Side Effects.—It was not part of this investigation to record effects such as changes in blood pressure, pulse rate, etc. These may be studied more profitably and easily in circumstances other than the lying-in wards of a maternity hospital, where patients are apprehensive and easily upset by any unusual investigation. No serious symptoms were noted after the administration of either drug, although three patients complained of a feeling of depression and weight in the head, and one patient of nausea and headache; the effects were of short duration. The doses received by these patients were 0.25 mg. ergotamine (intravenous), 0.5 mg. ergotamine (intramuscular), 1.5 mg. ergotamine (by mouth), and 0.5 mg. ergotoxine (intramuscular).

Dosage.—It may safely be said that in the case of both ergotoxine and ergotamine the optimum dosage for intramuscular injection is 0.5 mg. Doubling this dosage produced but slight increase of action: on the other hand, 0.25 mg. did not produce the full effect of the drug. Oral administration of ergotoxine and ergotamine, even in doses of 2 mg., did not yield consistent results. The contractions produced were much smaller and more erratic than those seen after the drugs had been given by injection. In several instances the contractions ceased after about an hour, to appear again about an hour later. Doses of 2.5 mg. produced a more definite result. Burn⁸ has made the observation that in the cat only about one-third of a dose of ergotoxine is absorbed from the alimentary canal after forty-eight hours. My results suggest that only a very small fraction of a dose is absorbed by the human subject during the two or three hours following oral administration.

These observations appear to justify a definite statement that ergotamine and ergotoxine are indistinguishable from each other in their clinical actions. If further experiments

should show that there is any difference in activity, that difference must be of such a small order that it is of no practical importance.

CONCLUSIONS

1. A method is described by which the response of the human puerperal uterus to oxytocic drugs may be directly recorded.

2. Both ergotoxine and ergotamine bring about strong contractions in the puerperal uterus when they are administered by injection.

3. Ergotoxine and ergotamine are indistinguishable from each other in their action on the puerperal uterus.

4. The effect comes on slowly, and takes fifteen to forty-five minutes to appear after intramuscular injection.

5. The most suitable dosage for intramuscular injection is 0.5 mg.

6. Oral administration gives slow and erratic results, even after comparatively large doses of the drug.

It is a pleasure to express thanks to Sir H. H. Dale for useful advice and encouragement in this work.

Note.—A further communication by the same author dealing with the action of ergot preparations on the puerperal uterus, with special reference to the activity of the liquid extracts, will be published in a subsequent issue of the *Journal*.

REFERENCES

- ¹ Moir, C.: *Lancet*, March 12th, 1932, p. 564.
- ² Bourne, A., and Burn: *Journ. of Obstet. and Gynecol.*, 1927, xxxiv, 249.
- ³ Dale, Sir H. H.: *Lancet*, 1930, ii, 1149.
- ⁴ Dale, Sir H. H., and Spiro: *Arch. Exper. Path. and Pharm.*, 1922, xcv, 337.
- ⁵ Burn, J. H., and Ellis: *Pharm. Journ.*, 1927, cxviii, 384.
- ⁶ Stoll, Professor A.: *Lancet*, 1930, ii, 1148.
- ⁷ Smith, S., and Timmis: *Ibid.*, 1930, ii, 994.
- ⁸ Burn, J. H.: *Quart. Journ. Pharm. and Pharmacol.*, 1929, ii, 515.

THE MENACE OF OBESITY *

BY

ERNEST BULMER, M.D., M.R.C.P.ED. AND LOND.

ASSISTANT PHYSICIAN, GENERAL HOSPITAL, BIRMINGHAM

The experience of life assurance companies is that weight, especially in relation to age, is an important factor in longevity, and the old tag *corpora sicca durant* has had statistical confirmation. The medical profession has been slow to apply these actuarial lessons to practice, and medical precept has lamentably lagged behind the dictates of fashion. Our advice has too frequently been sought for aesthetic rather than for hygienic reasons. An examination of some of the ascertained facts may be of interest. Should the national overweight continue to grow unchecked, the mortality from the degenerative, non-bacterial diseases will diminish the average expectation of life. This has been increased during the last century by the control of infectious diseases and by the reduction in infant mortality, but the scourge of degenerative disease remains to be tackled.

