patients. Preliminary results indicate that the initial high levels (Whitaker, 1960) fall coincident with satisfactory clinical response. Serum phosphohexose-isomerase has also been estimated serially (Boesen, unpublished) in many of these patients, and the level, although fluctuant, appears to correlate with the clinical course.

Two patients had dermatomyositis: one had been treated with prednisone with some improvement. The prednisone was discontinued before she underwent hypophysectomy for progression of her disseminated metastatic disease. The dermatomyositis improved after hypophysectomy while the patient was on maintenance cortisone. However, her disseminated metastatic disease continued to progress and she died of bronchopneumonia after hypophysectomy.

Conclusion

This larger series and recent series of surgical hypophysectomy of other workers (Jessiman *et al.*, 1959; Pearson and Ray, 1960; Atkins *et al.*, 1960) have confirmed our previous impressions. Hypophysectomy is no longer an experimental procedure. Its place has been established as a method of palliating advanced carcinoma of the breast. The risks of the operation are reduced with greater experience, although it can never be a routine procedure. The major problem remains the selection of patients for operation, for at present only about half the cases respond.

Summary

Pituitary ablation has been performed on 111 unselected patients with disseminated carcinoma of the breast over the past five years—104 by surgical hypophysectomy and 7 by stereotaxic procedure. The assessment and management of the cases are discussed. Regression or arrest has occurred in 42% of the patients assessed and the average expectation of life was increased by 12 months. A favourable response was more likely in patients who had responded well to previous endocrine therapy, and those in whom there was a long interval between the primary disease and the appearance of metastases. It is also possibly indicated by the menopausal status. Complications and metabolic effects of the operation are reviewed.

We are indebted to the British Empire Cancer Campaign for a whole-time grant to one of us (E. B.) and to the Royal Free Hospital endowment fund for financial assistance. We thank Dr. J. N. Willis and his registrars for their anaesthetics, Sisters N. Hitchcock and J. Daly for nursing care; Dr. Marion Gore, Dr. K. J. Gurling, Dr. D. C. Williams, and Mr. H. Williams for scientific collaboration; Miss I. Cade, Miss R. Robinson, and Mr. B. Whitaker for surgical assistance; Dr. I. Somerville (Chelsea Hospital for Women) for the gonadotrophin assays; and Mr. A. M. H. Bennett for allowing us to include cases in which he performed stereotaxic pituitary ablation.

REFERENCES

Atkins, H. J. B., Falconer, M. A., Hayward, J. L., and MacLean, K. S. (1957). *Lancet*, **1**, 489.
—— —— Hayward, J. L., MacLean, K. S., Schurr, P. H., and Armitage, P. (1960). Ibid., **1**, 1148.
Baron, D. N., Gurling, K. J., and Radley Smith, E. J. (1958). *Brit. J. Surg.*, **45**, 593.
—— (1959). *W. Afr. med. J.*, **8**, 125.
—— Gore, M. B. R., and Williams, D. C. (1960). *Acta Endocr. (Kbh.)*, **35**, Supp. 51, p. 981.
—— and Gurling, K. J. (1960). In *Recent Advances in Clinical Pathology*, edited by S. C. Dyke, p. 140. Churchill, London.
Bennett, A. M. H. (1960). *Brit. J. Radiol.*, **33**, 343.
Bulbrook, R. D., Greenwood, F. C., and Hayward, J. L. (1960). *Lancet*, **1**, 1154.
Franks, L. M. (1960). *Cancer*, **13**, 490.
Gore, M. B. R., and Baron, D. N. (1960). *J. Endocr.*, **21**, 303.
Gurling, K. J., and Baron, D. N. (1960). *Acta Un. int. Cancr.*, **16**, 181.
—— —— and Radley Smith, E. J. (1959). *J. clin. Endocr.*, **19**, 717.
Hadfield, J. (1959). *Ann. roy. Coll. Surg. Engl.*, **25**, 1.
Hershey, F. B. (1959). *Surg. Forum*, **9**, 614.
Hollander, V. P., Jonas, H., and Smith, D. E. (1958). *Cancer*, **11**, 803.
Huggins, C., Briziarelli, G., and Sutton, H., jun. (1959). *J. exp. Med.*, **109**, 25.
Jessiman, A. G., Matson, D. D., and Moore, F. D. (1959). *New Engl. J. Med.*, **261**, 1199.
Loraine, J. A. (1958). *Endocrine Aspects of Breast Cancer*, edited by A. R. Currie, p. 158. Livingstone, Edinburgh.
Luft, R., and Olivecrona, H. (1955). *Cancer*, **8**, 261.
—— —— Ikkos, D., Nilsson, L. B., and Mossberg, H. (1958). *Endocrine Aspects of Breast Cancer*, edited by A. R. Currie, p. 31. Livingstone, Edinburgh.
Nabarro, J. D. N. (1960). *Lancet*, **1**, 1293.
Pearson, O. H., and Ray, B. S. (1960). *Amer. J. Surg.*, **99**, 544.
Radley Smith, E. J., Gurling, K. J., and Baron, D. N. (1958). *Med. Press*, **240**, 657.
—— —— —— (1959). *Brit. J. Urol.*, **31**, 181.
Schon, M. (1958). *Cancer*, **11**, 95.
Strong, J. A., Bruce, J., and Falconer, C. W. A. (1959). *Lancet*, **2**, 1055.
Talalay, P., and Williams-Ashman, H. G. (1958). *Proc. nat. Acad. Sci. (Wash.)*, **44**, 19.
Whitaker, B. L. (1960). *Brit. J. Cancer*, **14**, 471.

