Ideally, drug research should proceed from basic sciences, through animal models to its final test - the clinical trials. In the field of supraventricular arrhythmias, however, the process has to unfortunately by-pass the animal models as we do not have satisfactory methods to produce the experimental counterpart of the human arrhythmias. In this presentation we will try to outline methodological guidelines for conducting clinical trials necessary to evaluate any new medication for supraventricular arrhythmias.

When preparing a strategy for the clinical trials, one first has to classify the supraventricular arrhythmias and define their natural history. The latter is extremely important for the proper evaluation of drug effect. The second ingredient in planning a clinical trial is the establishment of the objectives of the therapy.

From the point of view of drug evaluation, the supraventricular arrhythmia fall into three simple categories:

A. Supraventricular (atrial or junctional) premature beats.
B. Supraventricular (atrial or junctional) tachycardias.
C. Atrial flutter and fibrillation.

The approach to category A, namely the supraventricular premature beats, should be no different from that to premature beats in general. This aspect has been well dealt with elsewhere at this symposium. In this presentation we will therefore address ourselves to categories B and C.

The supraventricular tachycardia tend to appear in paroxysms which last from minutes to hours, and rarely, even days. The frequency varies tremendously among different patients and many
times also within the same patients. A chronic form of such an arrhythmia is a medical rarity. The objectives of treatment are thus twofold. One, to abolish a paroxysm when it appears, and two, to prevent recurrence of attacks.

Atrial flutter usually presents itself as paroxysmal arrhythmias, but may occur in chronic forms. Atrial fibrillation is abundant both in its paroxysmal and its chronic forms. In both atrial flutter and fibrillation (in their paroxysmal form), one may wish to terminate the arrhythmia and prevent recurrences. However, in the paroxysmal bouts, and all the more in the chronic form, one has to also deal with a different aspect of treatment, namely, the control of heart rate. The initial approach to atrial flutter and fibrillation, regardless of etiology and form (acute or chronic), is therefore slowing the heart rate. This is usually achieved by increasing the degree of atrio-ventricular block with drugs. In the chronic form of the arrhythmias (mainly the chronic atrial fibrillation) this is the only therapeutic objective.

In summary, there are three objectives to be achieved in the management of supraventricular arrhythmias:

I. Abolish paroxysms of arrhythmias.
II. Prevent recurrences of (or decrease) paroxysms.
III. Control heart rate in atrial flutter and fibrillation.

Different study designs should be utilized for the investigation of each of these objectives.

ETHICAL PROBLEMS

Two problems should be solved before plunging into any clinical trial in general, and into drug evaluation in supraventricular arrhythmias in particular. Should the patient be treated? Many of the supraventricular tachycardias occur in healthy individuals and their benign and rare appearances may render any preventive drug intervention unnecessary. The second problem deals with the applicability of placebo for a double blind study. The benign feature of many of the supraventricular arrhythmias, we feel, justifies the guarded use of placebo in patients who tolerate the arrhythmias well (for the various protocols, see below). However, instead of placebo as control,