Summary

In 30 patients with oral lichen planus regarded as severe enough to justify treatment, use of betamethasone (Betnovate) pellets 0.1 mg. was followed by substantial improvement or complete clearance of oral lesions in 20. Seven patients showed gradual or incomplete improvement.

Only 2 out of 30 patients failed to show any response to betamethasone, but treatment was not continued for more than one month in these cases.

Of two patients with mucous membrane pemphigoid the use of betamethasone pellets was followed by complete clearance of oral lesions. A third patient showed substantial improvement until he ceased to attend.

The only side-effect of treatment was development of thrush in four patients.

The assistance of Messrs. Glaxo in their generous supply of tablets and for other help for this trial is gratefully acknowledged.

REFERENCES

Altman, J., and Perry, H O. (1961). *Arch. Derm.*, 84, 179.
Andreasen, J. O., and Pindborg, J. J. (1963). *Nord. Med.*, 70, 861.
Bratlund, H., and Holten, C. (1954). *Dan. med. Bull.*, 1, 79.
Desbrosses, J. L. (1965). *Ann. Oto-laryng. (Paris)*, 82, 841.
Friedman, M., Fletcher, J., Hinton, J. M., Lennard-Jones, J. E., Misiewicz, J. J., and Parrish, J. A. (1967). *Brit. med. J.*, 1, 335.
McCarthy, P. L., and Shklar, G. (1964). *Diseases of the Oral Mucosa*. New York.
Warin, R. P. (1960). *Brit. J. Derm.*, 72, 288.
Williams, D. I., *et al.* (1964). *Lancet*, 1, 1177.

Use of Lignocaine in Treatment of Cardiac Arrhythmias

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Since the introduction of units for intensive observation and care of patients with acute myocardial infarction arrhythmias have been found in up to 70% of such patients (Yu *et al.*, 1965). This finding has emphasized the lack of antiarrhythmic drugs that are generally accepted as safe to use in these circumstances, especially when parenteral therapy is necessary. In acute myocardial infarction frequent ventricular ectopic beats may require treatment as urgently as the sustained ventricular arrhythmia that they commonly preface, especially if the ectopic beats are superimposed on the T wave of the preceding electrocardiographic complex (Fig. 1). Procainamide has been widely used, but the frequency of accompanying hypotension remains a drawback to its routine use in acute myocardial infarction.

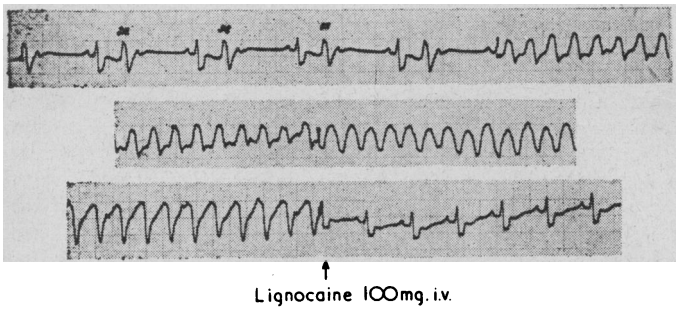

FIG. 1.—Rhythm strips showing ventricular ectopic beats precipitating ventricular tachycardia ; subsequently abolished by lignocaine.

Lignocaine, which is structurally similar to procainamide, was synthesized in 1943 by Löfgren, and subsequently extensively investigated as a local anaesthetic agent (Wiedling, 1964). Southworth *et al.* (1950) reported the successful use of lignocaine in association with alternating-current shock in a case of ventricular fibrillation arising during cardiac catheterization. Subsequent authors have confirmed the value of lignocaine in abolishing or preventing ventricular arrhythmias in animals under a variety of experimental conditions (Van Dongen, 1953 ; Melon *et al.*, 1953 ; Visentini, 1954 ; Frederickson and Morris, 1955 ; Cahn, 1955 ; Carden and Steinhaus, 1956 ; Harris *et al.*, 1956 ; Hitchcock and Keown, 1958 ; Austen and Moran, 1965). Greenspan *et al.* (1966) have shown lignocaine to be more effective than quinidine in restoring sinus rhythm in dogs with digitalis-induced ventricular arrhythmias ; Katz and Zitnik (1966) have similarly shown the superiority of lignocaine over direct-current shock in these circumstances.

