cause of spontaneous abortion, which still remains unknown.

Although only six of the abortuses have been recovered for detailed study, four of them were grossly abnormal. The abnormalities were distributed evenly between patients who received either solution A or solution B. It remains to be determined whether these abnormalities are environmentally or genetically determined.

It has taken over three years to collect the 50 cases published in this paper, and because of this relatively small number the investigation will continue to ensure that small, but perhaps ultimately significant, differences do not escape detection.

Summary

Fifty patients have been treated in a double-blind study of the effect of 17-hydroxyprogesterone caproate on abortion rate. Only patients showing a low or falling pregnanediol excretion were treated and included in this study. Of those receiving solution A, 18.5% aborted; of those receiving solution B, 21.7% aborted. The overall incidence of foetal wastage is 20%. Whichever of these solutions contains the progestogen these results do not so far support the claims that progesta-

tional therapy is of specific value in the prevention of abortion. This study is continuing.

Of six abortuses examined, four were grossly abnormal.

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METHYLDOPA IN THE TREATMENT OF HYPERTENSION

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Hypertensive patients have been shown to be highly sensitive to the pressor effect of catecholamines (Goldenberg *et al.*, 1948), although evidence for increased production of these adrenergic amines is absent in most forms of hypertension (von Euler, 1956).

Irrespective of the exact role of catecholamines in hypertension, control of their endogenous production might provide a means of lowering blood-pressure. Methyldopa is a compound shown *in vitro* to be an effective inhibitor of the decarboxylation of dihydroxyphenylalanine, a precursor of catecholamines (Sourkes, 1954). This effect was subsequently confirmed pharmacologically (Reichel and Dengler, 1958). Inhibition of 5-hydroxytryptophan, tyrosine, and tryptophan decarboxylation was also demonstrated (Oates *et al.*, 1960). On administration of methyldopa to hypertensive patients it immediately proved to be an antihypertensive agent (Oates *et al.*, 1960). This warranted a more extensive study in order to assess its value either as a sole agent or in combination with other drugs in the treatment of hypertension. Possible toxic effects of the drug on the liver, kidneys, and blood picture, and certain aspects of the catecholamine metabolism during administration of methyldopa, have been studied.

Materials and Methods

Twenty-eight subjects with persistent hypertension were selected for this study, their ages ranging from 22 to 72 (average 46 years). Seventeen had essential hypertension, eight had malignant hypertension (with papillary

oedema), two had hypertension with stenosis of a renal artery, and one had a phaeochromocytoma. All patients, except two with essential hypertension, had a urea clearance above 35%. Blood-pressure measurements were made by the arm-cuff-auscultatory technique. Methyldopa was administered as the L-isomer ("aldomet") supplied as capsules or film-coated tablets containing 250 mg. of the drug.† The toxicity of the drug was checked in each patient with serial analysis of the liver-function test and complete blood-cell counts. The urinary metanephrines were assayed in three cases by the method of Pisano (1960). The urinary excretion of catecholamines was determined in one patient by the method of De Schaepdrijver (1958). The protocols of individual studies are considered below in the appropriate sections.

Effect of Methyldopa on Blood-pressure

Acute Effect

Twenty-three hypertensive patients received the drug during their stay in hospital, their blood-pressure being taken three to five times daily in both the recumbent and the standing position. After two days in hospital a placebo capsule was given three times daily for two days to seven patients, after which they received methyldopa capsules on a similar schedule in daily doses ranging from 750 to 2,750 mg. for 2 to 10 days. When necessary the dose was increased every third day. Fourteen subjects were started immediately on methyl-

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†We are grateful to Dr. K. C. Mezey, of Merck Sharpe and Dohme International, for supplying the aldomet used in this study.

dopa, the drug being replaced by an identical number of placebo capsules for the three last days in hospital. Two patients with malignant hypertension were not put on placebo capsules, but were transferred from another hypotensive drug to methyl-dopa. Average blood-pressures were calculated for the placebo period or for the two last days on the previous antihypertensive drug and for the last two days on methyl-dopa.

