of treatment and then suddenly the rate was reduced. Pneumonia as an associated disease was present in Cases 3 and 4.

Only two drugs were used to reduce the heart rate—neostigmine and digitalis, the latter as tincture or digoxin. Neostigmine was effective in Case 1. The dose given was 0.125 mg. by intramuscular injection to an infant of 4 weeks. In the other five cases digoxin or tincture of digitalis by mouth was effective. Digoxin orally seemed to be the drug of choice. A suitable dose was 0.125 mg. repeated two or three times daily until the heart slowed. Even the smallest babies tolerated such a dose, and indeed it seemed necessary to control the rapid heart action.

Summary

Auricular paroxysmal tachycardia is less rare than is often supposed.

In the cases seen in hospital the so-called " paroxysm " usually lasted several days.

The common clinical picture in childhood is that of cardiac failure associated with an extremely rapid heart rate (200–350 beats a minute). The insidious onset of such failure is frequently missed in children unless looked for.

Pneumonia may be the assumed diagnosis, and indeed is often present in addition to the tachycardia. Both conditions demand treatment.

The incidence of congenital heart disease in association with auricular paroxysmal tachycardia seems to be quite low.

Digitalis would appear to be the drug of choice in treatment. Large doses are tolerated in infancy and seem necessary for recovery. A smaller maintenance dose for four to eight weeks should be given to prevent early recurrence of the tachycardia.

I wish to thank Dr. T. Colver and Professors R. S. Illingworth and E. J. Wayne, under whose care some of the cases were admitted to hospital; Dr. J. F. Goodwin for his advice, and especially for his interpretation of the E.C.G. tracings: and Dr. B. R. Eaton for his help in obtaining the tracings.

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The film " Streptomycin Drugs in the Treatment of Tuberculosis " has been withdrawn from the B.M.A. Film Library by Messrs. E. A. Squibb and Sons, from whom it was held on loan, because the methods of treatment and dosages depicted therein are now out of date.

EFFECT OF HYDRALAZINE IN HYPERTENSION

BY

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Hydralazine (1-hydrazinophthalazine ; " apresoline ") has recently been under investigation both in the laboratory and clinically as an antihypertensive drug. Pharmacologically, its exact action is not known. It is an antihistaminase and has a wide range of activity in antagonizing humoral pressor substances—that is, hypertensin, pherentasin (Schroeder, 1952), serotonin (Taylor *et al.* (1951), and *nor*adrenaline (Freis and Finnerty, 1950). There is suggestive evidence of a central action on the hypothalamus (Gross *et al.*, 1950 ; Craver and Yonkman, 1950) and on peripheral arterioles. It has been shown that, associated with a decrease in peripheral resistance—preferentially marked in the kidneys—and a decrease in blood pressure, there is a pronounced tachycardia and an increase in cardiac output due either to a central effect or to local action of the drug on the heart (Moyer *et al.*, 1951). There is an increase in the renal blood flow without constant increase in the glomerular filtration rate (Mackinnon, 1952) or any increase in tubular resorption of glucose, indicating that no additional nephrons are activated by the increase in renal blood flow (Moyer *et al.*, 1951). No previously known antihypertensive drug has been shown to have this combined effect of decreasing the blood pressure and increasing the renal blood flow.

The Investigation

Selection of Cases and Method of Recording.—In the present study the effect of hydralazine was observed on arterial hypertension in 12 cases—nine suffering from essential hypertension, one from hypertension complicating chronic pyelonephritis, and two from malignant hypertension. All had hypertensive symptoms. In two cases of essential hypertension (Cases 3 and 6) blood pressures showed wide fluctuations, often related to psychological disturbances. Auscultatory blood-pressure readings were taken frequently in upright, sitting, and recumbent positions during a control period of 3 to 13 days, and, after the drug was given, pressures were taken in the same positions at intervals for six hours ; averages of control readings, and these readings after the drug, are given in the Table overleaf.

Dosage.—Hydralazine was administered orally in all trials. A test dose of 25 mg. was first given, and the dose was gradually stepped up from 25 mg. eight-hourly to higher levels reaching 400 mg. three times a day, thus varying from 75 to 1,200 mg. a day in different patients. Every attempt was made to continue treatment unless it was considered futile or the side-effects were so unpleasant and persistent as to warrant discontinuation of the drug. The effect of the drug lasted from four to six hours, with a maximum at from one to two hours after administration. In addition to oral treatment, parenteral therapy with hydralazine in doses of 50 mg. intramuscularly was tried in two cases, only one of which is tabulated (Case 5). The effect of combined oral therapy with hexamethonium bromide and hydralazine, as suggested by Schroeder (1952), was studied in Cases 4, 7, 8, and 9. The maximum daily doses tried were 2,250 mg. of hexamethonium bromide and 450 mg. of hydralazine.