CAUSES OF OBESITY

The Controlling Mechanism.—The body weight after childhood represents the balance of two factors—the quantity of food ingested on the one hand, and the expenditure of energy in maintaining body heat and in glandular and muscular activity on the other. Some controlling mechanism must exist, and Grafe and Grunthal¹ have, as the result of experiment, suggested its localization in the hypothalamic region: this may explain the gross obesity in such diseases as chronic epidemic

encephalitis and hypothalamic tumours. The controlling mechanism is so perfect that the adult weight tends to remain constant in spite of an ever-varying food intake and energy output. Silver and Bauer² regard obesity as due to an upset in this mechanism, but they stress the importance of the hereditary factor.

The Endocrine Glands.—The part played by these glands in obesity is most controversial. The basal metabolic rate is usually within normal limits. Bauer² found clinically recognizable disorders of the endocrine glands in 2.6 per cent. of 276 cases, whilst Dunlop and Murray Lyon³ state that 62.8 per cent. of 493 cases gave "histories suggesting the possibility of glandular disturbance being a factor"; little evidence of such disturbance was found on physical examination. The endocrine factor, if it exists, must be a slight error operating over a long period.

Hyperinsulinaemia.—Nissl, En Shui, and Gordon,⁴ in a study of 500 obese people, found a normal intake of fat and protein but an immoderate consumption of carbohydrate; they suggest that this excessive carbohydrate causes pancreatic stimulation with hyperinsulinaemia, which in its turn provokes a craving for carbohydrate to check the uncomfortable symptoms of hypoglycaemia during brief fasts. There would appear to be much evidence and some theoretical considerations against this view.

CLASSIFICATION OF OBESITY

To review all the theories of the causes of obesity is without the scope of this paper, but the following classification suggests itself.

1. **Exogenous Group.**—This is a small but important group, due to gross and persistent immoderation in the intake of food and alcohol.

* A paper given before the Nuneaton and Tamworth Division of the British Medical Association, December 12th, 1931.

2. *Endocrine Group*.—This is a small group, and comprises cases of recognizable disorders of the thyroid, pituitary, suprarenal, and sex glands.

3. *Central Nervous System Lesions*.—This includes the few cases in which obesity results from disease—inflammatory or neoplastic—in the neighbourhood of the supposed metabolic centre in the hypothalamic region.

4. *Constitutional Group*.—Into this group the majority of cases fall, but little is known of the causative factors. Presumably there is a failure in the weight-regulating mechanism, and the majority of patients come of an obese stock. They maintain their weight without due regard to the usually accepted caloric balance. Carbohydrate is perhaps too readily converted into fat. There is much evidence that most cases are due to over-indulgence in carbohydrate—practically a carbohydrate addiction.

Taylor⁵ sums up well:

"We live in economic circumstances which permit of an easy functioning of the influences making for overweight. Foodstuffs are available in extraordinary variety and profusion. The per capita food requirement is declining. Economic restraint on eating is lacking, except in the poorest classes."

PRINCIPLES OF TREATMENT

Treatment is simple if the patient will co-operate; impossible otherwise. The more obese the patient the greater the rapidity of the weight reduction and of the likelihood of relapse. No sudden and drastic reduction is advisable—five or six pounds a month is the optimum. The object of treatment is cure of the carbohydrate addiction by a re-education of the patient's dietetic habits, so that he will be enabled to live permanently on a lower caloric intake.

Diet.—The scientific but rather impracticable method is to place the patient on an accurately measured diet calculated at about 20 per cent. below his needs at his ideal weight. Murray Lyon⁶ has had excellent results on the simple plan of using standard 1,000–1,200 calorie diets. Easily assimilable carbohydrates are replaced by bulky foods of low caloric but high satiety value. The patient must be made to live on his fat.

Stimulation of Energy Loss.—This aspect must be approached with caution, and in addition to exercise cold baths are a potent stimulus to metabolism.

Endocrine Cases.—These must receive their appropriate replacement therapy, and, although thyroid extract may be useful in constitutional obesity, myxoedema and not obesity is its correct indication.

SEX AND AGE DISTRIBUTION

Preble⁷ found in a study of 1,000 overweights, including in this category any person 10 lb. or more above the ideal weight, the following age and sex distribution.

TABLE I.—Distribution by Age Groups of 1,000 Overweights

Age	0-20	21-30	31-40	41-50	51-60	61-70	71 and Over	Total
Men ...	1	11	53	85	68	18	8	244
Women ...	7	65	178	238	196	62	10	756
Total ...	8	76	231	323	264	80	18	1,000

HYPERPIESIA AND OBESITY

That there is a definite relation between hyperpiesia and obesity is a matter of daily clinical experience, although many obese persons have a normal blood pressure. I have been unable to find any extensive analysis of cases. Terry⁸ found in a series of sixty-three obese women thirty-seven with hypertension. Preble⁷ in his series of 1,000 overweights, found that sixty-two had

a systolic pressure of over 200 mm. Hg; the average blood pressure in his cases is given in Table II.