DIETARY AND BIOCHEMICAL CONTROL OF PHENYLKETONURIA

BY

F. S. W. BRIMBLECOMBE, M.D., M.R.C.P., D.C.H.

J. D. BLAINEY, M.D., M.R.C.P.

MARGARET E. R. STONEMAN, M.D., D.C.H.

AND

B. S. B. WOOD, D.M., M.R.C.P., D.C.H.

Royal Devon and Exeter Hospital; Department of Experimental Pathology, University of Birmingham; and the Children's Hospital, Birmingham

The screening of young infants for the presence of phenylketonuria, if carried out comprehensively, may be expected to reveal about 40 new cases annually in the United Kingdom alone. Evidence is accumulating that dietary restriction of phenylalanine is effective in preventing subsequent mental deficiency, provided treatment is started in the early weeks of life (Horner and Streamer, 1956; Woolf *et al.*, 1958; Brimblecombe *et al.*, 1959; La Du, 1959; Knox, 1960). It is the purpose of this paper to discuss some practical problems in the management of these patients from the dietary aspect and from that of biochemical control, and also to report the difficulties encountered from excessive restriction of phenylalanine in two children diagnosed in early infancy.

Diagnosis

The introduction of a paper test (Baird, 1958) for the detection of phenylpyruvic acid in the urine has simplified the organization of mass screening of small infants by local health authorities. The test can be made either on a freshly wet napkin from which the urine can be squeezed out or on an ordinary specimen of urine. The paper test has the great advantage of

simplicity and of excluding the majority of false-positive reactions produced by routine testing with ferric chloride (Gibbs and Woolf, 1959). The urines of 18,981 of the 19,353 infants born in the City of Birmingham in 12 months in 1959–60 were tested with "phenistix" (Boyd, 1961); one infant and one older child were diagnosed as suffering from phenylketonuria. During the same period four suspected positive urines were sent for paper chromatography; none of these was a true positive and no satisfactory explanation of the weak colour change with the paper strip was discovered. It was not due to the presence of *p*-hydroxyphenylpyruvic acid as suggested by Gibbs and Woolf in false-positive reactions found by routine testing of urine with ferric chloride solution. In Devonshire during a similar 12-month period in 1959–60 6,571 routine paper tests on the urines of infants were carried out (98.9% of the infants at risk); one true-positive case was detected and only one false-positive test was observed.

Present recommendations on the technique of testing by different health authorities vary slightly; either two routine tests are carried out on each infant, one at 2 weeks and the second at 6 weeks of age, or, alternatively, a single test is made between the ages of 4 and 6 weeks. It is still impossible to assess the potential harm to an infant of an unchecked rise in the level of plasma phenylalanine between the ages of 2 and 6 weeks. If no permanent damage is ultimately found to result from this delay, the advantage to the local health authority of being able to limit the screening examination to a single urine test at 4 to 5 weeks is considerable. The danger of missing the occasional case in which phenylpyruvic acid is not present in adequate amounts in the urine to give a positive test until the fifth or sixth week of life has also to be considered, but this appears to be exceptional. Prolonged follow-up of infants in whom treatment has been started at different ages—that is, because of delay in diagnosis, etc.—must therefore be carried out before final conclusions can be reached regarding the optimal time after birth of routine testing for the disorder.