As can be calculated from Table I, the mean decrease in blood-pressure in the 13 patients with essential hypertension was 40/20 mm. Hg in the supine and 53/28 mm. Hg in the standing position at the end of a mean period of treatment of five days and with an average daily dose of 1,307 mg. of methyl-dopa. In the seven patients with malignant hypertension the mean blood-pressure reduction amounted to 56/38 mm. Hg in the supine and 61/34 mm. Hg in the standing position after an average of six days of treatment with 1,640 mg. of methyl-dopa. Two patients with renal-artery stenosis had a mean blood-pressure reduction of 26/11 mm. Hg in the supine and 57/22 mm. Hg in the standing position after three days of therapy with 1,500 mg. of methyl-dopa a day. The blood-pressure of the patient with a phaeochromocytoma was also lowered with respectively 16/12 mm. in the supine and 24/19 mm. in the standing position with a daily dose of 2,250 mg. of methyl-dopa.

Twelve out of the 23 patients were considered satisfactorily controlled, as judged by the standard of Dollery and Harington (1962), who consider control satisfactory if values at or below 160/100, in either the standing or the lying position, are obtained at repeated examinations. In two patients with essential hypertension no sizable fall of blood-pressure could be obtained, and in nine patients a slight hypotensive effect was demonstrable, but not sufficient according to the prevailing criteria. The degree of severity as rated by the fundus changes and aetiological mechanisms of the hypertension provided no clear-cut evidence regarding the way in which the hypertension would respond to methyl-dopa. In general, we found that the benign essential cases responded more favourably than the others. The onset of the antihypertensive action of the

drug was occasionally noticeable as early as three hours after administration of the first capsule, but usually the drug has to be given for 36 to 48 hours before it would start lowering the blood-pressure. After cessation of treatment the blood-pressure returned to pretreatment levels within 24 hours and often exceeded these levels for a day.

Long-term Effect

Seventeen patients were followed in the clinic, while taking the drug, for a period of 1 to 14 months (average five months). In this group, seven subjects, five with essential and two with malignant hypertension, were followed for an average of three months and received methyl-dopa only. Ten patients, six with essential and four with malignant hypertension, were treated initially with methyl-dopa only and after two to three weeks with an additional dose of hydrochlorothiazide, which was mostly incorporated in the methyl-dopa tablets. The dose of hydrochlorothiazide was kept constant during the whole period of observation, which averaged 6.8 months. Six patients were taking their own blood-pressure twice daily. The 11 others had their blood-pressure taken at least twice a week. The blood-pressures recorded are the means of the readings obtained during the last week of the observation periods on placebo and methyl-dopa tablets (Table II). The average fall of the blood-pressure in the group which received methyl-dopa only was 37/23 mm. in the recumbent and 38/27 mm. in the standing position at the end of the first month of therapy. The blood-pressure reduction was almost the same at the end of the observation period (average three months) with an identical dose of methyl-dopa.

Of the 10 patients treated with the combination methyl-dopa and hydrochlorothiazide, seven had their blood-pressure reasonably well controlled at the end of the first month of therapy. In four of them the blood-pressure rose after a few months. This necessitated an increase in the dose of methyl-dopa in three cases; without that the blood-pressure was lowered as much as at the end of the first month (Table II). Two of

TABLE I.—Blood-pressures of 23 Hypertensive In-patients Treated for a Short Term with Methyl-dopa

No. of Cases	Condition	Therapy		Blood-pressure (mm. Hg)							
				Placebo				Methyl-dopa			
				Lying		Standing		Lying		Standing	
		mg./Day	Days	Syst.	Diast.	Syst.	Diast.	Syst.	Diast.	Syst.	Diast.
13	E.H.	1,307 (180)	4.7 (1.5)	203 (19.2)	123 (14.4)	195 (17.6)	126 (10.2)	163 (20.6)	103 (13.1)	142 (17.8)	98 (11)
7	M.H.	1,640 (225)	6 (1.3)	235 (19)	139 (19.3)	234 (22.7)	134 (11.5)	179 (17.5)	101 (18.1)	173 (16.2)	100 (21.5)
2	R.H.	1,500	3	214	131	220	130	208	120	163	108
1	Phaeo	2,250	5	200	125	190	126	184	113	166	107

E.H. = Essential hypertension. M.H. = Malignant hypertension. R.H. = Hypertension with renal artery stenosis. Phaeo = Phaeochromocytoma. Standard deviations are given in parentheses.

