Cardiac Arrhythmias

The first use of PHT in cardiac disorders was reported by Leonard in 1958. Since it was the pioneer paper in this field, it will be summarized in some detail. It brings into focus three important points which develop throughout the literature: 1) PHT is an effective antiarrhythmic, prompt in its action; 2) PHT has a high margin of safety; 3) In the acute stage, substantial amounts of PHT may be required, adjusted to the severity of the condition.

Leonard, Archives of Internal Medicine (1958), 221 demonstrated the beneficial effect of PHT in controlling ventricular hyperirritability, complicating myocardial infarction in a patient. The patient was gravely ill with cardiographic findings of typical ventricular tachycardia. In spite of the previous history of complete heart block, it was felt that intravenous procaainamide, if carefully controlled, was the treatment of choice. The patient was receiving Arterenol to maintain his blood pressure at 110/70. Procaainamide was given intravenously. During a period of approximately two hours, 2300 mg of procaainamide was given, in spite of several episodes of marked hypotension, but finally discontinued because of disturbing widening of the QRS complex without reversion to a normal sinus mechanism. The patient's condition remained critical, and it was considered advisable to investigate the therapeutic potential of intravenous PHT. PHT was administered slowly intravenously in a dose of 250 mg. A cardiogram recorded approximately two minutes later revealed a normal sinus mechanism coupled with premature auricular contractions. In twenty minutes ventricular tachycardia had recurred. An immediate additional dose of 250 mg of PHT was given and within moments a normal sinus mechanism appeared. Four hours later ventricular tachycardia returned and was again successfully reverted to a normal sinus rhythm with 250 mg of intravenous PHT. Because the duration of effectiveness of PHT was unknown, a constant, slow intravenous infusion of 250 mg of PHT was started. The normal sinus mechanism was maintained in this fashion for successive periods of six and four hours. At these intervals ventricular tachycardia returned, but was promptly reverted with additional intravenous doses of 250 mg of PHT. At the time it was considered advisable to supplement the intravenous therapy with 3 grains of PHT and 500 mg of procaainamide every four hours orally. Eighteen hours after its initiation the intravenous PHT was discontinued. An electrocardiogram at this time showed posterior myocardial infarction with a normal sinus mechanism. On the following day procaainamide was discontinued, and the patient was maintained with 3 grains of PFU orally every six hours. There was no recurrence of signs of ventricular irritability. The patient made an uneventful recovery. The author suggests that PHT may represent a drug with a wide margin of safety that is effective in controlling serious ventricular hyperirritability.


Bernstein, Gold, Lang, Pappelbaum, Bazik and Corday, Journal of the American Medical Association (1965), 18 used oral PHT in the treatment and prevention of recurring cardiac arrhythmias in a group of sixty patients, who had been refractory to or intolerant of conventional medication. In thirty-seven patients with premature ventricular contractions, twenty-six returned to normal sinus rhythm, and seven had a decrease in the number of ectopic beats. In thirteen patients who had atrial tachycardia, ten had excellent response and two had moderate improvement. Six patients with paroxysmal atrial fibrillation had excellent response. Two patients with premature atrial contractions and one with premature nodal beats had excellent response. One patient with recurrent atrial flutter did not respond. Some side effects were observed. None were serious and all disappeared upon withdrawal of the medicine. The patients had been evaluated for periods up to nineteen months, the time the study was reported.


Conn, New England Journal of Medicine (1965), 61 found that PHT, administered intravenously to twenty-four patients with a variety of cardiac arrhythmias, was particularly effective in supraventricular and ventricular arrhythmias resulting from digitalis excess. It was also of benefit in controlling paroxysmal atrial and ventricular arrhythmias. In three cases of atrial fibrillation and two with atrial flutter no therapeutic effect was noted. Toxicity consisted of transient bradycardia and hypotension in one patient and short-term anticoagulant block with bradycardia in another. The author stated that PHT appears to be a significant addition to the drug therapy of cardiac arrhythmias.


Lugo and Sanabria, Acta Medicina Venezolana (1966), 517 reported the effectiveness of oral PHT, 100 mg q.i.d., in eleven patients with chronic Chagasic cardiac disease, with multifocal ventricular extrasystoles. In eight cases response was excellent with conversion to normal sinus rhythm which continued up to the eight months the patients were followed. In two cases there was excellent response, but the drug had to be discontinued because of skin rash. In one case with ventricular extrasystoles and atrial fibrillation, the extrasystoles were controlled.