Dietary Treatment

Restriction of the phenylalanine intake must remain the basis of treatment until replacement therapy with the liver enzyme responsible for the conversion of phenylalanine to tyrosine becomes a practical possibility. Methods of constructing a diet which restricts the phenylalanine intake adequately have been limited by insufficient knowledge of the phenylalanine content of many foods. Thus diets have tended to be both monotonous and unpalatable owing to the disagreeable taste of the hydrolysate which provides the greater part of the protein intake.

The accompanying Appendix giving the phenylalanine content of many food substances, although still incomplete, does allow more varied diets to be selected. The estimated phenylalanine content in these tables may be subject to 5–10% error in some food substances. In the low-protein foods, however, the total phenylalanine content is small and the error involved is unimportant. Most animal and vegetable proteins contain between 4% and 5% of phenylalanine, so that measurement of the nitrogen content of many foods allows a reasonable estimate of the phenylalanine content to be made. Wherever possible the phenylalanine contents of foods included in the Appendix are the results of direct analyses (Block and Weiss, 1956; Hughes, 1958; Commonwealth Agricultural Bureaux, 1956). Where such analyses were not available, the phenylalanine content has been calculated from the protein content of the food (McCance and Widdowson, 1946). The tables in the Appendix have been constructed to show the amount of food containing a given quantity of phenylalanine, since in practice this is the most valuable information in constructing diets.

Construction of Diet

1. Phenylalanine.—The degree of restriction of dietary phenylalanine required to achieve and maintain a normal level of plasma phenylalanine varies in different patients, depending mainly upon the rate of growth and the age. Most patients require limitation of intake to between 10 and 30 mg./kg./day, and in practice a diet containing 25 mg./kg./day is started, and is varied slightly according to the resulting changes of plasma phenylalanine concentration. The calculated quantity of phenylalanine is provided in the form of natural foods, the exact amount and type of protein being selected from the food tables (see Appendix). Thus an infant weighing 10 kg. on 25 mg./kg./day intake will require 250 mg. of phenylalanine, which can be selected from any of the foods listed. In young infants, milk or double cream will be chosen, but a more varied diet becomes important for older children. As the total quantity of natural protein which can be given is small and quite inadequate for nutritional needs, a supplement of phenylalanine-low casein hydrolysate has to be given to provide adequate protein. The amounts of fat and carbohydrate included in these natural foodstuffs also are totally inadequate and have to be supplemented.

2. Calorie Requirements.—The total calorie requirement depends upon the weight and age of the child (Table I). The calorie intakes suggested are 12% higher than those usually recommended for a normal diet, the additional quantity being necessary on account of the synthetic nature of the protein (Rose *et al.*, 1954; Blainey and Gulliford, 1956).

TABLE I.—*Daily Food Requirements*

Age in Years	Calories per kg.	Protein* (g./kg.)	Fat† (g./kg.)	Carbohydrate‡ (g./kg.)
0–1	125	4·6	4·7	16·7
1–3	115	4·2	4·3	15·3
4–6	105	3·8	4·0	14·0
7–9	90	3·3	3·4	12·0
10–12	80	2·9	3·0	10·7
13–15	70	2·6	2·6	9·3
15–18	60	2·2	2·3	8·0

* 15% calorie intake. † 35% calorie intake. ‡ 50% calorie intake.

3. Requirements of Phenylalanine-low Protein Hydrolysate.—The main protein requirements are next calculated. These should amount to 15% of the total calorie intake (approximately 4 calories/g. protein) and is supplied as phenylalanine-low casein hydrolysate, the commercial preparations of which also include some carbohydrate, fat, vitamins, and mineral salts. For young infants up to 6 months, "minafen," a high-calorie phenylalanine-low artificial milk powder, can be prepared for use by the simple addition of an appropriate volume of water, and, apart from the essential natural protein requirements described above, together with vitamins A, C, and D, no further supplement is necessary, as this is a complete balanced food

preparation. In older children more variety in the diet is highly desirable and "cymogran" may be used to supplement the nitrogen requirements other than those supplied by natural protein. An equivalent of 40 g. of protein is supplied by every 100 g. of the preparation. Table II gives the actual daily requirements of cymogran per kg. body weight for each age, for two levels of phenylalanine intake.