TABLE II.—Average Blood-pressures of 17 Hypertensive Patients Treated for a Long Term with Methyl-dopa

No. of Cases	Therapy		Blood-pressure (mm. Hg)											
			Placebo				After 1 Month				Final			
			Lying		Standing		Lying		Standing		Lying		Standing	
	Months	mg./Day	Syst.	Diast.	Syst.	Diast.	Syst.	Diast.	Syst.	Diast.	Syst.	Diast.	Syst.	Diast.
7	3 (0.7)	M1,140 (370)	206 (22.4)	124 (5.1)	207 (17.8)	123 (9.8)	169 (12.8)	101 (9.4)	169 (19.1)	96 (9.5)	172 (12.2)	100 (10.4)	171 (15.2)	98 (8)
10	6-8 (3.5)	M1,600 (990) H80	210 (17.1)	133 (11.7)	201 (14.2)	133 (10.3)	165 (21.7)	111 (9.2)	170 (12.1)	117 (4.7)	182 (16.4)	119 (19.4)	179 (12.2)	121 (7.1)

M = Methyl-dopa. H = Hydrochlorothiazide. Standard deviations are given in parentheses.

these patients had essential and one had malignant hypertension. The three remaining patients, of whom two had malignant hypertension, became resistant in less than two weeks to doses of methyldopa as high as 3, 4, and 5 g., and hydrochlorothiazide did not alter this. These patients were nevertheless maintained on those high doses of methyldopa for longer periods, but the blood-pressure remained unchanged. Finally 14 of the 17 patients included in the long-term follow-up study had their blood-pressure pretty well under control with methyldopa only or with the combination of hydrochlorothiazide and methyldopa at the end of the observation period.

Apart from differences in the hypotensive effect of methyldopa during the months it was administered, we also noticed diurnal variations in the blood-pressure-lowering effect in five patients who were taking their

Effect of methyldopa on morning and evening standing blood pressure.

own pressure readings. They were asked to take methyldopa capsules at 6 a.m., 1 p.m., and 7 p.m. and to measure their pressure three hours after the ingestion of the drug. In each of them we found the blood-pressure to be significantly lower in the morning than at night, both in the recumbent and in the standing position. This difference is graphically presented in the Chart for the standing position.

Effect of the Addition of Hydrochlorothiazide on the Blood-pressure-lowering Action of Methyldopa

Acute Effect.—Methyldopa was given for seven days to four patients, after which hydrochlorothiazide was added for two weeks. The blood-pressure was taken twice daily and the mean values of the readings obtained during the two last days of each period of observation were compared (Table III). On average, 72.5 mg. of hydrochlorothiazide added to 1,375 mg. of methyldopa produce an additional blood-pressure drop of 29/20 mm. in the supine and 30/21 mm. in the standing position (Table III). This effect cannot be attributed to the hypotensive effect of hydrochlorothiazide alone, which in all cases produced only a very slight or even no blood-pressure reduction at all.

Long-term Effect.—In four patients, in whom the addition of hydrochlorothiazide to methyldopa had produced an initial significant reduction in blood-pressure, we withdrew the thiazide after several weeks for a period of seven days. The mean of the two daily blood-pressure readings obtained during the last two days of the period with and without the thiazide were compared. As shown in Table IV, two of the four patients had a blood-pressure rise. This effect was

TABLE IV.—Chronic Effect of Hydrochlorothiazide on Anti-hypertensive Action of Methyldopa