Karlner, Diseases of the Chest (1967), 187 described fifty-four patients who received intravenous PHT on fifty-seven occasions for abnormal cardiac rhythm. Nineteen of twenty-three who had digitalis-induced arrhythmias responded with abolition or marked suppression of a ventricular ectopic focus, or with conversion of supraventricular arrhythmias to a regular sinus mechanism. Of twenty-eight patients whose arrhythmias were unrelated to digitalis, seven responded favorably. As a result of this study the author confirmed the usefulness of PHT in a variety of cardiac arrhythmias, especially those which appear to be related to digitalis excess. Rapidity of action and relative paucity of side effects make PHT an effective antitarrhythmic agent.


Mercer and Osborne, Annals of Internal Medicine (1967), 248 reported on their six years' experience in the treatment, with PHT, of 774 cases of cardiac arrhythmias. The authors state that intravenous PHT is highly efficacious in the treatment of ventricular arrhythmias associated with anesthesia, cardiovascular, cardiac catheterization, and cardiac surgery. On the basis of their experience they consider PHT to be superior to quinidine and procaainamide in these arrhythmias. PHT also had a good effect against digitalis-induced ventricular arrhythmias and an even better effect against digitalis-induced atrial tachycardia. The authors reviewed the literature, including their own series, on the oral use of PHT. There were reported successes in twenty out of twenty-four cases of supraventricular arrhythmias, twenty-six out of thirty-eight cases of ventricular arrhythmias and five out of eight cases of unclassified paroxysmal tachycardia.


Bashour, Edmonson, Gupta and Prati, Diseases of the Chest (1968), 418 reported on twelve patients who were treated with PHT, all of whom had clinical evidence of digitalis toxicity. Most patients had more than one type of arrhythmia. During intravenous administration of PHT, continuous electrocardiographic monitoring was usually performed, and after conversion to sinus rhythm or subsidence of the arrhythmia, monitoring of the cardiac rhythm was continued for a period of ten minutes. In five of the cases, atrial fibrillation was present with other arrhythmias. Two of these arrhythmias were of recent origin and were restored to normal sinus
rhythm by PHT. Three cases of chronic atrial fibrillation did not respond to treatment. Four of the patients were uremic. The successful termination of their cardiac arrhythmias, especially ventricular tachycardia, with PHT, was of special interest. In uremic patients with arrhythmias the usual therapeutic measures are both less effective and more hazardous.


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Eddy and Singh, British Medical Journal (1969), 987 treated thirty-seven patients with cardiac arrhythmias with intravenous PHT. Twenty-one had acute myocardial infarctions and sixteen had other conditions. There was a favorable response in eighteen of the twenty-one cases of myocardial infarction and in six of the other sixteen cases.


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Gattenloher and Schneider, Munchener Medizinische Wochenschrift (1969), 1052 reported fifteen patients in whom they studied cardiac hemodynamics. PHT, in doses of 125 and 250 mg, did not alter or interfere with cardiac output or stroke volume. In the eight patients with digitalis-induced arrhythmias, they noted return to normal sinus rhythm. They conclude that PHT is not only effective but may be lifesaving in digitalis-induced arrhythmias. (See also Ref. 2230.)


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Helfant, Steuffert, Patton, Stein and Damato, American Heart Journal (1969), 720 report on the use of intravenous PHT in a variety of cardiac arrhythmias. In a controlled study, eight of eleven patients treated with PHT prior to cyclopropane anesthesia did not develop arrhythmias; whereas, in the control group, eight of nine patients did develop arrhythmias. In another phase of the study, PHT restored sinus rhythm in all eight patients who developed arrhythmias during the administration of various anesthetics. In a second group with ventricular arrhythmias, unresponsive to procainamide, PHT abolished or decreased the ectopia in ten of twelve patients. In a third group of twelve patients given prophylactic PHT prior to DC counter-shock, none developed arrhythmias. In patients on digitalis, twenty-one of twenty-four with ventricular arrhythmias, and six of eleven with supraventricular arrhythmias responded to PHT. The authors confirmed PHT's effectiveness and safety in the prevention and treatment of cardiac arrhythmias.