TABLE II.—*Daily Requirements of Cymogran, Fat, and Carbohydrate in Diet*

Age	Calories per kg.	Cymogran (g./kg.)	Fat (g./kg.)	Carbohydrate (g./kg.)
*Phenylalanine 25 mg./kg. Body Weight**				
1–3	115	14·0	3·0	10·0
4–6	105	11·5	2·5	9·5
7–9	90	9·5	2·3	8·2
10–12	80	8·5	2·0	7·3
13–15	70	7·2	1·8	6·4
15–17	60	5·9	1·6	5·6
Adult	45	4·0	1·3	4·4
Phenylalanine 10 mg./kg. Body Weight†				
1–3	115	14·0	3·0	9·0
4–6	105	12·5	2·5	8·5
7–9	90	10·7	2·3	7·0
10–12	80	9·5	2·0	6·3
13–15	70	8·0	1·8	5·1
15–17	60	7·0	1·6	4·5
Adult	45	5·0	1·3	3·5

* This diet allows 0·5 g. natural protein/kg./day to supply phenylalanine needs.
† This diet allows 0·2 g. natural protein/kg./day to supply phenylalanine needs.

4. Calculation of Additional Calories and Fat.—To achieve a balanced diet, 50% of the calorie requirements should be supplied as carbohydrate, 35% as fat, and 15% as protein (the relative proportions of cymogran are 38%, 20%, and 40% respectively). Thus after the protein needs and *some* of the calorie requirements in the older child have been supplied, *further* carbohydrate and fat are essential for normal weight gain and nutrition and also to maintain the effectiveness of the phenylalanine restriction, as an inadequate supply of calories, especially in carbohydrate, leads to negative nitrogen balance and elevation of the blood levels of phenylalanine (Blainey and Gulliford, 1956). Gluten-free wheat starch, sugar, vegetable fat, and many of the low-protein foods may be used, and recipes have been developed for cakes, biscuits, sweets, vegetables, and fruit dishes to make the diet interesting. Table II gives the actual requirements for a given age and body weight of the carbohydrate and fat which must be added to the cymogran supplement to ensure adequate calories and a balanced diet. These supplements do not include the fat and carbohydrate in the natural protein allowance, which will normally be insignificant. If the commercial preparations of low-phenylalanine protein hydrolysate are used—for example, cymogran and minafen—no additional minerals or vitamins need be added.

This description of the dietary requirements in phenylketonuria contains only basic essentials. A more detailed account of the individual amino-acid content, total protein, fat, carbohydrate, and calorie contents of a wide variety of foods, together with recipes for the preparation of special dishes and foods for low-phenylalanine diets, was presented by one of us (Stoneman, 1959) as a thesis for the M.D. degree of Manchester University. These diets have been used successfully by us in the management at home of a number of infants and children with phenylketonuria since 1957, the only serious difficulty arising with the disagreeable taste of the hydrolysate and with excessive phenylalanine restriction in two infants. In these, a fall of plasma phenylalanine to subnormal level resulted from a too-severe restriction of intake, the babies became listless and ill, with loss of weight and, in one case, with the development of a severe eczematous rash which cleared rapidly on the addition of more phenylalanine to the diet. It appears that infants under 12 months may require a higher basic intake of phenylalanine than older children, possibly because of the rapid rate of growth of muscle at this age.

