are of vital importance in choosing the correct test.^{3,4} The types of hypotheses that a researcher may wish to test can be divided into two categories.

In the medical sciences, a researcher who designs and carries out an experiment almost invariably has specific hypotheses or predictions that he aims to test. These hypotheses have been formulated before the experiment was conducted and are reflected in its design. Usually, the number of comparisons required to test such *a priori* hypotheses will be small when compared with the total number of comparisons that potentially could be made. These *a priori* hypotheses will, of course, always be tested in the analysis. When the *a priori* comparisons form or are part of an orthogonal set (*i.e.*, the outcome of each comparison is independent of

the outcomes of all other comparisons), multiple comparison procedures are not required and the hypotheses should be tested individually.⁴ In practice, the *a priori* hypotheses often will not be mutually independent. Even in this case, Winer⁴ states that, when the number of *a priori* hypotheses is small, they should be tested individually at the chosen level of significance.

It also may happen that, having tested his *a priori* hypotheses (or, rarely, having none), and wishing to make the most of the resources invested in the experiment, the researcher deliberately sets out to sift through his data to see if any unexpected but possibly interesting effects have been uncovered. Or, perhaps, the results of the experiment suggest that some interesting effect may exist that had not been anticipated. In any complex experiment, there are a large number of such *a posteriori* comparisons (it should be noted that a deliberate selection of the two most extreme means implies the comparison of all possible pairs of means), and consequently some large differences are likely to arise by chance. To disallow such *post hoc* data snooping would do nothing to aid the advance of science; indeed, unexpected findings sometimes may be the most important. However, these *a posteriori* comparisons are of a clearly different nature to those made to test *a priori* hypotheses. Readers of the scientific literature should be protected from the deluge of spuriously significant results that would appear if this distinction was not made. Therefore, most researchers will wish to control the Type 1 error for the set of *a posteriori* comparisons as a whole, and so should use an appropriate multiple comparison procedure.

If the approach outlined above is followed, then the argument that use of multiple comparison procedures leads to requirements for larger sample sizes and greater investment in experiments² clearly does not apply to those hypotheses that the experiment was designed to test. What does become clear is the crucial importance of identifying and specifying the hypothe-