combined degeneration of the cord is to be retained it would appear logical to limit its use to lesions of the central nervous system. Unfortunately, even neurologists find it difficult to decide on the clinical features which clearly distinguish lesions of the posterior columns of the cord from lesions of the peripheral nerves. It is generally agreed that tendon reflexes, vibration sense, and positional sense may be reduced or absent and also that ataxia may be present in both conditions. There appear to be no infallible criteria which will distinguish the two lesions except histological examination of the affected structures.

Accordingly, the differential diagnosis during life has to be made on the basis of certain suggestive findings. Thus, hyperaesthesia of calf muscles strongly supports the diagnosis of peripheral neuritis, while loss of vibration sense extending up to the pelvis favours a lesion of the posterior columns. Lastly, a markedly disproportionate increase in the degree of impairment of muscle and joint sensibility and vibration sense on the one hand, as compared with the degree of loss of superficial sensations of touch and pinprick on the other, supports the view that the posterior columns are affected. The presence of an extensor plantar response (positive Babinski sign) clearly indicates that a lesion of the central nervous system is present, but it must be remembered that in pernicious anaemia the lateral columns of the cord are affected much more rarely and usually much later than are the posterior columns. It should also be noted that peripheral neuritis may be due to a specific deficiency of vitamin B₁₂ or it may result from anoxaemia of the peripheral nerves as a consequence of anaemia and cardiac weakness. In the former case it may be present when anaemia is minimal in degree and it will respond dramatically to vitamin B₁₂ therapy. In the latter case it may occur in association with any form of anaemia, but only if the degree of anaemia is sufficiently severe, and it will not respond to vitamin B₁₂ therapy, but will disappear when the haemoglobin level is raised by any method, including blood transfusion.

In assessing the incidence of subacute combined degeneration of the cord in the Edinburgh series of 250 patients, cases have not been included in which the only neurological features were of paraesthesiae and the subjective sensation of unsteadiness, since both these symptoms can be due to causes other than disease of the nervous system. Patients were classified as having involvement of the posterior columns if ataxia was a prominent feature, if tendon reflexes and positional sense were reduced or absent, and if vibration sense was lost as high up as the pelvis. They were classified as having lesions of the pyramidal tract if a spastic gait was present with increased tendon reflexes, extensor plantar response, and a greater or lesser degree of paralysis. These groups are therefore comparable to the two groups described by Cabot (1908) as the "ataxic type" and the "spastic type." Table III shows that involvement of the central nervous system was present in only 11% of Cabot's series and in 7% of the Edinburgh series. This is in contrast to the frequency of occurrence of paraesthesiae as indicated in Table II.

One of the most striking features of Table III is the difference in the degree of anaemia present in the three series when medical advice was first sought. Whereas 21% of Cabot's series had a blood count of less than one million red cells per c.mm., only 1% of the Edinburgh series had a similar degree of anaemia. Panton's series also showed a very high incidence of severely anaemic cases, the average red cell count being 1.39 million per c.mm.

Summary and Conclusions

Evidence is presented to show that the clinical picture of pernicious anaemia is very different to-day from that seen prior to the introduction of liver therapy. This difference is due to the fact that as a consequence of the improved facilities for early diagnosis and treatment which are now available the degree of anaemia in

patients seeking medical advice at the present time is much less than was the case fifty years ago. Hence it is not surprising that certain clinical features which were held to be of particular diagnostic importance in the pre-liver era—namely, jaundice, splenomegaly, acute glossitis, diarrhoea, and subacute combined degeneration of the cord—were present in less than 10% of the patients with pernicious anaemia investigated in the Blood Clinic in Edinburgh during the past ten years. Accordingly, undue emphasis on such features in textbooks of medicine and in lectures is to be deprecated, since it will hinder rather than help early diagnosis.

It is essential to tell undergraduate and postgraduate students that there are no pathognomonic symptoms or signs which will establish the diagnosis of pernicious anaemia; that tiredness, breathlessness, paraesthesiae, and chronic atrophic glossitis are presenting features which occur frequently in other types of anaemia and in particular in cases of iron-deficiency anaemia; and that diagnosis must be based on accurate blood examination, supplemented sometimes by special methods of investigation.