TABLE II.—Average Blood Pressure by Age Groups in 1,000 Overweights

Age	0-20	21-30	31-40	41-50	51-60	61-70	71 and Over
Systolic ...	111	130	136	152	162	172	163
Diastolic ...	72	84	89	98	102	103	103

DIABETES MELLITUS AND OBESITY

Diabetes is almost unknown in wasting diseases. It is increasing more rapidly as a cause of death than cancer, apoplexy, and organic heart disease. In Germany during the war its incidence as a cause of death was halved, presumably from under-nutrition; and this experience is reflected, to a less extent, in the vital statistics of the other countries who suffered restriction in their food supply. In 1,063 cases of diabetes Joslin⁹ found marked obesity as a precursor in 40 per cent. He states that diabetes, unlike the other degenerative diseases, does not increase in incidence with age except in the obese; in the lean it remains fairly constant throughout life. He regards the disease as a penalty of obesity, although there are other factors in its causation. Preble⁷ in 700 overweights found an incidence of diabetes of 75.7 per 1,000, against an estimated incidence in the general population of 10 to 20 per 1,000. Yet more striking is Joslin's analysis of 1,000 cases given in Table III. This is most

TABLE III.—Variations from Normal of the Maximum Weight at or Prior to the Onset of 1,000 Cases of Diabetes Calculated for Height, Age, and Sex.

Ages	No. of Cases	Below Standard Weight per cent.			Normal Average Zone +5 to -5	Above Standard Weight per cent.										Per-centage of each decade below normal zone
		30 to 21	20 to 11	10 to 6		6 to 10	11 to 20	21 to 30	31 to 40	41 to 50	51 to 60	61 to 70	+ 71			
1-10	16	0	3	2	5	3	2	—	—	1	—	—	—	31		
11-20	59	2	11	8	24	6	4	2	1	—	1	—	—	36		
21-30	131	—	15	13	41	15	29	9	4	—	3	—	2	21		
31-40	178	1	9	12	28	22	34	25	15	14	10	6	2	12		
41-50	291	2	8	7	31	19	59	59	40	30	18	10	8	6		
51-60	233	—	4	7	16	28	39	48	45	14	13	5	4	5		
61-70	84	—	—	2	8	10	17	23	14	7	1	1	1	2		
71-80	18	—	—	1	6	3	2	3	2	1	—	—	—	6		
1-80	1,000	5	50	52	159	106	186	169	121	67	46	22	17			

easily understood if comparison is made in turn of an underweight column with the corresponding overweight column; it will be seen that 107 cases occurred in the underweights, compared with 634 cases in the overweights.

MORTALITY IN THE OBESE

The chief source of information is the American Medico-Actuarial Mortality Investigation from life insurance figures: this dealt with a group of 744,672 cases. Table IV gives the percentage ratio of actual to expected deaths according to weight and age. The ratio is easily ascertained: from the standard mortality tables the expected number of deaths can be found, and the actual number was given by the life insurance companies. If fewer die than is expected the ratio is below 100, and if more die it is in excess of 100. The weight is known only at the age of entry—that is, at the medical examination. The lives were all accepted at standard rates, and therefore the group, except so far as weight is concerned, is a selected one.

Chart showing cause of death of 17,792 men (modified from the Medico-Actuarial Tables).

The figures in the left-hand column refer to the age at entry, those on the right to the ratio of deaths per 10,000 at risk.

TABLE IV.—Medico-Actuarial Mortality Investigation¹⁰
Graduated Percentages—Actual Deaths of Expected Deaths According to the Number of Pounds Variation from the Average Weight

Age at Entry	Variation from Average Weight in Pounds													
	-35 to -45	-25 to -30	-15 to -20	-10	-5	Average	+5	+10	+15 to +20	+25 to +30	+35 to +45	+50 to +60	+65 to +70	
20-24	135	127	115.5	107	105.5	104	102	99	97	102	104	110	125	
25-29	122	116	108.5	102	101	100	99	97.5	96.5	104	108	116	132	
30-34	112.5	108	102.5	98	97.5	97	96.5	96	97	109	118.5	131	149	
35-39	105	101	97.5	94.5	95	95	96	96.5	101	112.5	133	151	172	
40-44	99	95.5	93	91.5	93	94	96.5	97	108	115	141	157	181	
45-49	93.5	91	89.5	89.5	91.5	93.5	97.5	100	112	116.5	139	155	178	
50-53	88.5	88	87	88.5	90.5	94.5	99	102	112.5	116.5	132	150.5	172	
54-56	86	86	86	88	90.5	95.5	99.5	102.5	112	116	122	142	162	
57-59	86	86	86	88	90.5	95.5	99.5	102	111.5	114.5	117.5	134	153	
60-62	86	86	86	88	90	95	98.5	101	110.5	112.5	114	130	148	