Case No.	Condition	Therapy (mg day)	Weeks on Thiazide	Blood Pressure (mm. Hg)			
				On Thiazide		Off Thiazide	
				L	S	L	S
1	E.H.	M 1,500 H 90	12	153/103	161/103	154/91	170/103
2	M.H.	M 1,500 H 90	12	150/115	155/115	160/115	145/110
3	E.H.	M 1,500 H 90	20	163/94	165/102	177/108	181/116
4	E.H.	M 2,000 H 100	32	180/117	136/95	181/119	153/106

M=Methyldopa. H=Hydrochlorothiazide. L=Lying. S=Standing.

apparent in Case 3, both in the supine and in the standing position, and in one instance (Case 4) in the standing position only. Cases 1 and 2 did not show any consistent blood-pressure rise after one week off thiazide.

Comparison Between the Hypotensive Effect of Methyldopa and Guanethidine

Seven patients were put alternately on guanethidine and methyldopa and the effect of both drugs on the blood-pressure was compared (Table V). Five patients (Cases 5, 6, 7, 10, and 11) were transferred from guanethidine to methyldopa and two (Cases 8 and 9) from

TABLE III.—Acute Effect of Hydrochlorothiazide on Antihypertensive Action of Methyldopa

Case No.	Condition	Therapy (mg./Day)	Blood-pressure (mm. Hg)					
			Before		On Methyldopa		On Combined Treatment	
			L	S	L	S	L	S
1	E.H.	M 1,500 H 90	220/120	210/110	178/105	168/110	160/102	156/102
2	M.H.	M 1,500 H 90	240/170	250/170	210/140	205/140	170/105	120/90
3	E.H.	M 1,000 H 60	210/130	175/120	180/118	184/123	160/88	168/105
4	E.H.	M 1,500 H 50	230/130	175/120	190/120	168/115	150/110	158/108
Average		M 1,375 H 72.5	220/138	202/130	189/121	181/122	160/101	151/101

M=Methyldopa. H=Hydrochlorothiazide. L=Lying. S=Standing.

methyldopa to guanethidine. All the patients were maintained on a constant daily dose of each drug for at least 10 days, except one (Case 8) in whom methyldopa was increased every four days. No patient received one of the drugs for more than a month. The differences between the means of the blood-pressure readings obtained during the two last days of the aforementioned dose of each drug are recorded in Table V. Four

alkaline phosphatase, the bilirubin determination, the B.S.P. excretion test, the assay of the transaminases, and in six patients also the determination of pyruvic acid and α -ketoglutaric acid. A complete urine examination was carried out on each visit. These tests were performed prior to treatment, after one week, at the end of each month for four months, and after the eighth month. We found a significant increase

TABLE V.—*Hypotensive Effect of Methyldopa Compared with that of Guanethidine*

Case No.	Therapy	Placebo		Guanethidine			Methyldopa		
		B.P. (mm. Hg)		Treatment (mg.)	B.P. (mm. Hg)		Therapy (mg.)	B.P. (mm. Hg)	
		L	S		L	S		L	S
5	M.H.		214 140	G 150 H 100		-10/+5	M 6,000 H 100		+5/+5
6	E.H.	230 130	175 120	G 50 H 50	-20/-10	-10/-15	M 1,000 H 50	-70/-30	-25/-22
7	E.H.	220 115	205 115	G 150		-45/-35	M 750	-40/-22	-53/-28
8	M.H.	200 135	242 126	G 100	-7/-12	-10/-5	M 1,500	-22/-30	-20/-30
9	M.H.	220 140	195 130	G 70 H 100	-40/-30	-70/-40	M 3,000 H 100	+5/+5	-10/+15
10	E.H.	200 140	190 136	G 25 H 100	-15/-23	-48/-25	M 2,500 H 100	-11/-11	-25/-23
11	E.H.	180 135	190 139	G 40 H 100	-20/-23	-24/-33	M 1,500 H 100	-35/-30	-45/-34

G = Guanethidine. H = Hydrochlorothiazide. M = Methyldopa. E.H. = Essential hypertension. M.H. = Malignant hypertension. L = Lying. S = Standing.