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CLINICAL SIGNIFICANCE OF WEIGHT TRENDS DURING PREGNANCY

BY

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Regular measurement of body weight during pregnancy is clinically valuable. For example, progressive loss of weight helps to confirm the seriousness of vomiting, while a sudden increase of weight may precede the appearance of oedema. It is usually easier to explain a sudden alteration in the rate at which an individual patient gains weight than to explain why overall gains in different patients vary so widely. A few patients gain very little weight, while others gain 50 lb. (22.7 kg.) or more. The impression that many patients who develop pre-eclampsia have high average rates of gain is well substantiated, but there is comparatively little exact numerical information.

The statistical evaluation of weight changes in pregnancy is difficult. A true and complete picture could be obtained only by weighing all pregnant women in a representative community at frequent intervals from conception until delivery, which is practically impossible. It is usual to circumvent the technical difficulties by reporting only on patients fulfilling certain arbitrary criteria. For example, Humphreys (1954) studied 1,000

"normal" mothers, the criteria of normality including such items as first antenatal visit before the 13th week of gestation and last antenatal visit within seven days of delivery; while Scott and Benjamin (1948) selected 360 women weighed regularly at four-weekly intervals from the 16th week. It is difficult to know whether selection on such lines introduces much distortion of results. Some of the difficulties can be avoided by restricting analyses to weight changes during a limited period of pregnancy. Hamlin (1952) has suggested that the 10-week period, 20-30 weeks,* is especially significant in relation to the prevention of eclampsia and pre-eclampsia by weight regulation. Data for this period can be obtained for the majority of cases, since most women come under antenatal care before mid-pregnancy, and few are delivered before the 30th week.

In centres where weight gain is controlled as part of antenatal care it is impossible to obtain a "natural" picture. During the years under review no attempt was made to restrict the amount of weight gained by patients.

Primigravidae are more liable to develop pre-eclampsia and many other complications than multigravidae; therefore studies in which various parities are taken together are not easily interpreted. The analysis which follows relates the "natural" rate of weight gain in primigravidae, especially during the period 20-30 weeks, to the clinical outcome. The findings are discussed in relation to proposals by Hamlin (1952), Dieckmann (1952), and others that severe restriction of the rate of gain helps to prevent eclampsia and pre-eclampsia.

Methods

Patients were weighed at the first antenatal visit and again, as a rule, four to six weeks later. Most were then weighed monthly until 28-30 weeks of pregnancy, and more often during the final weeks. Accurate lever balances were used, and patients wore underclothes only. The week of pregnancy within which each weight was taken was accurately calculated in cases where reliable menstrual data were available. Since many patients did not attend during the first trimester, data for the first 13 weeks of pregnancy are too sparse to have any representative value. Trends in late pregnancy are necessarily derived from patients whose pregnancies continued until term or near it.

Records Used and Methods of Analysis

The analysis was restricted to records of legitimate first pregnancies of women resident in the city of Aberdeen and delivered in the Aberdeen Maternity Hospital as booked patients during the six years 1949-54. Multiple pregnancies were excluded. Out of 5,297 records, 1,083 were rejected because either the period of gestation was uncertain or the number of weighings was not large enough to provide the required data with sufficient accuracy. Patients whose records were thus excluded had a slightly lower average age and belonged more often to a lower social class than the remainder. The 4,214 cases analysed have pre-eclampsia, prematurity, and perinatal death rates very similar to those of all hospital-booked primiparae, and it is therefore thought that selection does not invalidate the conclusions drawn from the analyses which follow.

Since the average rate of weight gain is well known to be related to the occurrence of pre-eclampsia, the records were first divided into three clinical groups as follows: (a) Cases of pre-eclampsia with albuminuria (6.5% of all cases). (b) Cases with other hypertensive complications,

mostly mild pre-eclampsia without albuminuria (25.4%). This group includes a few cases diagnosed as essential hypertension. (c) Cases without hypertensive complications ("normotensive") (68.1%). The first group corresponds to "severe pre-eclampsia" as defined by Nelson (1955), who has discussed the problems of definition for epidemiological purposes. For the sake of brevity these relatively severe cases will in future be referred to as "pre-eclampsia," without qualification. "Hypertension" connotes a diastolic blood pressure recorded as 90 mm. Hg or above on two or more occasions separated by at least a day, or showing a definite or progressive pattern if the rise occurs in labour.