In a large series of over 500 cases Hitchcock and Keown (1959) have shown the efficacy of lignocaine in the management of cardiac arrhythmias during cardiac surgery in man. This work has been confirmed by Weiss (1960). Likoff (1959) successfully used lignocaine for the control of various arrhythmias arising during surgery. De Sanctis (1965), Minuck (1965), and Bedynek *et al.* (1966) reported the use of lignocaine in the treatment of ventricular ectopic beats and ventricular tachycardia of non-surgical origin. It therefore appeared to be a drug worthy of further evaluation. This report is based on experience over the past year in a coronary intensive care unit, a cardiac surgical recovery ward, and the general medical wards.

Material and Methods

Fifty-five patients were treated with lignocaine for a variety of arrhythmias. The drug was usually given intravenously, though some patients received it by intramuscular injection. Initially 1–2 mg. of lignocaine per kg. body weight was used, repeated, if necessary, every 20 minutes to a maximum of 500 mg. Subsequently it was found more satisfactory to use a "loading" dose of 1–2 mg./kg. followed by the slow infusion of 1–2 mg./minute in a drip. For this purpose 500 mg. of lignocaine was added to 500 ml. of 5% dextrose in water ; it was then infused at 10 to 20 drops a minute, according to the patient's response, and continued for up to 48 hours. Five hundred units of heparin was added to prevent the thrombophlebitis that commonly accompanied prolonged infusion of lignocaine into one vein.

Cardiac outputs were determined in three patients before and 10 minutes after receiving 2 mg. of lignocaine per kg. intravenously. One had a normal heart, one a small left ventricular aneurysm, and the third a cardiomyopathy. Pulmonary artery and brachial artery pressures were recorded, and cardiac out-

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puts were determined by both indicator dilution and the Fick methods.

Results in Different Arrhythmias

(1) *Sinus Tachycardia.*—Lignocaine did not influence the heart rate in the three patients with sinus tachycardia in whom it was used.

(2) *Supraventricular Ectopics* (12 patients).—Supraventricular ectopic beats were treated in two patients after myocardial infarction, in two after open-heart surgery, and in another two after thoracotomy ; in all six cases sinus rhythm was restored by lignocaine. Six patients with frequent atrial ectopic beats following cardioversion of atrial fibrillation had their ectopics abolished by lignocaine. Despite maintenance therapy atrial fibrillation recurred in one of these patients within 12 hours.

(3) *Supraventricular Tachycardia.*—No obvious effect was observed in four patients with this arrhythmia.

(4) *Atrial Fibrillation.*—Ten patients with chronic atrial fibrillation were given lignocaine. In none of these cases was the rhythm affected.

(5) *Ventricular Ectopics* (18 patients).—Fourteen patients who developed ventricular ectopic beats after acute myocardial infarction were treated with lignocaine. In twelve of them the ectopics were abolished ; in two they were significantly reduced (Fig. 2). Two other patients with chronic ischaemic heart disease, and long-continued ventricular ectopic beats, did not respond to lignocaine. Ventricular ectopic beats occurring in two patients after open-heart surgery were abolished by lignocaine.

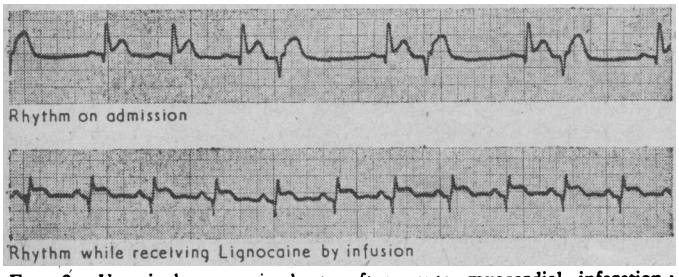

FIG. 2.—Ventricular ectopic beats after acute myocardial infarction ; abolished by lignocaine infusion.

