

du diagnostic précoce et du traitement chirurgical de la cryptorchidie et de corriger certaines idées fausses.

## References

1. WARD B, HUNTER WM: The absent testicle. A report on a survey carried out among schoolboys in Nottingham. *Br Med J* 1: 1110, 1960
2. SCORER CG: Incidence of incomplete descent of the testicle at birth. *Arch Dis Child* 31: 198, 1956
3. *Idem*: The descent of the testis. *Arch Dis Child* 39: 605, 1964
4. BAUMRUCKER GO: Incidence of testis pathology. *Bull US Army Dept* 5: 312, 1946
5. SOUTHAM AH, COOPER ER: Pathology and treatment of retained testis in childhood. *Lancet* I: 805, 1927
6. FARRINGTON GH: The position and retractibility of the normal testis in childhood with reference to the diagnosis and treatment of cryptorchidism. *J Pediatr Surg* 3: 53, 1968
7. ROBINSON JN, ENGLE ET: Some observations on the cryptorchid testis. *J Urol* 71: 726, 1954
8. JOHNSON DE, WOODHEAD DM, POHL DR, et al: Cryptorchism and testicular tumorigenesis. *Surgery* 63: 919, 1968
9. COLLINS DH, PUGH RC: *The Pathology of Testicular Tumours*. Edinburgh, E & S Livingstone, 1964
10. FOWLER R, STEPHENS FD: The role of testicular vascular anatomy in the salvage of high undescended testes. *Aust NZ J Surg* 29: 92, 1959
11. BRENDLER H, WOLFSOHN MA: Surgical treatment of the high undescended testis. *Surg Gynecol Obstet* 124: 605, 1967

# Permanent demand pacing for hypersensitive carotid sinus syndrome

Dwight I. Peretz, M.D., M.Sc., F.R.C.P.[C], F.A.C.P., F.A.C.C., Alfred N. Gerein, M.D., C.R.C.S.[C] and Robert T. Miyagishima, M.D., F.R.C.S.[C], Vancouver, B.C.

**Summary: Ten patients with proved hypersensitivity of one or both carotid sinuses and with symptoms of recurrent lightheaded spells and syncope had implanted a permanent transvenous demand pacemaker. In a follow-up course ranging from 6 to 55 months there has been no recurrence of lightheadedness or syncope in any of the patients. Six of the ten have had their battery packs replaced owing to routine battery exhaustion.**

The carotid sinus is a major vagal centre for regulation of heart rate and peripheral vascular tone. In normal humans, stimulation of the carotid sinus area at the bifurcation of the internal and external carotid arteries produces a mild slowing of heart rate and insignificant fall in blood pressure.<sup>1,2</sup> In some individuals, more commonly in the elderly, there is a hypersensitivity of the carotid sinus reflex so that stimulation by pressure over the carotid sinus or increase in pressure within the carotid sinus will cause a marked slowing of cardiac rate, or even asystole, with lightheadedness or syncope.

Hypersensitivity of the carotid sinus with hemodynamically significant bradycardia or syncope is not as uncommon as one would suspect from the small number of cases reported in the literature over the years. The carotid sinus reflex, hypersensitivity of the carotid sinus and carotid sinus syncope have been well described and little can be added to the description provided in 1933 by Weiss and Baker.<sup>1</sup>

The syndrome consists of sudden episodes of fainting or lightheadedness which occur spontaneously, often in circumstances recognized by the patient, such as while looking upward or stroking the side of the neck, and the whole symptom complex is often reproducible by carotid sinus massage. The symptomatic episodes are usually extremely short, measured in seconds, and are only occasionally preceded by an aura which may be visual, auditory, vertiginous or hallucinatory. In our experience, seizure phenomena have not been displayed. The patients rarely have symptoms unless in the vertical posture, contrary to idiopathic Stokes-Adams syncope and epileptic attacks.

Recovery from the syncope is usually extremely prompt and there is no post-ictal phase. Diagnosis is dependent on reproduction or partial reproduction of the symptoms by carotid sinus massage, often with the patient sitting in a chair, and simultaneous electrocardiographic evidence of asystole or marked bradycardia. In our patients we have reproduced syncope in only three cases, whereas in the other seven there was asystole in excess of five seconds or a marked sinus bradycardia with a feeling of "faintness". In our opinion reproduction of the actual syncope is not necessary provided the clinical story is present and hypersensitivity of the carotid sinus vagal output as described can be demonstrated.