The problem was to determine whether the weight trends in each clinical group differed according to the stage of pregnancy at which weighing began. This was done by drawing average curves for 11 groups of normotensive patients, in which antenatal care began at different stages.

The scatter was so small that it was thought justifiable to pool the results. The scatter in groups of patients with pre-eclampsia and other hypertensive complications was also small.

The Chart shows the average weight gain curves from the 13th to the 38th week for all cases in each of the three clinical groups. The normotensive patients had the lowest average starting weight (118 lb.; 53.5 kg.),

Average weight-gain curves in three clinical categories of primigravidae.

the highest (124 lb.; 56.2 kg.). The average rate of gain, especially in the final trimester, was greatest in pre-eclamptic and least in normotensive cases. These findings justified the separation, *ab initio*, of the three clinical groups.

For each patient, weights in the 13th, 20th, 30th, and 36th weeks were determined, by interpolation if necessary, and the average weekly rates of gain in the three intervening periods calculated. These average weekly rates of gain were the data used for most purposes. The number of cases in each period is different, because some patients had not reported early enough, or were delivered too early or were weighed too irregularly, for inclusion in all three periods.

Results

Average Weight Gains and Variations of Gain

Table I shows the average gain per week in each of the three periods and three clinical groups, together with their standard errors. In normotensive patients the average rate

TABLE I.—Average Rates of Gains in Three Periods of Pregnancy

Clinical Group		13-20 Weeks	20-30 Weeks	30-36 Weeks
Pre-eclampsia with albuminuria	No. of cases	166	274	267
	Av. gain/week (lb.) (g.)	1.00 (-0.36) 454 (16)	1.23 (-0.27) 558 (12)	1.50 (-0.68) 680 (31)
"Other hypertensive complications"	No. of cases	533	1,072	1,067
	Av. gain/week (lb.) (g.)	0.95 (-0.19) 431 (9)	1.14 (-0.13) 517 (6)	1.08 (-0.17) 490 (8)
Normotensive	No. of cases	1,362	2,868	2,833
	Av. gain/week (lb.) (g.)	0.92 (-0.11) 417 (5)	1.03 (-0.07) 467 (3)	0.87 (-0.09) 395 (4)

Standard errors are shown in parentheses. In each period the differences between means for clinical groups are statistically significant.

*To simplify notation, periods like 20th-30th or 30th-36th weeks are written as 20-30 and 30-36 weeks respectively. The average time of recording "20th week" weights is, of course, 19.5 weeks; and similarly for other times.

of gain was greater in the period 20–30 weeks than either before or after, whereas in pre-eclampsia the rate of gain tended to increase as pregnancy progressed and was greater at all stages than in the average normotensive case. Further analysis shows that in the period 20–30 weeks the proportion of patients gaining more than 1.6 lb. (726 g.) per week is nearly three times as high in those who eventually develop pre-eclampsia as in those who remain normotensive. This ratio becomes 6 to 1 in the period 30–36 weeks, owing no doubt to oedema adding to the rate of gain in pre-eclampsia. There is, nevertheless, so much overlap that the predictive value of rates of gain is relatively small. The rates of gain are significantly less variable in the period 20–30 weeks than either earlier or later. This is to be expected, since complicating factors such as vomiting and oedema which affect rates of gain are least common in the period 20–30 weeks.

The 20–30 weeks series includes 11 patients who had eclamptic fits. The distribution of weight gains in these is very similar to that for cases of pre-eclampsia.