(6) *Ventricular Tachycardia.*—Lignocaine was successful in correcting this arrhythmia in four patients after cardiac infarction (Fig. 1). In one of them lignocaine prevented the recurrence of ventricular tachycardia. In another, with widespread ischaemic heart disease, lignocaine failed to prevent the recurrence of ventricular tachycardia. Lignocaine was used in many more instances for this arrhythmia, but usually in conjunction with cardioversion and other medication, thus making the assessment of its value in these cases difficult.

(7) *Ventricular Fibrillation.*—Lignocaine was used in four cases of ventricular fibrillation before any other measure. In only one case did it restore sinus rhythm. In this emergency cardioversion was attempted as soon as possible, and several drugs were usually given. Despite these other agents it was felt that in some cases lignocaine did facilitate the restoration of sinus rhythm, and it assisted in the maintenance of sinus rhythm in others.

Haemodynamic Study.—In the three patients studied lignocaine did not significantly alter the pulmonary or brachial artery pressure or cardiac output.

Side-effects.—No significant complication of lignocaine therapy was observed in any of these patients. An insignificant reduction in systolic blood pressure occurred in five patients, and dizziness, blurred vision, and drowsiness occurred in two patients receiving maximal doses of lignocaine. Local thrombophlebitis was encountered with prolonged infusion of lignocaine. The development of this complication could be prevented by the use of small doses of heparin in the infusion.

Discussion

Lignocaine has been used by continuous intravenous infusion in anaesthetic practice (de Clive-Lowe *et al.*, 1954). The duration of antiarrhythmic action of a single intravenous dose of 1 mg./kg. is 10 to 20 minutes. It has therefore been recommended that each dose be rapidly administered intravenously (Weiss, 1960 ; Harrison *et al.*, 1963). However, we have found it necessary to use a loading dose of lignocaine, followed by continuous intravenous infusion, for the adequate control of arrhythmias.

Like previous authors, we have found lignocaine to be of especial value in acute ventricular arrhythmias such as those encountered after myocardial infarction and during and after cardiac surgery. In the more chronic arrhythmias and in acute supraventricular tachycardias it is of less value.

It has been reported that an excess of lignocaine may produce drowsiness, analgesia, euphoria, twitching, discomfort on breathing, speaking, or swallowing, blurred vision, sensations of heat, cold, and numbness, and sweating ; with larger doses, apprehension, disorientation, and fits may occur ; fits have been reported with doses above 750 mg./hour. With severe overdosage cardiovascular depression and respiratory arrest occur. Hypoxia increases the risk of cardiovascular toxicity. Lignocaine decreases myocardial irritability and prolongs conduction time, depolarization time, and the refractory period. Little depression of the sino-atrial node occurs. Its rapidity of action has been related to its rapid diffusion to and penetration of cell membranes (Hitchcock and Keown, 1959 ; Frieden, 1965).

Lignocaine has been found to produce no significant circulatory depression in man in doses of 1 to 2 mg./kg. (Harrison *et al.*, 1963). In fact, at this dose level Kao and Jalar (1959) demonstrated an increase in cardiac output, heart rate, stroke volume, and arterial pressure in the anaesthetized dog. These effects were shown to be due to a central action of the drug. With larger doses peripheral vasodilatation, hypotension, bradycardia, and decreased cardiac output occur. We have shown that in three patients lignocaine in a dose of 2 mg./kg. did not alter cardiac output or intravascular pressures. This drug would therefore seem to have an important advantage over other commonly used antiarrhythmic agents, propranolol, quinidine, and procainamide.

In this small series we have been impressed by the safety of lignocaine as well as by its efficacy. The mechanism of the drug's antiarrhythmic action remains unknown.