patients (Cases 6, 7, 10, and 11) showed a blood-pressure reduction with each drug, although not always to the same extent. In Case 5 the pressure did not drop with either 150 mg. of guanethidine or 6 g. of methyldopa. Case 8 responded very nicely to 1.5 g. of methyldopa but not to 100 mg. of guanethidine. On the other hand Case 9 showed no blood-pressure reduction on 3 g. of methyldopa, but responded well to 70 mg. of guanethidine. We were not always able to increase the dose of each drug up to the desired level either because of the reluctance of some patients to take so many methyldopa tablets (Cases 8, 9, and 10) or because of the highly disturbing morning weakness experienced by two patients on low doses of guanethidine (Cases 6 and 11). These two patients manifested no side-effects on methyldopa although the pressure was lower.

Side-effects and Toxicity

The side-effect most frequently observed was slight drowsiness, which was not always noticed by the clinician, but which was experienced subjectively by the patient for a few days (Table VI). This occurred in

TABLE VI.—*Side-effects and Their Frequency Encountered in 28 Patients on Methyldopa*

Drowsiness	11 cases	Absence of ejaculation	2 cases
Dry mouth	8 "	Diarrhoea	1 case
Depression	2 "		

11 of our 28 patients, and several volunteered that after being placed on placebo capsules they actually had felt much more relaxed on methyldopa. Other side-effects were dryness of the mouth, which occurred in eight patients ingesting the drug for a rather prolonged period of time, and diarrhoea, which appeared in one patient one day after initiation of therapy and necessitated its interruption after two days. Depression was seen in two patients who had a tendency to it. Two patients complained of disturbed ejaculation, which became manifest while they were taking methyldopa and which did not disappear after they had stopped taking the drug for one week.

The possible appearance of toxic effects was closely followed in all patients by means of a haemogram and liver-function tests, including the flocculation test, the

in B.S.P. retention after eight days in two patients. One was in congestive heart failure, which might explain this finding. Therapy was stopped and the patient was never seen again. The other patient had been in congestive failure, and we thought that her general condition could not account for this sudden rise in B.S.P. retention. Liver biopsy was performed, but did not provide any explanation. Methyldopa was nevertheless stopped, being replaced by guanethidine. One month later she returned to our out-patient department and a B.S.P. test performed at that time was normal; no other abnormalities were found.

Effect on Urinary Excretion of Catecholamines and Metanephrines

Since methyldopa has been shown to be an inhibitor of dopa decarboxylase, one might expect the drug to reduce the excretion of catecholamines and of its metabolites such as metanephrines. The 24-hour excretion rates of catecholamines were determined before and after the administration of a dose of methyldopa sufficient to produce a significant blood-pressure reduction in one hypertensive patient. The urinary excretion of metanephrines was determined in three hypertensive patients whose blood-pressure had also dropped with methyldopa.

After methyldopa the urinary excretion of adrenaline dropped to zero (Table VII). The values which were

TABLE VII.—*Effect of Methyldopa on Urinary Excretion of Adrenaline*

	$\mu\text{g.}/24 \text{ hours}$		$\mu\text{g.}/24 \text{ hours}$
Control	10.4 19.7 13.0	On methyldopa ..	0 0 0

obtained for noradrenaline were much higher than during the control period. It was shown by paper chromatography that these results were due to the presence of a substance other than noradrenaline (De Schaepdrijver, personal communication, 1962). The urinary excretion of metanephrines did not show any significant changes during methyldopa therapy (Table VIII).

TABLE VIII.—Effect of Methyldopa on Urinary Excretion of Metanephrine

Subject	mg./24 Hours	
	Control	On Methyldopa
1	0.50	0.37
	0.47	0.45
	0.60	1.03
2	0.60	0.20
	0.40	0.30
	0.34	0.50
3	0.70	0.55
	0.50	0.72
	0.60	0.78

Discussion

Our data confirm the antihypertensive effect of methyldopa. This effect was noticed in a variety of hypertensive conditions ranging from benign essential to malignant hypertension, or to hypertension with renal-artery stenosis or due to a pheochromocytoma.