The total weight gains for the period 13–36 weeks are estimated to be 21.9, 24.6, and 28.3 lb (9.9, 11.2, and 12.8 kg.) for normotensive, "other hypertensive," and pre-eclampsia cases respectively; for all cases together 23.1 lb. (10.5 kg.). To these may be added 2.5 lb. (1.1 kg.) for the first trimester (Chesley, 1944); while the gain from the 36th to the 40th week in normotensive cases was 3.2 lb. (1.5 kg.) and in all cases 4 lb. (1.8 kg.). Thus the gain during the whole of pregnancy is estimated to be 27.6 lb. (12.5 kg.) for normotensive cases alone and 29.6 lb. (13.4 kg.) for all cases in which pregnancy continued until term. A comparable figure for pregnancies complicated by pre-eclampsia would have limited significance, since a relatively high proportion terminate before the 40th week.

Average rates of weight gain do not vary greatly according to the social class, height, or age of patients. Women in the upper social classes and tall women gain slightly more in each period than the others, but the differences are too small to have clinical importance. Older women tend to gain slightly less than those who are young.

The rates of weight gain cannot be related to the usual non-pregnant weight for height (fatness or leanness), since the weight before pregnancy is seldom known. It was therefore decided to study the weight for height at the 20th week in relation to the rate of gain during the period 21–30 weeks. An "obesity index" was calculated for each patient by relating the weight at the 20th week to the median weight at the 20th week for all patients of the same height. The average weight gains did not vary much in relation to the "obesity index." Underweight women tended to gain at slightly lower rates than usual. Since "obesity" was assessed at the 20th week of pregnancy, a high index may, of course, mean simply that the women concerned had put on a relatively great amount of weight during the first half of pregnancy. This may be why women who were moderately overweight at the 20th week had a slightly higher than average rate of gain during the next 10 weeks. On the other hand, women who were unusually heavy at 20 weeks did not gain more than the average.

Clinical Outcome in Relation to Weight Gain

The differences of weight gain in the three main clinical groups are shown in Table I and the Chart. In the analyses which follow, the data for all cases are grouped according to weight gain and the incidence of certain complications in each weight gain category is shown. The weight data used are those for the periods 20–30 and 30–36 weeks; analyses of clinical phenomena in relation to rates of weight gain before the 20th week are of limited value, since the necessary weight data are not available for more than half the cases (Table I). The cases omitted are known to have relatively high rates of prematurity and of perinatal death; they were, for the most part, women who first attended the clinic after mid-pregnancy.

TABLE II.—*Clinical Outcome in Relation to Amount of Weight Gained in the 16-Weeks Period, 20–36 Weeks*

Weight Gained		Pre-eclampsia %	Pre-maturity*	Percentage of Prematures* with Pre-eclampsia	Perinatal Mortality per 1,000	No. of Cases
lb.	kg.					
<8	<3.6	2.6	12.1	9	36.0	273
8	3.6	3.3	8.3	9		671
12	5.4	3.1	5.5	16	11.9	1,090
16	7.3	5.7	4.4	25	27.8	1,009
20	9.1	9.2	4.9	35		651
24	10.9	13.5	5.7	47		296
28+	12.7+	26.0	8.5	66		177

* Birth weight 5½ lb. (2,500 g.) or under.

Table II shows the trends in relation to the amount of weight gained in the 16 weeks period 20–36 weeks. Amongst women who gained 8 lb. (3.6 kg.) or less—that is, at an average rate not exceeding 0.5 lb. (227 g.) a week—the incidence of pre-eclampsia was 2.6%. The incidence increased steadily with increasing rate of weight gain until, in women gaining 28 lb. (12.7 kg.) or more, equal to an average gain of at least 1.75 lb. (794 g.) a week, it was ten times as great (26%). The incidence of prematurity (birth weight 5½ lb. (2,500 g.) or less) shows an opposing trend, falling as the weight gain increases, except that it rises again when the gain becomes very large, owing to the fact that a high proportion of the prematures in the groups with the high weight gain were the result of pre-eclampsia. The high rate of prematurity (defined as low birth weight) associated with low weight gains appears, in the main, to arise from poor foetal growth resulting in the birth of relatively small babies and not from the effects of the well-recognized diseases of pregnancy. But as the rate of weight gain increases, the proportion of prematures associated with pre-eclampsia rises steeply, and in the groups with the highest weight gain the relatively high rate of prematurity is due primarily to premature termination of pregnancy either spontaneously or after induction of labour owing to pre-eclampsia.