Summary

Lignocaine has been used in 55 patients suffering from a variety of arrhythmias. After a loading dose of 1 to 2 mg./kg. it was given by continuous intravenous infusion (0.1%). It was found to be particularly successful in treatment of acute ventricular arrhythmias, notably those occurring after acute myocardial infarction, during and after cardiac surgery, and in the treatment of atrial ectopic beats, though of less value in sustained atrial arrhythmias.

Since the completion of this report the value of lignocaine in these circumstances has been supported at a W.H.O. meeting in Edinburgh (Annotation, *Lancet*, 1967).

REFERENCES

Austen, W. G., and Moran, J. M. (1965). *Amer. J. Cardiol.*, 16, 701.
Bedynek, J. L., Weinstein, K. N., Kah, R. E., and Minton, P. R. (1966). *J. Amer. med. Ass.*, 198, 553.
Cahn, J. (1955). Cited by Wiedling (1964).

Carden, N. L., and Steinhaus, J. E. (1956). *Circulat. Res.*, **4**, 680.
de Clive-Lowe, S. G., Gray, P. W. S., and North, J. (1954). *Anaesthesia*, **9**, 96.
De Sanctis, R. W. (1965). *J. Amer. med. Ass.*, **191**, 632.
Frederickson, E. L., and Morris, L. E. (1955). *Fed. Proc.*, **14**, 340.
Frieden, J. (1965). *Amer. Heart J.*, **70**, 713.
Greenspan, K., Lord, T. J., Steinmetz, E. F., and Fisch, C. (1966). *J. Indiana med. Ass.*, **59**, 148.
Harris, A. S., Aguirre y Guerra, C., Liptak, R. A., and Brigham, J. C. (1956). *J. appl. Physiol.*, **8**, 499.
Harrison, D. C., Sprouse, J. H., and Morrow, A. G. (1963). *Circulation*, **28**, 486.
Hitchcock, P., and Keown, K. K. (1958). *Fed. Proc.*, **17**, 378.
—— —— (1959). *Sth. med. J. (Bgham, Ala.)*, **52**, 702.
Kao, F. F., and Jalar, U. H. (1959). *Brit. J. Pharmacol.*, **14**, 522.
Katz, M. J., and Zitnik, R. S. (1966). *Amer. J. Cardiol.*, **18**, 552.
Lancet, 1967, **2**, 665.
Likoff, W. (1959). *Amer. J. Cardiol.*, **3**, 427.
Melon, J. M., Cahn, J., and Dubrasquet, M. (1953). Cited by Wiedling (1964).
Minuck, M. (1965). *Canad. med. Ass. J.*, **92**, 16.
Southworth J. L., McKusick, V. A., Pierce, E. C., and Rawson, F. L. (1950). *J. Amer. med. Ass.*, **143**, 717.
Van Dongen, K. (1953). *Arch. int. Pharmacodyn.*, **96**, 45.
Visentini, P. (1954). Cited by Wiedling (1964).
Weiss, W. A. (1960). *Anesth. Analg. curr. Res.*, **39**, 369
Wiedling, S. (1964). *Xylocaine : The Pharmacological Basis of its Clinical Use*, 2nd ed. Stockholm.
Yu, P. N., Fox, S. M., Imboden, C. A., and Killip, T. (1965). *Mod. Conc. cardiovasc Dis.*, **34**, 27.

Follow-up Study of Refractory Obesity Treated by Fasting

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The treatment of obesity by a period of fasting in hospital has achieved popularity since its introduction by Bloom in 1959, and the few reports of its long-term effects have been encouraging (Hunscher, 1966; Harrison and Harden, 1966). We present the follow-up results of fasting in patients having "refractory" obesity in whom this form of treatment has not previously been specifically studied; these are not encouraging.