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Lesbre, Cathala, Salvador, Florio, Lescure and Meriel, Archives des Maladies du Coeur et des Vaisseaux (1969), 1264 investigated the antiarrhythmic value of PHT in a variety of arrhythmic disturbances with the following results:

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<tr>
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</tr>
<tr>
<td>Ventricular extrasystoles</td>
<td>17 / 16</td>
</tr>
<tr>
<td>Bouts of tachycardia</td>
<td>3 / 3</td>
</tr>
<tr>
<td>First-degree block</td>
<td>8 / 5</td>
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</tr>
<tr>
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</tr>
<tr>
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</tr>
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TOTAL 106 / 84

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Gautam, British Heart Journal (1969), 721 reports on the use of intravenous PHT in treating serious cardiac arrhythmias following open heart surgery in fourteen patients. PHT was rapidly and highly effective in abolishing supraventricular and ventricular arrhythmias in thirteen of these patients. Higher doses were required for the more serious arrhythmias. The author states that the rapidity of its action and the relative paucity of side effects make PHT an effective antiarrhythmic agent.


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Bielak and Pokora, Polski Tygodnik Lekarsky (1970), 2331 report their experience in 106 patients with either oral or intravenous PHT for various arrhythmias caused by infarction, digitalis toxicity, valvular heart lesions, chronic cardiopulmonary disease and myocarditis as follows:

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The authors also evaluated the prophylactic use of PHT, 300 mg/day. No arrhythmias were recorded in sixty-three of 125 patients with acute myocardial infarction. Twenty-two patients with ectopic ventricular beats were successfully treated with PHT. In twelve of these patients, ectopic beats, returned when PHT was discontinued. In a group of ten patients with recurring atrial arrhythmias, five had no recurrences.


Hansen, Medizinische Klinik (1970),2569 reported the use of PHT in 150 patients who developed arrhythmias during digitals treatment. One hundred and three of 115 with ventricular arrhythmias responded favorably. Seventy-nine of these converted to normal sinus rhythm. In twenty-four patients who had atrial fibrillation and extrasystoles, the ventricular extrasystoles disappeared, but the fibrillation was unaltered. Seven patients with supraventricular tachycardia were also controlled. In seven of twelve patients with paroxysmal atrial fibrillation and five of seven patients with supraventricular tachycardia were also controlled. In seven of twelve patients with paroxysmal atrial fibrillation and five of seven patients with supraventricular tachycardia were also controlled.


Hansen and Wagener, Deutsche Medizinische Wochenschrift (1971),1121 in a controlled study of 200 patients with PHT and 300 patients without PHT, evaluated the effect of PHT when added to cardiac glycoside administration. By combining PHT and glycosides, the incidence of arrhythmias was reduced from 21% in the non-PHT group to 2.5% in the PHT-treated group. The authors state that this clinical experience indicates that PHT administration reduces the toxic effects of glycosides in man without affecting their inotropic effects. Thus, the use of PHT improves the chance of effective treatment in heart failure.

1121. Hansen, H. W. and Wagener, H. H., Diphenylhydantoin in the treatment of heart failure. Thus, the use of PHT improves the chance of effective treatment in heart failure.

Kemp, Journal of the American Geriatrics Society (1972),1214 studied the effect of PHT on ventricular ectopic rhythms. These arrhythmias were not caused by digitalis. PHT was given to five patients and five patients were given placebo. For the first three weeks the dosage of PHT was 100 mg q.i.d. During the rest of the three-month study the dosage was reduced to 100 mg t.i.d. The numbers of premature ventricular contractions during a five minute continuous ECG monitoring period were recorded before therapy, after three weeks of therapy, and after three months of therapy. At the end of the three-month period, premature ventricular contractions were absent in 16 (96%) of the PHT patients but 2 (10%) of the patients in the control group. In the control group, contractions increased in two patients, and were moderately decreased in three.


O'Reilly and MacDonald, British Heart Journal (1973),1390 reported on the successful use of PHT in treating two cases of ventricular arrhythmias induced by hypokalemia. (Hypokalemia results in below normal potassium in nerve and muscle cells. Relevant to the above discussion, the potassium difference, Refs. 157, 387, 728, 731, 1012, 1025, 1225, 1379, 1418, 1642, 1662, 2224, 2374, 2458.) The authors emphasize the usefulness of PHT in the management of the notoriously resistant and malignant arrhythmias associated with hypokalemia, where the usual antiarrhythmic agents are at best ineffective and may even be dangerous.


2458. Doemer, W., Wolfe and Giffreich, British Heart Journal (1974),1488 detailed the successful treatment with PHT of a patient who attempted suicide with a massive digoxin overdose. (In addition to the digoxin, seventeen 400 mg tablets of meprobamate had also been ingested.) Serum digoxin levels reached 35 ng/ml. Pronounced hyperkalemia was noted fourteen hours after ingestion. The patient responded to seven doses of 25 mg intravenous PHT over a period of thirty-six hours. The patient had complete heart block and PHT improved this to a first-degree block. The authors note that low doses of PHT were effective in this case and they suggest that it should be used early in the treatment of acute digoxin overdose.