The point of lowest mortality for age at entry 20-34 lies in the group 15 to 20 pounds above average weight, and for age at entry 35-49 in the group 5 to 10 pounds under the average weight. For age 50 and over the lowest mortality is in the underweight group.

EFFECT OF OBESITY ON CAUSE OF DEATH

The chart has been constructed from figures given in the Medico-Actuarial Mortality Investigation.¹⁰ The ratio of deaths per 10,000 at risk has been recorded for certain diseases; in each case the ratio has been ascertained for three age groups at entry (that is, at the initial medical examination), and comparison has been made of the standard weights with those 50 lb. or more overweight, and with those 25 lb. or more underweight. The overweight group shows an improvement in mortality only in pulmonary tuberculosis.

CHOLECYSTITIS, CHOLELITHIASIS, AND OBESITY

The association of these conditions with obesity is a commonplace, and I do not propose to put forward any statistical evidence.

CONCLUSIONS

1. There is an increase in the average weight of certain sections of the community.
2. Overweight after the age of 35 years increases the general mortality.
3. The cause of obesity is usually increased carbohydrate diet.
4. Treatment is simple and dietetic.
5. Obesity and hyperpiesia are associated.
6. Diabetes is probably a penalty of obesity in the majority of cases.
7. Degenerative disease of a fatal nature in the heart, arteries, kidneys, and liver are two and a quarter times

commoner in the obese than in the standard weights, and three and three-fifths times commoner than in the underweights.

8. Chronic cholecystitis and gall-stones are much more frequent in the obese.

REFERENCES

- ¹ Grafe, E., and Grunthal, E.: *Klin. Woch.*, 1929, viii, 1013.
- ² Silver, S., and Bauer, J.: *Amer. Journ. Med. Sci.*, 1931, clxxxi, 769.
- ³ Dunlop, D. M., and Lyon, R. M. Murray: *Edin. Med. Journ.*, October, 1931.
- ⁴ Nissl, C. W., En Shui Tai, and Gordon, B.: *New York State Med. Journ.*, July 15th, 1931, 187.
- ⁵ Taylor, A. E.: *Sci. Monthly*, May, 1931.
- ⁶ Lyon, D. Murray: *Clin. Journ.*, July 1st, 1931.
- ⁷ Preble, W. E.: *Boston Med. and Surg. Journ.*, April 6th, 1923, 618.
- ⁸ Terry: *Journ. Amer. Med. Assoc.*, 1923, lxxxii, 1283.
- ⁹ Joslin, E. P.: *Treatment of Diabetes Mellitus*, 1924.
- ¹⁰ Medico-Actuarial Mortality Investigation, New York, 1913, ii.

THE SYMPTOMATIC END-RESULTS OF OPERATIONS FOR CHOLECYSTITIS

A REVIEW OF 153 CASES

BY

J. COSBIE ROSS, CH.M.LIVERP., F.R.C.S.ENG.

RESIDENT SURGICAL OFFICER, LIVERPOOL ROYAL INFIRMARY

In recent years there has been a tendency to emphasize the radiographic and biochemical evidence of cholecystitis at the expense of the clinical history. That the clinical history is of vital importance, and must be used in conjunction with Graham's test if the best results are to be obtained, is expressed by R. L. Sanders in reviewing the end-results of 500 cases of cholecystectomy, when he says: "Most of the surgeon's disappointments in the end-results are related to cases in which there are cholecystographic evidence and surgical indications for operation, but not a good clinical history."

In this connexion I considered it might be of value to attempt to estimate the prospects of complete or partial cure of the symptoms, particularly in some of the pathological subdivisions of the disease. Especial attention was directed to cases where cholecystitis was present without stones.

It has been pointed out that one-fifth only of the total number of cases of cholecystitis have definite attacks of biliary colic, whereas all appear to suffer with flatulent dyspepsia. What happens to these milder symptoms after operation? Post-operative adhesions between the duodenum and the liver, said to be probably the commonest cause of disappointing results in gall-bladder surgery might perpetuate those vague dyspeptic symptoms and render the result incomplete. Judged by the