Materials and Methods

The Table includes the relevant pretreatment data of the 25 patients studied. All were clinically obese, overweight by at least 40% of their standard (U.S.A. Medico–Actuarial Investigation 1912), and satisfied the criteria for refractory obesity as originally defined (Duncan *et al.*, 1960). Thus all had regularly attended the department, but their weight had either increased or remained unchanged during the six months before inpatient fasting despite the use of anorectic agents in nine subjects. All were shown by appropriate investigation to be free from endocrine disease, none was in cardiac failure, but several had complications of obesity, such as hernia, osteoarthritis, varicose veins, or flat feet.

On admission to hospital patients were given a 400–500-calorie diet for one or two days. During the subsequent fast they were allowed to drink as much water, unsweetened black coffee or tea, or acaloric fruit juices or cordial as they wished, but no solid food was permitted. A vitamin preparation (Multivite) was given routinely and mineral supplements, hypnotics, and sedatives if required. Patients were weighed every second day and encouraged to be ambulant. Estimations of the blood electrolytes, bicarbonate, and uric acid and urine tests for ketones were regularly made, but no serious biochemical changes occurred and no patient had to terminate the fast prematurely. For a few days before leaving hospital each patient took a daily diet of 400 calories. At the time of discharge all were given further instruction in an appropriate 400–1,000-calorie daily diet and were weighed in the outpatient department wearing normal clothing; this weight was taken as the weight on discharge.

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Weight Data of Fasted Patients

Case No.	Age	Sex	Standard Weight (lb.)	Excess Weight (lb.) Before Fast		Excess Weight At Start of Fast		Time Fasted (Days)	Weight Lost During Fast (lb.)	Excess Weight After Fast				Follow-up Period (months)	Weight Change Since End of Fast (lb.)	Latest Weight as Change From Weight Before Fast
				6 months	3 months	lb.	% standard			Immediately	3 months	6 months	When Last Seen			
1	24	F	139	61	65	61	43	18	23	38	—	—	—	—	—	—
2	48	F	144	59	60	60	42	12	12	48	56	—	—	—	—	—
3	30	M	160	224	227	230	144	40	58	172	168	202	217	7	+45	−13
4	57	F	144	90	93	94	65	31	43	51	55	63	66	8	+15	−28
5	38	M	159	77	77	78	49	34	35	43	55	68	71	8*	+28	−7
6	45	F	146	209	209	209	143	40	33	176	184	186	195	8	+19	−14
7	20	F	129	81	85	81	62	12	9	72	79	81	82	10	+10	+1
8	43	F	141	114	116	119	86	26	22	97	103	109	123	10	+26	+4
9	61	F	136	169	168	176	130	21	24	152	168	164	168	10*	+16	−8
10	55	F	145	108	112	115	79	23	24	91	107	121	123	11*	+32	+8
11	20	F	141	102	104	106	75	17	21	85	87	89	107	12*	+22	+1
12	37	M	154	115	118	120	78	21	32	88	75	79	92	12	+4	−28
13	38	F	132	110	118	124	94	27	28	96	110	126	132	12*	+36	+8
14	62	F	136	64	64	64	47	29	13	51	59	64	67	12*	+16	+3
15	51	F	117	178	181	179	153	16	19	160	175	177	191	13	+31	+12
16	50	F	134	265	267	272	203	32	42	230	238	248	266	14*	+36	−6
17	45	F	159	73	79	83	52	16	22	61	46	46	78	14*	+17	−5
18	40	F	134	132	130	134	100	15	22	112	125	131	136	18*	+24	+2
19	51	F	149	159	159	159	107	26	18	141	144	159	161	18	+20	+2
20	50	F	138	78	78	95	69	36	34	61	72	72	100	19	+39	+5
21	53	F	145	111	119	129	90	27	26	103	113	117	133	21	+30	+4
22	37	F	149	101	110	114	77	34	31	83	89	103	113	22	+30	−1
23	43	F	137	121	121	121	88	10	20	101	105	111	121	22*	+20	±0
24	33	F	130	67	70	73	56	16	16	57	91	99	105	23	+48	+32
25	39	M	170	214	218	240	141	17	20	220	219	240	321	24	+101	+81

* Patients subsequently defaulted.