Rotmensch, Graff, Azyenberg, Amir and Laniado, Israel Journal of Medical Sciences (1977),2058 reported on three cases of suicide attempt with massive digoxin overdoses. Intravenous PHT was dramatically effective in controlling digitals arrhythmias in these three cases. The authors suggest that PHT's early use is in the treatment of this type emergency.

Da Paola, Gondin, Hara and Mendonca
See also: Myocardial Infarction

3163. Suarez-Kurtz, G., Meneges Lorga, A., and Moraes, F.D., Effects of phenytoin on the ventricular tachyarrhythmias of chronic patients with chronic chagasic myocarditis. Significant (> 90%) reduction of couplets, bigeminy and runs of ventricular tachycardia were observed in 50 - 67% of the patients, whereas the frequency of isolated PVCs was significantly (> 70%) reduced in only 2 patients (18%). Proarrhythmic activity was not observed and adverse side effects were of mild intensity and usually transient, except in one patient, who developed pruritus and skin rash in the presence of toxic phenytoin serum levels (27 mg/ml). The authors report that their results suggest that phenytoin may be useful for the control of repetitive forms of ventricular tachyarrhythmias in selected patients with chronic chagasic myocarditis.


Cardiac Arrhythmias in Children

Garson, Kugler, Gillette, Simonelli and McNamara, The American Journal of Cardiology (1980), 1847 reported the use of PHT in treating six young patients with chronic postoperative ventricular arrhythmias and abnormal hemodynamics following surgery for congenital cardiac defects. Arrhythmias varied from ten or more premature ventricular complexes per hour to bigeminy and ventricular tachycardia. PHT alone controlled the arrhythmias in five patients. In the sixth, a combination of PHT and disopyramide was effective. 1847. Garson, A., Kugler, J. D., Gillette, P. C., Simonelli, A. and McNamara, D. G., Control of late postoperative ventricular arrhythmias with phenytoin in young patients, Am. J. Cardiol., 46(2): 290-4, 1980.

Garson and Gillette, Pacing and Clinical Electrophysiology (1981), 2528 studied the effects of PHT in fifty-one young patients with chronic arrhythmias consisting of multiform premature ventricular contractions (PVCs), couplets and ventricular tachycardia. The patients were divided into three groups according to hemodynamics. PHT was the initial drug used, followed by the addition or substitution of other drugs if effective response was not obtained. Five patients were not responsive to any treatment. PHT alone corrected the arrhythmias in thirty-nine patients: twenty-two with severe, and sixteen with moderate hemodynamic abnormalities, and one with normal hemodynamics. The authors observed that PHT was most effective in patients with the most abnormal hemodynamics, and say that PHT is the drug of choice for children with ventricular dysrhythmias.


Rocchini, Chun and Dick, American Journal of Cardiology (1981), 2251 reviewing their records on treatment and follow-up of children with ventricular tachycardias of various etiologies, report that PHT abolished arrhythmias in four patients with ventricular tachycardia following tetralogy of Fallot repair. A combination of PHT and propanolol effectively controlled symptoms and abolished ventricular tachycardias in two patients with prolonged Q-T interval.


Kavey, Blackman and Sondheimer, American Heart Journal (1982), 2654 reported the effects of oral PUF in nineteen patients, seen consecutively, who developed ventricular premature complexes (VPCS) late after surgery for congenital heart disease. Arrhythmias included ventricular tachycardia, couplets and frequent multiform or uniform VPCS, documented by twenty-four-hour ambulatory ECG. Sixteen had undergone previous repair of the tetralogy of Fallot and three had had aortic valve surgery. Nine of these children had been unresponsive to previous treatment. PHT decreased ventricular dysrhythmias in all nineteen patients. The arrhythmias were completely suppressed in fifteen, and in four they were reduced to uniform VPCS. The authors state that the high rate of success in treating these patients who are at particular risk for sudden death, and the relative lack of side effects suggest that PHT is the drug of choice for this patient group.


Maxwell, Martin and Yaster, Anesthesiology (1994), 3171 present case reports of two newborns who developed cardiac dysrhythmias while receiving epidural bupivacaine either by continuous infusion or by repeated bolus dosing. In both cases, the dysrhythmias were successfully treated with intravenous phenytoin after other therapies, including bretylium, had been unsuccessful. 3171. Maxwell, L.G., Martin, L.D., Yaster, M., Bupivacaine-induced cardiac toxicity in neonates: successful treatment with intravenous phenytoin, Anesthesiology, 80(3): 682-6, 1994.