The descriptions of the treatment of carotid sinus syncope in the past, including a detailed and exhaustive review of the subject in 1970,<sup>3</sup> allude to surgical denervation of the carotid sinus area, radiotherapy, parasympatholytic agents and sympathomimetic agents, but there was no mention in the literature up to that time of cardiac pacing on demand to prevent the syncopal attacks associated with hypersensitivity of the cardioinhibitory reflex. In the last year there have been two single case reports<sup>4,5</sup> on the treatment of carotid sinus syncope with demand transvenous cardiac pacing, and it was listed as an indication for demand pacing by one of the authors in 1971.<sup>6</sup>

## Materials and methods

Ten patients without demonstrable

From the P. A. Woodward Intensive Care and Coronary Care Unit, Division of Cardiopulmonary Diseases, Department of Medicine, St. Paul's Hospital, and the Faculty of Medicine, University of British Columbia, Vancouver, B.C.

Reprint requests to: Dr. Dwight I. Peretz, Director, P. A. Woodward Medical Intensive Care and Coronary Care Unit, St. Paul's Hospital, 1081 Burrard Street, Vancouver 1, B.C.

episodes of atrioventricular block were seen for episodes of lightheadedness and/or syncope in an office and consultative cardiological practice between January 1968 and August 1972. All were found to have hypersensitivity of their right and/or left carotid sinus as the cause of their symptoms. Nine were in sinus rhythm, one having a wandering pacemaker with frequent sinus arrest. Nine were males, the age range for the group being 47 to 88 years, with an average age of 64 years. They all complained of recurrent episodes of lightheadedness and/or one or more episodes of syncope. During the initial examination auscultation of the heart was carried out in order to determine cardiac rate during carotid sinus stimulation. If the patient went into bradycardia or asystole, then this was reconfirmed with the patient supine and attached to an electrocardiograph. Palpation and auscultation of each carotid artery were done in order to detect any obstruction. The bifurcation of the carotid artery was palpated to determine whether or not it was prominent. The right and then the left carotid sinus areas were compressed against the transverse process of the adjacent vertebrae with the head turned to the contralateral side and the examiner's other hand palpating the ipsilateral superficial temporal artery. Pressure was placed upon the carotid sinus firmly but without occluding the pulsation in the ipsilateral superficial temporal artery. If marked bradycardia resulted (less than 30 per minute) massage was maintained with the patient first lying and then sitting to determine if symptoms would become manifest (Fig. 1). If asystole of over five seconds' duration developed during massage, then pressure was removed and the patient asked to cough; if syncope occurred during the asystole, the patient was struck on the chest (Fig. 2).

If bradycardia was the sole cardiac arrhythmia produced by carotid sinus massage we demanded reproduction of the presenting complaint before accepting the patient as a case of "hypersensitive carotid sinus syndrome". If asystole of over five seconds was induced by light carotid sinus massage we did not require reproduction of syncope.

Atropine in sufficient dosage should abort the sensitivity of the carotid sinus. The patients were all given 0.6 mg. atropine sulfate intravenously at five-minute intervals up to a maximum of 1.8 mg. or until their sinus rate increased to more than 100 per minute. In each of our cases this prevented the appearance of significant bradycardia or asystole.

## Results

Table I summarizes the important data from these patients. Nine were in sinus rhythm, one having a wandering pacemaker and frequent episodes of sinus arrest, with his usual rate often as low as 30 per minute. This patient apparently has the "sick sinus syndrome" but none the less, vagal stimulation with ca-

rotid sinus massage produced asystole consistently. One patient had sustained an inferior myocardial infarction in the remote past, and another had a left bundle branch block, with no history of previous myocardial disease. A third patient had a rate-dependent left bundle branch block which appeared at rates of less than 40 per minute, with no aberrant conduction when his rate was more than 40 per minute. In this patient (H.M.) the right carotid sinus alone was sensitive, and upon stroking it his rate would decrease to 20 per minute and a left bundle branch block would immediately develop with a fall in blood pressure, increase in premature ventricular contractions and syncope. Coughing would initiate exactly the same response. In a fourth patient (H.McR.) a