The cases of hypertension which are most easily controlled with methyldopa are the mild and moderately severe ones. From our experience it appears that such cases continue to be well controlled after several months with the same dose as initially, which rarely exceeds 1.5 g.

The severe cases will generally require higher doses. Because of the well-known potentiation of the antihypertensive effect of methyldopa by a diuretic, we added hydrochlorothiazide to methyldopa with the hope that this might reduce the dose of methyldopa which these patients need.

The potentiation of the blood-pressure-lowering effect of methyldopa by hydrochlorothiazide was manifest in all the patients whose blood-pressure had already dropped to some extent on methyldopa only, and this confirms the observations of other investigators (Payne *et al.*, 1961; Dollery and Harington, 1962). After several weeks the blood-pressure of some of the patients treated with the combination of methyldopa and hydrochlorothiazide was, however, slowly rising again. This might be due to the inefficacy of hydrochlorothiazide after prolonged administration, as some of our results suggest, but the possibility of the appearance of a resistance against methyldopa cannot be excluded. That some patients might become refractory to methyldopa is well known (Cannon *et al.*, 1962; Dollery and Harington, 1962), and three of our patients whose blood-pressure had dropped dramatically within a few days with 1.5 g. a day showed no blood-pressure reduction while taking as much as 5 g. daily two weeks later. Only more-prolonged follow-up will show how serious this handicap may become. Meanwhile the blood-pressure of all but three of our patients with essential as well as malignant hypertension was kept reasonably well controlled for months with methyldopa or with the combination of methyldopa and hydrochlorothiazide. In our opinion this is the treatment of choice whenever diuretics and rauwolfia derivatives fail to lower the pressure. The main reasons for this preference are its efficacy in lowering the blood-pressure in both the standing and the recumbent position without marked orthostatic drop and its being extremely well tolerated.

Methyldopa should not necessarily be considered less potent than such drugs as guanethidine. This feeling is supported by the results we obtained in a small group

of patients who were put alternately on guanethidine and methyldopa. Some patients appeared to respond very nicely to reasonable doses of methyldopa and not to guanethidine. The opposite was also true, so that the use of both drugs might be considered in the treatment of severe hypertension.

The fact that in five patients methyldopa appeared to lower the blood-pressure in the morning rather than at night is another interesting feature which we also noticed in patients treated with guanethidine (Lauwers *et al.*, 1961). To our knowledge there is no satisfactory explanation for it; and many factors such as the accumulation of fluid which the subject may show at night may be involved.

As regards the toxicity of the drug, we have not noticed any disturbing manifestation attributable beyond any doubt to methyldopa. The appearance of agranulocytosis, observed in one patient by Hallwright (1961) during treatment, seems to be the only substantiated instance of toxicity precipitated by this drug. The side-effects were in general well tolerated and sometimes even welcome, such as the feeling of relaxation which some patients felt and which decided them to continue taking the drug even though it had no effect on the blood-pressure.

Although one might expect that the decarboxylation-inhibiting properties of methyldopa would be related to the hypotensive action of the drug, there is at present no convincing evidence that this is the case. The determinations of the urinary excretion of metabolites of catecholamines have not procured fresh evidence. Cannon *et al.* (1962) found no changes in the excretion of vanillic mandelic acid, whereas Schaub *et al.* (1962) did find a reduction after intake of methyldopa, but this decrease did not coincide with the fall in blood-pressure.

We have not found a reduction in the excretion of metanephrines after methyldopa. But since we know that methyldopa can be metabolized to L- α -methyl-noradrenaline, which in turn undergoes 3-O-methylation (Gillespie *et al.*, 1962; Carlsson and Lindqvist, 1962), we will have to separate the α -methyl from the physiological metanephrines before we can properly interpret our results. The disappearance of adrenaline in the urine of our patient following methyldopa is, however, suggestive of an inhibition of the decarboxylation. But the determination of the urinary excretion of noradrenaline did not support this, as the chemical method used could not separate noradrenaline from a very similar compound appearing in the urine following methyldopa. What would appear to contradict inhibition of decarboxylation as being related to the blood-pressure-lowering effect of methyldopa is the fact that analogues of methyldopa, which *in vitro* possess a much greater decarboxylase inhibiting activity, have been found to exert a less-marked antihypertensive activity (Cannon *et al.*, 1962).