Oral Therapy with Hydralazine

Case No.	Age and Sex	A. Type of Hypertension and B. Clinical Condition	Control Period (days)	Average Control B.P.			In-patient Treatment (days)	Largest Dose (mg./day)	Average B.P. During Treatment			Severity of Side-effects	Remarks
				Standing	Sitting	Recumbent			Standing	Sitting	Recumbent		
1	42 M	A. Essential hypertension B. Angina pectoris. Heart +. E.C.G., L.V. ++. Fundi: A/V nipping +. Renal function: fair	4	188/128	188/129	183/126	33	900 orally	179/119	178/120	176/116	Mod. severe	Treatment abandoned because of: (1) no appreciable effect on hypertension; (2) side-effects
2	32 M	A. Essential hypertension B. Congestive cardiac failure (early). Hypertensive encephalopathy. Heart +. E.C.G., L.V. +++. Fundi: haemorrhages and exudates. No papilloedema. Left optic atrophy (old central retinal artery thrombosis). Renal function: fair	3	200/125	200/122	202/120	18	1,200 orally	199/117	200/117	196/113	Slight	Treatment abandoned because of no appreciable effect on hypertension
3	60 M	A. Essential hypertension B. Angina pectoris. Heart +. E.C.G., L.V. ++. Fundi: nothing abnormal detected. Renal function: good	13	210/109	216/112	213/110	30	600 orally	189/94	187/98	186/97	Slight	Control B.P. showed much fluctuation, which continued at lower levels during treatment period. Later out-patient observation showed that the slight B.P. reduction of first month was not maintained
									Average B.P. in last week of out-patient follow-up while on treatment				
									201/112	208/113	212/115		
4	62 F	A. Hypertension complicating chronic pyelonephritis. B. Heart +. E.C.G., L.V. +. Fundi: exudates in left fundus. No papilloedema. Renal function: advanced renal failure	4	215/125	220/122	215/122	11	300 orally	189/110	192/112	184/103	Mod. severe	Treatment abandoned because of (1) side-effects—patient refused to continue treatment with the drug; (2) inadequate response
							Combined therapy with hexamethonium bromide and hydralazine						
							20	Hex. brom. 750 Hydral. 300	169/101	170/102	170/100	Mod. severe	Effect of combined therapy with oral hexamethonium bromide and hydralazine studied on readmission of patient. The favourable response in hospital not maintained in the out-patient follow-up
									Average B.P. in last week of one month's out-patient treatment				
									208/123	207/123	197/120		
5	53 M	A. Essential hypertension B. Angina pectoris. Heart +. E.C.G., L.V. ++. Fundi: A/V nipping +. Renal function: fair	4	200/120	210/125	210/120	2	50 mg. I.M. inj. daily	142/89	156/95	168/99	Severe	Parenteral therapy had appreciable effect on B.P. but had to be abandoned because of side-effects. Oral therapy then resorted to
							6	450 orally	173/105	183/107	190/109	Mod. severe	Treatment abandoned because of (1) side-effects; (2) inadequate response
6	39 F	A. Essential hypertension B. Heart: L.V. +. E.C.G. within normal limits. Fundi: nothing abnormal detected. Renal function: good	5	164/109	164/109	164/106	10	300 orally	153/96	155/96	151/95	Mod. severe	B.P. in control and treatment periods showed fluctuations because of large psychological overlay. Treatment abandoned because of side-effects and inadequate response
7	50 F	A. Essential hypertension B. Heart +. E.C.G., L.V. +. Fundi: A/V nipping. Renal function: good	4	212/122	214/122	210/120	23	Hex. brom. 1,500 Hydral. 450	164/98	170/98	167/100	Mod. severe	Considerable reduction of B.P. shown by patient while in hospital not maintained in out-patient follow-up
									Average B.P. after two weeks out-patient treatment				
									225/135	227/132	222/130		
8	59 F	A. Essential hypertension B. E.C.G., L.V. strain or ischaemia. Fundi: N.A.D. Renal function: good	5	224/137	216/137	217/135	8	Hex. brom. 2,250 Hydral. 450	205/127	200/128	200/128	Mod. severe	No appreciable reduction of B.P. achieved
9	51 M	A. Essential hypertension B. Heart +. E.C.G., L.V. ++. Fundi: haemorrhages and exudates. No papilloedema. Renal function: good	5	233/142	226/135	232/138	14	Hex. brom. 2,250 Hydral. 450	208/132	206/128	206/127	Slight	No appreciable reduction of B.P. achieved

Side-effects.—In all patients the side-effects were similar in nature but not in severity, and were much more pronounced after parenteral administration. Cases 2, 3, 8, and 9 got over these reactions after about a week's treatment, but others could not get used to the drug at all. The side-effects noted were: (1) headaches, heaviness, and throbbing in the head; (2) flushing and sweating of the face—a sense of heat in the face and head; (3) dryness of the mouth, nausea, vomiting, anorexia, and epigastric discomfort; (4) a feeling of chill and shivering; (5) yawning and sleepiness; (6) tachycardia; (7) slight hyperpnoea; (8) transient erythematous rash; (9) lethargy, tiredness, and loss of interest in everyday affairs; and (10) giddiness on standing, especially after parenteral therapy.