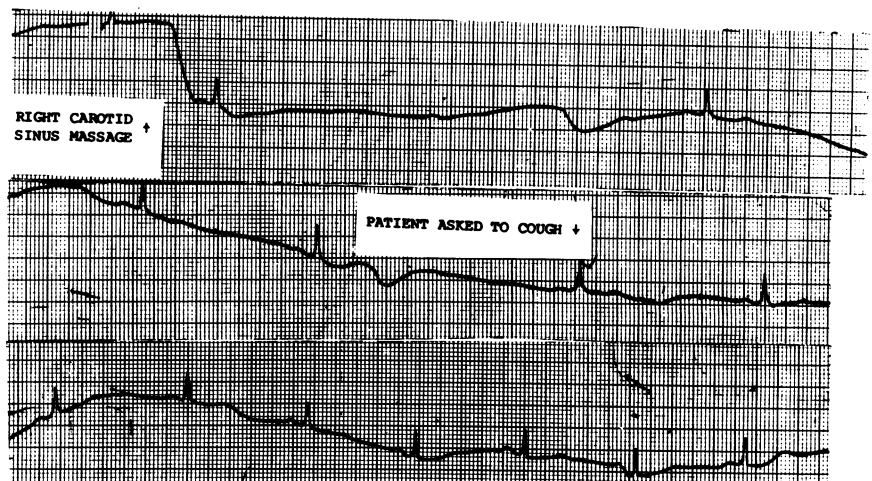


FIG. 1—Slowing of cardiac rate due to carotid sinus hypersensitivity.

**Table I**  
**Data of 10 patients with hypersensitive carotid sinus syndrome**

Patient	Age	Sex	Pacemaker inserted	Symptoms	Carotid sinus sensitivity
S.P.	75	Male	January 1968	Recurrent lightheadedness and syncope, 3 yrs.	R
H.M.	47	Male	June 1969	Syncope x 1	R
J. McD.	63	Male	September 1969	Fainted 9 times	R = L
J.P.	54	Male	October 1969	Dizziness and syncope, 2 yrs.	L > R
H.H.	66	Male	March 1970	Syncope x 6	R = L
J.N.	61	Male	November 1970	Lightheadedness 1 yr., fainted x 2	R > L
W.G.	88	Male	March 1971	Lightheadedness several times weekly	R = L
H.McR.	65	Male	March 1971	Fainted many times after coughing	R > L
R.M.	54	Male	October 1971	Wandering pacemaker, sinus arrest, syncope	R > L
G.R.	67	Female	February 1972	Syncope x 7, many lightheaded episodes	R

marked sinus bradycardia of 28 per minute was induced by massage over the right or left carotid sinus, and by coughing several episodes of documented asystole lasting up to nine seconds were initiated.

The right carotid sinus was sensitive in all cases, the right being more sensitive than the left in three, equal in sensitivity to the left in three, and the only sensitive sinus in three. In one case only was the left carotid sinus more sensitive than the right on initial examination. One patient (H.H.) was in congestive cardiac failure and was initially seen while taking digitalis. Upon discontinuation of his cardiac glycosides hypersensitivity of the carotid sinus could no longer be elicited. He, however, required digitalis to remain free of congestive cardiac failure, and subsequently had a permanent transvenous demand pacemaker inserted and digitalis once again added to his therapeutic regimen.

All 10 patients had permanent transvenous endocardial pacemakers inserted in the demand mode at approximately 62 electronic impulses per minute (Fig. 3). All are alive and none have had any recurrence of lightheadedness or syncope since insertion of the pacemaker. These results are very much superior to those reported in the literature from any other form of therapy. There was no mortality and no significant morbidity in any patient due to implantation of the pacemaker. One patient had a

thrombosis of the axillary vein following insertion, but this cleared with anticoagulant and anti-inflammatory therapy.

### Discussion

The hypersensitivity reaction to external or internal pressure upon the carotid sinus is customarily classified into:

1. Cardioinhibitory reflex characterized by a sharp drop in blood pressure associated with asystole or marked bradycardia. This reflex is inhibited with atropine.
2. Depressor or vasomotor reflex characterized by a sharp drop in blood pressure but no slowing of the heart rate. This reflex is inhibited with epinephrine.
3. "Cerebral" reflex with loss of consciousness but no change in blood pressure or pulse rate.