Summary

Methyldopa, an inhibitor of the decarboxylation of certain aromatic amino-acids, has been used in the treatment of 23 hospitalized patients with hypertension; 12 were considered satisfactorily controlled as judged by the standards of Dollery and Harington (1962). Seventeen patients were followed in the clinic and received methyldopa alone or in combination with a thiazide for periods ranging from 1 to 14 months

(average 5 months). In 14 of them the blood-pressure was maintained within reasonable limits.

Treatment failed to lower the blood-pressure to any significant extent in two in-patients. Three out-patients became rapidly refractory to the hypotensive effect of methylodopa.

Methylodopa was shown to be highly effective in the most severe cases of hypertension, but in some cases for only a short time.

The average effective dose in moderate and severe hypertension was 1.5 g. of methylodopa. Thiazide diuretics potentiated the hypotensive action.

The results obtained with guanethidine and methylodopa in the treatment of seven hypertensive patients are compared. It appeared that both drugs might be considered in the treatment of severe hypertension and that methylodopa was usually better tolerated.

Our results as regards the urinary excretion of catecholamines and metanephrine did not show any parallelism between the inhibition of the biosynthesis of noradrenaline and the blood-pressure reduction.

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"Recently C. P. Snow, the novelist, once a scientist, has described the phenomenon of two cultures. It is most often encountered, he writes, in our universities. Those devoted to science and those in the humanities no longer communicate with each other. Their cultures separate them and they speak different languages. They are unhappy and irritated when not left to themselves. But what Sir Charles Snow is describing is only one example of a much more general phenomenon prevalent to-day in society. Within science itself, separate groups have formed. Each uses a technical lingo incomprehensible to other groups. Even doctors of medicine use strange genteelisms and expertise in laboratory and hospital. When they talk to patients, or write reports, they continue to use it, as though hoping to impress someone. Or else they forget the fact that simpler diction would be better suited to humane purposes and to scholarly performance. The rancher, the business man, the technologist, the musician and even the beatnik and the crook have a language of their own. As the years pass, they find general communication increasingly difficult." (Professor Wilder Penfield, O.M., F.R.S., "Scholar's Use of Idleness," *Med. J. Aust.*, December 22, 1962.)

ASSESSMENT OF CONDENSER-HUMIDIFIERS WITH SPECIAL REFERENCE TO A MULTIPLE-GAUZE MODEL

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If a patient's upper respiratory tract is bypassed by means of an endotracheal tube or a tracheostomy the humidifying properties of this part of the tract are lost. If it is thought necessary to replace this loss by external means there are three main possibilities. Water droplets may be added to the inspired gas by means of a nebulizer; water vapour may be added by passing the inspired gas over heated water; or a "condenser-humidifier" may be used.

In general a condenser-humidifier is a device through which the patient's respirations pass and which contains some element of large surface area such as a multiple-bore tube (Toremalm, 1960) or wire gauze as in Walley's (1956) device, or in the instruments manufactured by Drägerwerk and by Messrs. Garthur (London) Ltd. During expiration warm moist gas from the patient passes through the relatively cool element; therefore the gas is cooled and the element is warmed, and water condenses out of the gas on to the element. During inspiration gas enters the device and in passing through the relatively warm wet element becomes warmed and humidified.

In principle, at least, by using a nebulizer or by passing inspired gas over heated water any desired humidity can be produced, because external supplies of water and heat or power are available. In a condenser-humidifier, however, no such external supplies are present and its performance must therefore be subject to some limits. The object of this investigation was to determine these limits for condenser-humidifiers in general and for the multiple-gauze condenser-humidifier manufactured by Messrs. Garthur (London) Ltd. in particular.

Fig. 1.—Condenser-humidifier manufactured by Messrs. Garthur (London) Ltd.