the A-V block occurs at the level of the bundle branches
the deficit in blood supply must be in both the anterior
and posterior circulations of the heart since branches to
this area are supplied from both anterior and posterior
perforating arteries. Thus involvement of both bundles
necessarily implies extensive myocardial damage.1–4

In our experience, patients with A-V block having a
widened QRS all developed cardiac failure or shock
even if these complications were not present at the
moment of the onset of the block. Regardless of the
electrocardiographic location of the infarction, the
mortality rate despite pacing is about 90%.

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The author replies:

I feel that this view is too simplified to be of practical
importance. It is generally known that the QRS duration
is important in prognosis. However, it is certainly not
our experience that all patients with wide QRS develop
failure or shock, or that the related mortality is “about
90%.” Our studies regarding experiences in this area
have been reported in a subsequent issue of Circulation.
Any effective subgrouping will require use of more than
just one descriptor. It is for this reason that we included
location of infarction, degree of heart failure experi
cenced by the patient, and site of A-V block as criteria
for inclusion within the subgroup that we reported. It
may be necessary, in fact, for a fourth or fifth descriptor
to be added on a larger number of patients to be able to
accurately choose the best management for the
individual patient.

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Bretylium and Ventricular Arrhythmias

To the Editor:
The paper “Deleterious Effects of Bretylium in Cats
with Digitalis-induced Ventricular Tachycardia” by
Gillis, Clancy and Anderson (Circulation 47: 974,
1973) documents the worsening of ventricular arrhyth
mias which bretylium can induce in the anesthetized
cat intoxicated with deslanoside. The purposes of this
letter are threefold: (1) to support the authors’
conclusion that the catecholamine releasing action is
related to the ventricular arrhythmias bretylium
produces, (2) to speculate on how bretylium aggra
vates ventricular arrhythmias, and (3) to set these
observations in the cat into clinical perspective.

The communication by Gillis and coworkers shows
deleterious effects of bretylium on ventricular tachycar
dia caused by excess digitalis. A number of mechanisms
can produce ventricular tachycardia in digitalis toxicity
or otherwise. These include: (1) enhanced normal
automaticity, (2) abnormal automaticity in Purkinje
fibers and (3) simple or complex forms of reentry in
Purkinje fibers and/or ventricular muscle.1–2 The data
presented by Gillis, Clancy and Anderson suggest that
bretylium may aggravate changes in automaticity
induced by bretylium. Two previous studies evaluated
the effects of bretylium on normal automaticity in
isolated preparations of mammalian cardiac Purkinje
fibers and ventricular muscle cells.3–4 These studies
showed that bretylium induces or increases the rate of
spontaneous firing in these preparations for 10 to 15
minutes, after which it has a variable effect on rate.3,4
Low concentrations of quinidine were shown to have
the opposite effect, i.e., to reduce automaticity in the
same preparations.4 The ability of bretylium to enhance
or evoke automaticity in cardiac Purkinje fibers is
completely nullified by pretreatment with propranolol
or reserpine;3,4 this finding suggests that the augmenta
tion of automaticity bretylium is due to release of
norepinephrine (NE) from the postganglionic sympa
thetic nerve terminals in the isolated preparations.

How bretylium-induced NE release from sympathetic
nerve endings in ventricular tissues might aggravate
ventricular arrhythmias is not certain. Several effects
of catecholamines on mammalian ventricular tissues are
almost certainly relevant; the catecholamines can:
(1) enhance Purkinje fiber automaticity by causing
potassium current (IK) to decline more rapidly during
diastole,5 (2) hyperpolarize depolarized cardiac tis
sues, either by increasing IK or by increasing elec
trogenic Na+ pumping, particularly when depolariz
ation is produced by stretch,6 (3) induce slowly
propagating active potentials in depolarized tissues
(active responses which are qualitatively different from
the normal action potential)7 and (4) augment the
diastolic oscillations (“abnormal automaticity”) seen in
digitalis toxicity.8 Any one or combination of these
effects could under appropriate conditions result in
ventricular tachycardia. Which of these mechanisms
leads to the aggravation of digitalis-induced arrhyth
mias reported by Gillis, Clancy and Anderson remains
to be elucidated.

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No matter what the mechanism by which bretylium aggravates experimental ventricular arrhythmias, it would seem reasonable to treat clinical digitalis arrhythmias by some other means since treatment with diphenylhydantoin, lidocaine and potassium is so effective and relatively safe. Further, bretylium has been noted, on occasion, to aggravate human ventricular arrhythmias of other causes, e.g., those encountered in patients with ischemic heart disease. In some cases, the increase in arrhythmias seems related to bretylium's ability to block neuronal uptake of catecholamines and thus greatly potentiate the cardiac action of circulating catecholamines (present due either to adrenal secretion or therapeutic infusion).

On the other hand, it should be emphasized that bretylium can be quite effective as an antiarrhythmic drug and should be considered for acute therapy of arrhythmias which are resistant to other agents; in this circumstance, it is often successful. Also, a small but important experience with long-term oral bretylium therapy suggests that, used in this mode, it may prevent recurrence of dangerous ventricular arrhythmias. Interestingly, tachyphylaxis for antiarrhythmic effect does not occur as it does for the antihypertensive effect of bretylium. In fact, were it not for the frequent and significant parotid pain which attends long-term therapy, bretylium would even be a reasonable candidate for the effective, well-tolerated drug which is so badly needed for long-term antiarrhythmic prophylaxis in patients with coronary heart disease.

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Bretylium and Ventricular Arrhythmias
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