Drugs are said to have no effect on the third or cerebral type of reflex. Many doubt its existence and there is evidence that it is probably a result of occlusion of cerebral flow rather than a carotid sinus reflex.<sup>3,7</sup> In our experience we have only seen patients with the cardioinhibitory type of syndrome.

Certain drugs are known to increase the vagal tone and may unmask hypersensitivity of the carotid sinus. Of particular importance in this respect are cardiac glyco-

sides, morphine and meperidine. One of our patients demonstrated this with digitalis.

The "sick sinus syndrome" may present in a fashion similar to the hypersensitive carotid sinus syndrome but the manifestations of wandering pacemaker with changing configuration of the P waves and length of PR interval, junctional escape beats and sinus arrest are apparent.

It is interesting to note that in two recent papers<sup>2,3</sup> the statement that "milder forms of the disease respond to reassurance and drug therapy" is, in our opinion, a dangerous concept. Presumably by "milder forms" is meant infrequent syncopal attacks and those which last but a short period of time. However, in everyday life, many potentially extremely serious consequences could occur from even a few seconds' loss of consciousness, particularly when driving an automobile or working in certain situations. For this reason and because of the low risk of implantation of permanent transvenous demand pacing units,<sup>6</sup> it is our opinion that all patients with hypersensitive carotid sinuses who have demonstrated episodes of lightheadedness or syncope should have such a pacemaker implanted.

We have found that reproducibility of hypersensitivity of the carotid sinus is not consistent. On several occasions a drop in cardiac rate produced by initial stimulation and documented by auscultation could not be reconfirmed a few minutes later by the time the patient had been connected to an electrocardiograph. Occasionally several days elapsed with the patient on the cardiac monitor and carotid sinus massage performed several times daily, before hypersensitivity could be reconfirmed. One would suspect, therefore, that a number of patients with carotid sinus hypersensitivity will escape detection because they fail to show the cardioinhibitory response on the initial testing. If the clinical story is suggestive and no other etiological possibilities such as carotid or vertebral artery insufficiency, or primary cerebral disease is found, then repeated examination over several days is needed before the examiner can be satisfied that carotid

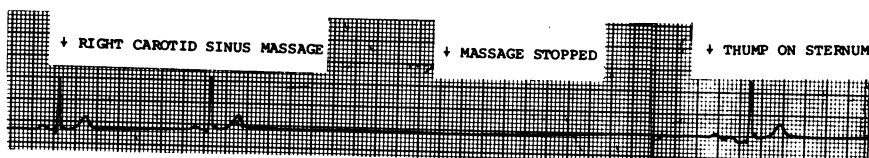


FIG. 2—Five seconds of asystole following carotid sinus massage with response to striking sternum. The patient had lost consciousness.

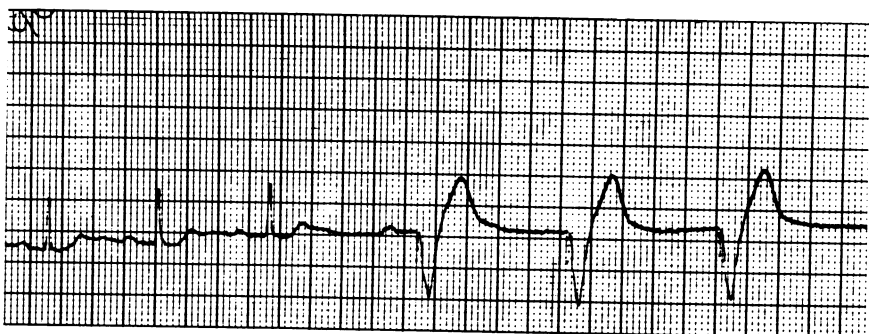


FIG. 3—Carotid sinus massage following implantation of permanent demand pacemaker; electronic pacemaker can cut in, aborting syncope or lightheaded episodes.

sinus hypersensitivity does not exist.

## Résumé

*Stimulateur cardiaque automatique à demeure pour les cas de syndrome du sinus carotidien*

Chez dix malades souffrant d'hyperréflexivité de l'un ou des deux sinus carotidiens et présentant des symptômes de vertige et de syncope, on a implanté par voie intra-veineuse un stimulateur cardiaque à demeure opérant automatiquement. L'évolution a été suivie pendant une période variant de 6 à 55 mois. On n'a noté chez aucun malade de récurrence des étourdissements ou des syncopes. Chez six des 10 malades, il a fallu, à un moment donné, remplacer la pile épuisée.