The perinatal mortality rates shown in Table II are underestimates, since pregnancies ending much before the 36th week, which have a very high mortality rate, are not included in the data.

Table III shows the incidences of pre-eclampsia, "other hypertensive complications," prematurity, and perinatal death according to the rate of weight gain in the periods 20–30 weeks and 30–36 weeks separately. The grouping of rates of gain is arbitrary, being designed to give reasonably adequate numbers in all categories.

Pre-eclampsia and "other hypertensive complications" both show the same pattern, the highest rates being found when the rate of gain is high in the 30–36 weeks period, irrespective of the rates of gain between 20 and 30 weeks. In the period 20–30 weeks, women gaining more than 1.2 lb. (544 g.) a week had a relatively high expectation of pre-eclampsia, unless the rate of gain subsequently fell below 1 lb. (454 g.) a week in the period 30–36 weeks.

In the case of prematurity, the highest rates are found where the weight gain has been low in the period 20–30 weeks, and especially when the rate of gain has been unusually low or unusually high in the period 30–36 weeks. The rate was only 3%, less than half the average, when the gain was moderate in both periods—that is, 0.8–1.2 lb. (363–544 g.) a week from the 20th to the 30th week, and 0.6–1 lb. (272–454 g.) a week from the 30th to the 36th week.

The advantage of this moderate rate of gain is even more strikingly demonstrated in the perinatal mortality rate. The very low death rate found, 11 per 1,000 births, could be as low as it is by pure chance; however, the statistical probabilities indicate that a rate higher than 20 is unlikely. This low death rate probably reflects the fact that in this weight-gain group the foetus has the best chance of escaping the hazards of pre-eclampsia and of prematurity. In general, the trends of perinatal mortality follow those of prematurity rather than of pre-eclampsia.

TABLE III.—Incidence of Certain Complications by Rates of Weight Gain in the Periods 20–30 and 30–36 Weeks of Pregnancy

Gain per Week, 20–30 Weeks		Gains per Week, 30–36 Weeks				
lb.	g.	<0.6 lb. <272 g.	0.6 lb.— 272 g.—	1 lb.— 454 g.—	1.4 lb.+ 635 g.+	All†
<i>Pre-eclampsia (%)</i>						
<0.8	<363	2.3	2.9	5.5	17.5	4.0
0.8—	363—	2.0	2.8	6.2	16.7	5.1
1.2+	544+	3.5	3.0	6.8	18.7	9.7
All	..	2.3	2.9	6.4	18.1	6.5
<i>"Other Hypertensive Complications" (%)</i>						
<0.8	<363	17.7	20.2	26.8	36.5	21.0
0.8—	363—	21.5	19.3	26.3	39.1	23.8
1.2+	544+	21.1	25.4	30.5	36.7	30.3
All	..	19.7	21.2	28.3	37.3	25.4
<i>Prematurity (%)</i>						
<0.8	<363	10.1	8.8	8.5	7.9	10.1
0.8—	363—	6.9	3.0	5.9	9.4	6.1
1.2+	544+	7.0	3.6	3.9	6.2	5.9
All	..	8.4	4.6	5.4	7.2	7.0
<i>Perinatal Mortality, per 1,000*</i>						
<0.8	<363	39.0	20.5	(—)	(31.7)	30.4
0.8—	363—	34.7	10.9	22.9	31.3	26.0
1.2+	544+	42.3	41.4	22.7	34.1	38.0
All	..	37.7	21.5	19.3	33.2	31.3
<i>Numbers of Cases‡</i>						
<0.8	<363	436 (10.5)	341 (8.2)	164 (3.9)	63 (1.5)	1,021† (24.1)
0.8—	363—	404 (9.7)	643 (15.4)	437 (10.5)	192 (4.6)	1,692† (40.2)
1.2+	544+	142 (3.4)	362 (8.7)	485 (11.6)	498 (11.9)	1,501† (35.6)
All	..	982 (23.6)	1,346 (32.3)	1,086 (26.1)	753 (18.1)	4,214† (100.0)

* Rates in brackets based on fewer than five deaths.