Results

Parenteral Therapy.—Despite its pronounced hypotensive effect in the early stages, this method had to be abandoned because of unpleasant side-effects (Case 5).

Oral Therapy.—In Cases 1, 3, 4, 5, and 6 this caused some lowering of pressures in the first few days of the trial, but hypertension quickly became resistant even to the higher doses of the drug, and the sum total of results was not encouraging. In Case 2 the treatment had no effect at all on the hypertension. In one case (not mentioned in the Table) the patient had such unpleasant side-effects from the test dose of 25 mg. that she refused to take further doses of hydralazine, and preferred injections of hexamethonium bromide: the test dose was without effect on the blood pressure. In two cases of malignant hypertension oral therapy was tried between effective injections of hexamethonium. No further action was noted on the blood pressure: the results are not tabulated.

Combined Oral Therapy (Hexamethonium Bromide and Hydralazine).—This method was tried in Cases 4, 7, 8, and 9. There was some lowering of the pressures in the first few days of the trial, but the hypertension quickly became resistant even to higher doses of the drugs.

Discussion

Various claims of beneficial results from oral hydralazine are not substantiated by the experience recorded above. Page (1951) has stated that good responses to oral doses may not be achieved until patients have been on the drug for 10 days or more. This claim is not supported by our results, but rather the reverse—that is, apparently good results at the beginning are not maintained after a week or two. When patients are receiving hexamethonium it has often been noted that vasodilatory influences such as meals, hot weather, or intercurrent fever may enhance the blood-pressure-reducing action of the drug. However, the addition of hydralazine to hexamethonium therapy did not seem to make the latter treatment any more effective.

Summary

The effect of hydralazine alone and in combination with oral hexamethonium bromide was studied in 12 patients suffering from hypertension. In most of these there was a slight reduction of blood pressure at the beginning of treatment, but this was not maintained later in spite of a great increase in dosage. Persistence of unpleasant side-effects was noted in most of the patients.

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EFFECT OF P.A.S. ON THE THYROID GLAND

BY

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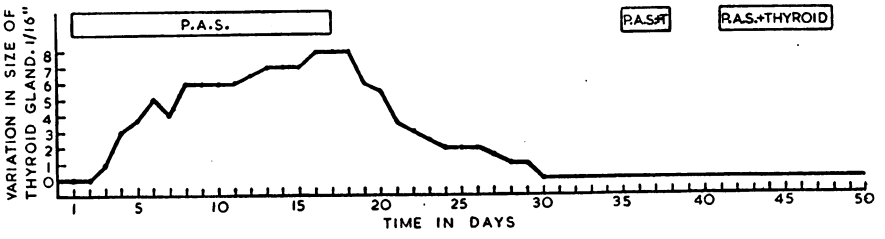
Enlargement of the thyroid gland after the administration of P.A.S. has been reported on several occasions (Bergquist and Mare, 1951; Clausen and Kjerulf-Jensen, 1951; Komrower, 1951). In the following case observations showed that the P.A.S. was the direct cause of the enlargement and that the administration of thyroid extract along with the P.A.S. prevented it. An unusual feature was the development of exophthalmos.

Method Used to Estimate Variation in Size of the Thyroid Gland.—A plaster-of-Paris cast was made of the patient's chin and sternal notch, a pencil being placed between the two and incorporated in the plaster. When this was held in position by the patient the neck was fixed at a constant angle. Three fixed points were next placed on the patient's neck overlying the thyroid gland, and the distance between them was measured daily. It was thought that any variation in the measurement reflected an increase or decrease in the size of the thyroid. By this method it was possible to detect a variation of 1/16 in. (1.5 mm.).



Case Report

The patient, a young man aged 19, suffered from bilateral pulmonary tuberculosis with extensive cavitation of both lungs. On two occasions prior to the present observations the patient had developed an enlargement of the thyroid while receiving P.A.S.; this rapidly subsided when the drug was stopped.

In December, 1951, the administration of P.A.S. was again started, 7.5 g. being given daily in divided doses; the effect on the thyroid gland is shown in the accompanying Graph.

Enlargement of the gland was first noted on the third day; it continued until the seventeenth day (total dosage, 123.5 g.), administration being stopped because of toxic symptoms consisting of loss of appetite, vomiting, headache, dizziness, and slight exophthalmos. On stopping the drug the thyroid began to decrease, and by the twenty-ninth day had returned to its original size. It would seem that the P.A.S. was the direct cause of the enlargement, and that the enlargement was proportional to the total dosage given.