## References

1. WEISS S, BAKER JP: The carotid sinus reflex in health and disease: its role in the causation of fainting and convulsions. *Medicine* 12: 297, 1933.
2. EVANS E: The carotid sinus: its clinical importance. *JAMA* 149: 46, 1952
3. THOMAS JE: Hyperactive carotid sinus reflex in carotid sinus syncope. *Mayo Clin Proc* 44: 127, 1969
4. VOSS DM, MAGNIN GE: Demand pacing and carotid sinus syncope. *Am Heart J* 79: 544, 1970
5. BAHL OP, FERGUSON TB, OLIVER JC, et al: Treatment of carotid sinus syncope with demand pacemaker. *Chest* 59: 262, 1971
6. BERNSTEIN V, ROTEM CE, PERETZ DI: Permanent pacemakers: 8-year follow-up study. *Ann Intern Med* 74: 361, 1971
7. GURDJIAN EC, WEBSTER JE, HARDY WO, et al: Non-existence of the so-called cerebral form of carotid sinus syncope. *Neurology (Minneapolis)* 8: 8, 1958

# CATAPRES®

clonidine hydrochloride

## COMPLETELY NEW CLASS OF ANTIHYPERTENSIVE AGENT WITH UNIQUE MODE OF ACTION

### PRESCRIBING INFORMATION

#### CATAPRES® clonidine hydrochloride

##### Composition

2-(2,6-dichlorophenylamino)-2-imidazoline hydrochloride.

##### Indications

Catapres has been used successfully to treat hypertension of all grades of severity.

##### Contraindications

There are no known absolute contraindications to the use of Catapres.

##### Warnings

If Catapres therapy is discontinued for any reason, withdrawal should be done gradually over several days rather than abruptly. There have been rare instances of rebound hypertensive crises following sudden discontinuation of high doses of the drug. This can be effectively controlled by reinstating Catapres at the previous dosage level; however if more rapid control is necessary, intravenous infusions of alpha adrenergic blocking agents such as intravenous phentolamine (5-10 mg doses at 5 minute intervals up to a total of 30 mg) are effective in reducing the blood pressure.

##### Precautions

Patients with a known history of depression should be carefully supervised while under treatment with Catapres, as there have been occasional reports of further depressive episodes occurring in such patients.

As an abrupt withdrawal of Catapres followed in rare instances by an excess of circulating catecholamines, caution should be exercised in the concomitant use of drugs which affect the metabolism or the tissue uptake of these amines (MAO inhibitors and tricyclic antidepressants respectively).

A few instances of a condition resembling Raynaud's phenomenon have been reported. Caution should therefore be observed if patients with Raynaud's disease or thromboangiitis obliterans are to be treated with Catapres.

As with any drug excreted primarily in the urine, smaller doses of Catapres are often effective in treating patients with a degree of renal failure.

The use of Catapres during the first trimester of pregnancy is subject to the normal precautions surrounding the use of any drug. Animal tests have shown no evidence of foetal abnormality.

##### Adverse effects

The most commonly encountered side effects are initial sedation and dry mouth. However these effects are seldom severe and tend to be dose related and transient.

There are occasional reports of fluid retention and weight gain during the initial stages of treatment with Catapres. This side effect is usually transient, but the addition of a diuretic will correct any tendency to fluid retention in these cases.

Other occasional drug-related side effects which have been noted in literature include dizziness, headache, nocturnal unrest, nausea, euphoria, constipation, impotence (rarely), and agitation on withdrawal of therapy. Facial pallor has occasionally been noted at high dosage levels.

No toxic reactions have been observed on investigating blood status, renal function and liver function. Long-term treatment has shown no adverse effect on blood urea nitrogen levels, and in patients with pre-existing renal damage there is no suggestion of further impairment of the renal blood flow despite a fall in arterial blood pressure.

##### Dosage

Initially 0.05-0.1 mg four times daily. This dosage may be increased every few days until satisfactory control is achieved. When used alone the final dosage usually ranges between 0.2 and 1.2 mg daily. The last dose of the day should be given immediately before retiring to ensure blood pressure control during sleep.