† Including cases for which adequate 30–36 weeks' weight data were not available, and cases delivered from the 31st to the 36th weeks.

‡ Numbers in brackets are percentages in each "cell."

When analyses of the type shown in Table III are repeated, grouping the weight-gain categories in different ways, the same kind of pattern emerges. The same is true when patients are first subdivided according to weight for height or by "physical grade"—that is, the judgment of the obstetrician at the patient's first antenatal attendance as to her general physique and well-being. Women who were over average weight at 20 weeks had, however, higher rates of pre-eclampsia and lower rates of prematurity than underweight women in nearly all categories.

The last part of Table III shows the numbers involved and their percentage distribution. Forty per cent. of primigravidae were in the moderate weight-gain group for the period 20–30 weeks—that is, gained between 8 and 12 lb. (3.6 and 5.4 kg.). Nearly one-quarter gained less than 8 lb. (3.6 kg.). Only 15% of all cases were in the most favourable group, that which gained 8–12 lb. (3.6–5.4 kg.) from the 20th to the 30th week, and 6–10 lb. (2.7–4.5 kg.) from the 30th to the 36th week.

Discussion

The methods of analysis described were devised primarily to elucidate the clinical significance of various weight-gain patterns, the physiological basis of which will not be discussed. We have shown elsewhere (Thomson and Billewicz, 1955) that the rate of weight gain during pregnancy is positively correlated with the calorie value of the maternal diet.

The weight gains found are consistent with those previously reported. Our estimated average total gain in normal pregnancy, 27.6 lb. (12.5 kg.), and average rate of gain in the period 30–36 weeks, 0.87 lb. (395 g.) a week, are reasonably close to estimates for the total gain and for rate of gain during the last trimester made by Chesley (1944) and by Humphreys (1954).

The relationship between weight gain and incidence of pre-eclampsia follows expectation. As Chesley and others have already noted, the incidence of pre-eclampsia rises as the rate of weight gain increases, but measurement of the

rate of gain over a period of time such as 20–30 weeks has little predictive value in the individual case. It has often been suggested that the occurrence of a sudden acceleration in the rate of gain is of more clinical significance than a high average rate of gain. Our records show that this "sign" of incipient oedema or hypertension, while not without value, is not very reliable as a means of prediction.

Primigravidae who develop mild pre-eclampsia have a higher average "starting weight" (observed at the end of the first trimester) than those who develop severe pre-eclampsia or those who remained normotensive. This cannot be wholly explained in terms of age and height differences, and its significance is not clear.

The primigravida aged 30 or over is slightly taller and heavier and has a very slightly lower average rate of weight gain than the younger primigravida. As Nelson (1955) has shown, she also has an increased tendency to develop mild pre-eclampsia, but little or no special liability to severe pre-eclampsia; though when severe pre-eclampsia does supervene the foetal mortality is relatively high. But our more extensive data do not confirm Nelson's suggestion that the tendency to high rates of weight gain with severe pre-eclampsia in primigravidae occurs only under the age of 30. We have no evidence to support the claim of Tompkins, Wiehl, and Mitchell (1955) that women with abnormally low weight gains also have a raised incidence of pre-eclampsia.

It is reasonable to expect some correlation between rates of weight gain and birth weights, since the weight of the foetus accounts for part of the increase of maternal weight. This has been observed, for example, by Kerr (1943) and Beilly and Kurland (1945), and the present data confirm it. In our data, median birth weights rise steadily from 6.7 to 7.5 lb. (3 to 3.4 kg.) as the 20–30 week rates of gain increase from under 0.6 lb. (272 g.) to over 1.8 lb. (816 g.) a week. The high incidence of prematurity (birth weight 5½ lb. (2,500 g.) or less) associated with low maternal weight gains seems to be due more to depression of the foetal growth rate than to curtailment of the length of gestation. In cases of severe pre-eclampsia, usually associated with high rates of weight gain, depression of foetal growth as well as curtailment of pregnancy is usual (Baird, Thomson and Billewicz, 1957); both facts account for the excess of very small prematures in pregnancies where the 20–30 week weight gain was very large.

Where there is no policy of weight restriction during pregnancy, moderate rates of gain are clearly associated with the most favourable clinical experience. Thus, patients who gained 8–12 lb. (3.6–5.4 kg.) from the 20th to the 30th week, and at a slightly lower rate after the 30th week, had pre-eclampsia, prematurity, and perinatal mortality rates only about half the average. Higher rates of gain were associated especially with pre-eclampsia and lower rates especially with prematurity.

It does not follow logically that, if excessively high or low gains are avoided by dietary regulation and other measures, the clinical outcome will be as favourable as in those women who gain the "correct" amounts of weight when left to their own devices. But there is some evidence that restriction of excessive gains is helpful in preventing eclampsia; the evidence that such restriction prevents pre-eclampsia is less satisfactory, perhaps because pre-eclampsia is less easy to define.

Of recent reports along these lines, those by Hamlin (1952, 1953) are the most spectacular. He claimed the abolition of eclampsia (no cases in 6,600 booked patients) and a considerable reduction of severe pre-eclampsia in a large Australian hospital, thanks to an intensive programme of antenatal care, including measures aimed at limiting the amount of weight gained and the admission to hospital of cases of mild pre-eclampsia. Hamlin says that most primiparae who are allowed to gain more than 8 lb. (3.6 kg.) in the 20–30-weeks period will progress inexorably towards pre-eclampsia and eclampsia, but gives no evidence. Hughes (1951), reporting on the same Australian campaign,

merely observes that a gain exceeding 1 lb. (454 g.) a week after the fifth month of pregnancy points to the need for close observation of the patient. Of Aberdeen primiparae who remained normotensive throughout, 73% gained more than 8 lb. (3.6 kg.) in the period 20–30 weeks, compared with 85% of those who developed fairly severe pre-eclampsia. Hamlin's statement is therefore certainly not valid in Aberdeen.

Hamlin (1953) and also Nixon (1955) have republished a "normal" curve of weight during pregnancy derived from Dieckmann, Smither, and Rynkiewicz (1952); this shows a gain of only 7.7 lb. (3.5 kg.) during the period 20–30 weeks. It is not clear how the patients from whom the curve was derived were selected, nor whether they were required to restrict their weight gains as part of antenatal care. In his monograph on the toxæmia of pregnancy Dieckmann (1952) recommends limiting the weight gain to 200 g. a week during the last 28 weeks of pregnancy, which implies a 20–30 weeks' gain of less than 5 lb. (2.3 kg.). He acknowledges that such targets may be difficult to attain even under ideal conditions: "The fact that we were only able to restrict one-third of the patients to what we consider the maximum gain during an intense nutrition study indicates how difficult it is to restrain calorie intake in these patients."

There is no doubt that, even without a policy of weight regulation, good out-patient antenatal care, backed by adequate hospital facilities, can do much to prevent eclampsia and the more serious consequences of pre-eclampsia. Between 1938–42 and 1954–5 the incidence of eclampsia in primigravidae booked in Aberdeen Maternity Hospital fell from 8 to 2 per 1,000,* and the stillbirth rate in cases of eclampsia and pre-eclampsia from 151 to 25 per 1,000 births. Nelson (1955) has discussed the reasons. We do not know whether progress would have been accelerated if weight regulation had been practised as part of routine antenatal care. The problem now is whether results can be further improved, and especially whether the need for antenatal beds required for the treatment of pre-eclampsia can be reduced by weight regulation.† These questions can be answered only by means of an *ad hoc* trial under controlled conditions.

Preliminary trials have shown that full scientific control is practically impossible to achieve because the measures needed for regulating weight changes inevitably mean that antenatal care is intensified in other respects; again, within one centre, the ideas promulgated at an experimental antenatal clinic soon begin to "infect" staff at the routine clinics from which control cases are drawn. These facts make the value of a policy of weight regulation difficult to assess scientifically. It will be some time before the data of our current trial can be quoted. It seems more easy, by careful dietary supervision, to restrict a rate of gain which has been excessive than to augment a rate of gain which seems unduly low.