##### Catapres used with a diuretic


Catapres has been used successfully together with chlorthalidone, and the thiazide and furosemide diuretics. Lower doses of Catapres or the diuretic may be used to achieve the same degree of blood pressure control whenever a diuretic is added to the Catapres regimen or vice versa. In these circumstances, most mild-to-moderate hypertensives can be controlled using only 0.3-0.6 mg of Catapres daily in divided doses.

Severe hypertensives have been successfully treated with a diuretic and higher doses of Catapres (frequently up to 1.2 mg daily and occasionally up to 5 mg daily). When extremely high doses of Catapres are necessary dosage adjustments should be made over a period of several months.

##### Catapres used with other antihypertensive agents

Catapres has been used together with methyldopa, guanethidine, bethanidine and hydralazine, and further reductions in blood pressure have been achieved.

##### Availability

Catapres is available as a white single-scored 0.1 mg tablet, impressed with the motif  on one side and the Boehringer Ingelheim symbol on the reverse. Supplied in bottles of 50 and 500 tablets.

For further prescribing information, consult the Catapres Product Monograph or your Boehringer Ingelheim representative.

## OVER 500 PUBLISHED STUDIES ON CATAPRES HAVE APPEARED IN THE WORLD-WIDE LITERATURE TO DATE.

#### References:

1. Cecil-Loeb Textbook of Medicine, ed. P.B. Beeson and W. McDermott, W.B. Saunders Co., 13th edition, 1971, p. 1061.
2. Onesti, G. et al. "Antihypertensive Effect of Clonidine", Supplement II to Circulation Research, Vol. XXVIII and XXIX, May 1971, pp. 53-69.
3. Onesti, G. et al. "Clonidine: A New Antihypertensive Agent", *Am. J. Cardiology*, 28:74-83, July 1971.
4. Muir, A.L. et al. "Circulatory Effects at Rest and Exercise of Clonidine, an Imidazoline Derivative with Hypotensive Properties", *The Lancet*, July 26, 1969, pp. 181-185.
5. Smet, G. et al. "Clinical Observations on a New Antihypertensive Drug, 2-(2,6-dichlorophenylamino)-2-imidazoline hydrochloride", *Am. Heart J.*, 77:473-478, April 1969.
6. Hoobler, S.W. and Sagastume, E., "Clonidine Hydrochloride in the Treatment of Hypertension", *Am. J. Cardiology*, 28:67-73, July 1971.
7. Putzeys, M.R. and Hoobler, S.W., "Comparison of Clonidine and Methyldopa on Blood Pressure and Side Effects in Hypertensive Patients", *Am. Heart J.*, 83:464-468, April 1972.
8. Parsons, W.B. and Morledge, J.H., "Antihypertensive Effect of a New Imidazoline Compound (Clonidine) and Chlorthalidone, Individually and in Combination", *Am. J. Cardiology*, 26:258-261, Sept. 1970.
9. Macdougall, A.I. et al. "Treatment of Hypertension with Clonidine", *Br. Medical J.*, 3:440-442, August 22, 1970.
10. Raftos, J., "The Use of 'Catapres' in the Treatment of Severe Hypertension", *Med. J. Australia*, Oct. 4, 1969, pp. 684-687.
11. Mroczek, W.J., Leibel, B.A. and Finnerty, F.A., "Comparison of Clonidine and Methyldopa in Hypertensive Patients Receiving a Diuretic", *Am. J. Cardiology*, 29:712-717, May 1972.
12. Khan, A. et al. "Clonidine (Catapres): A New Antihypertensive Agent", *Current Therapeutic Research*, 12:10-18, Jan. 1970.
13. Sung, P-K, et al. "Effects of Clonidine and Chlorthalidone on Blood Pressure and Glucose Tolerance in Hypertensive Patients", *Current Therapeutic Research*, 13:280-285, May 1971.
14. Mroczek, W.J., Davidov, M. and Finnerty, F.A., "Prolonged Treatment with Clonidine: Comparative Antihypertensive Effects Alone and with a Diuretic Agent", *Am. J. Cardiology*, 30:536-541, Oct. 1972.



**Boehringer Ingelheim (Canada) Ltd.**  
2121 Trans Canada Highway, Dorval 740, P.Q.

B-18-73