The clinical hazards associated with very low "natural" rates of weight gain do not seem to have been systematically studied in the past, though the increased risk of prematurity (especially when the mother is underweight at the beginning of pregnancy) has been noted by Tompkins *et al.* (1955). Women who fail to gain an adequate amount of weight present a problem at least as important as those who gain excessively.

The rule of moderation is probably as sound when applied to weight gains during pregnancy as to many other aspects of existence. As a realistic target, we would suggest gains within the range of $\frac{1}{2}$ to $1\frac{1}{2}$ lb. (340 to 567 g.) a

week as being consistent with excellent clinical results. Roughly half of all primigravidae will "naturally" gain weight within this range from the 20th to the 30th week of pregnancy, and it may be that the proportion could be increased by measures practicable at out-patient clinics. The mean rate of gain, 1 lb. (454 g.) a week, is easily remembered, and the patients' progress easily assessed from one clinic visit to the next. There is no real justification for the lower rates that have been widely advocated. Weight restriction is not easy, and the mother who fails to comply with a rigorous schedule may become unnecessarily burdened with guilt; while the one who succeeds, possibly with considerable stress, may be running an increased risk of prematurity.

Summary

An analysis of the weight gains of primigravidae, not subjected to weight regulation, confirmed that the average rate of gain is higher in pre-eclampsia than in normal pregnancy, and that the incidence of pre-eclampsia rises as the rate of weight gain increases. These facts are of little value for predicting pre-eclampsia in the individual case.

The incidence of prematurity (birth weight $5\frac{1}{2}$ lb. (2,500 g.) or less) is highest when weight gains are consistently low, falls as the rate of gain increases, and then rises again with high rates of gain. Pre-eclampsia is an important cause of prematurity in the high but not in the low weight-gain groups.

The most favourable outcome of pregnancy—in terms of pre-eclampsia, prematurity, and perinatal death—is associated with a moderate rate of weight gain, at least throughout the second half of pregnancy. A gain of about 1 lb. (454 g.) a week is suggested as a sound and realistic average to aim at. The more rigorous restriction of weight gain which has been advocated is not justified on present evidence and may be harmful.

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"Infections in Laboratory Animals" is the subject of the fourth volume (1956) of *Collected Papers* published by the Laboratory Animals Bureau. It records the proceedings of a symposium held at the Royal Veterinary College, London, last April, and consists of seven papers on the following subjects: "Epidemiology and Laboratory Mice" (Mr. A. A. Tuffery); "Control of Ectromelia in Mouse Colonies" (Dr. M. H. Salaman); "Control of Infection in Laboratory Cats and Dogs" (Professor W. L. Weipers); "Infections in Laboratory Monkeys" (Dr. A. P. Goffe); "Control of Disease in Rabbits" (Dr. J. Stuart Paterson); "Control of Disease in Laboratory Poultry" (Dr. R. F. Gordon); and "Salmonella in Laboratory Animals" (Dr. Joan Taylor and Mr. J. D. Atkinson). In addition there are the opening remarks and summary of the meeting by the chairman, Professor J. W. Howie. The volume (pp. 68) is obtainable from the Laboratory Animals Bureau, M.R.C. Laboratories, Holly Hill, Hampstead, London, N.W.3, price 7s. 6d.

*The current average incidence of eclampsia in booked cases of all parities, 0.8 per 1,000, is comparable with rates reported from a number of major American hospitals in 1947–9 (Dieckmann, 1952). In the latter, presumably, weight regulation has been practised for many years.

†About 16% of all Aberdeen booked primigravidae are admitted to the antenatal wards for treatment of pre-eclampsia and allied conditions, which account for over 40% of the total antenatal bed-days due to primigravid admissions of all kinds, and absorb an average of about 4 antenatal beds per 1,000 booked primigravidae per annum. The equivalent figures for booked patients of all parities are 12% admitted, 26% of all bed-days, and 3 beds per 1,000 patients per annum.