Biochemical Control of the Diet

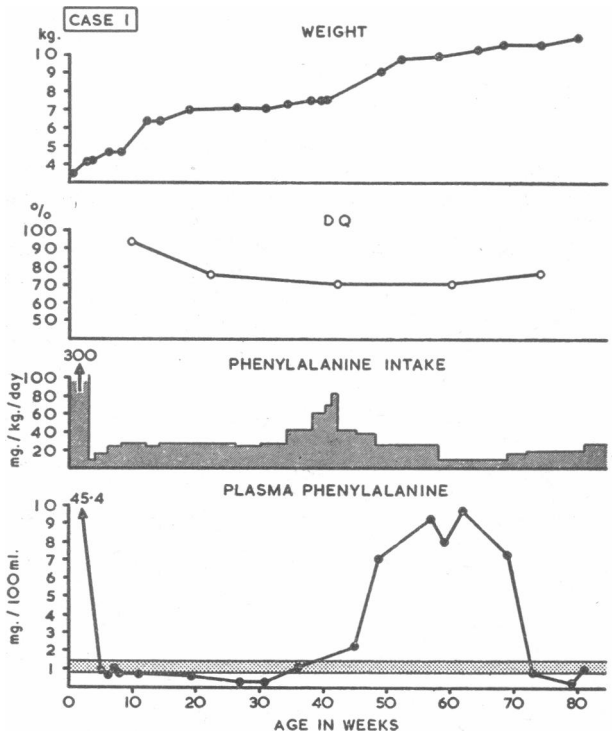
The optimum level of phenylalanine in the blood to obtain normal mental development has not been defined, but it would seem reasonable to maintain the serum chemistry as near normal as possible. The only satisfactory index of strict biochemical control has been found to be the estimation at regular intervals of the plasma phenylalanine concentration. Neither the qualitative nor the quantitative estimation of urinary phenylpyruvic acid with ferric chloride solution or paper strips provides adequate control, since the urine becomes free from phenylpyruvic acid at a plasma level of phenylalanine of 8–12 mg./100 ml. (Armstrong and Low, 1957; Blainey and Leyton, 1961) and while abnormal indole compounds are still present in the urine in large amounts. It has not proved possible to use the excretion of indole compounds as the index of biochemical control, partly because the estimation of the latter is laborious as a routine measure, but more on account of the D-tryptophan content of the commercial hydrolysates, referred to above, which is largely excreted as indole lactic acid and indole acetic acid.

Biochemical control of the patients in Exeter and Birmingham has been maintained by repeated estimations of plasma phenylalanine using a specific and accurate microbiological method of assay (Henderson and Snell, 1948). Other methods (Table III) that have been recommended are enzymic (Hsai *et al.*, 1958; La Du and Michael, 1960), chemical (Armstrong and Tyler, 1955), and paper chromatography (Woolf *et al.*, 1958). The first is accurate and simple, provided that a stable and reproducible phenylalanine decarboxylase can be prepared; but this has proved difficult and somewhat unpredictable in practice. The provision of a stable and reliable enzyme would facilitate the control of these cases very greatly. The chemical method is simple, but unfortunately not specific, as other substances—for example, tryptophan—are estimated with the phenylalanine, and the normal values are higher so that it is difficult to detect slight departures from normality. Paper chromatography is reliable in skilled hands, but is only semi-quantitative, and it is difficult to detect marked reduction in serum phenylalanine below normal values.

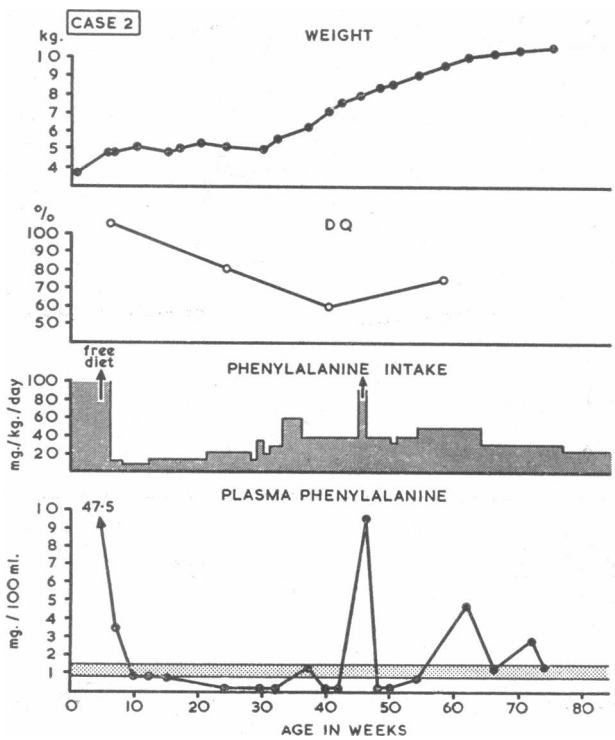
TABLE III.—*Normal Value of Plasma Phenylalanine (mg./100 ml.)*

Method	Author	No. Tested	Mean (S.E.)	Range
Kapeller–Adler ..	Armstrong and Tyler (1955)	—	—	3·0 to 5·0
Enzymatic	Hsai *et al.* (1958)	19	0·91 (±0·31)	0·39 to 1·49
,, ...	La Du and Michael (1960)	30	1·55	0·84 to 2·64
Microbiological assay	Blainey	65	1·06 (±0·47)	0·65 to 1·85

Urine phenylalanine may also be estimated in the same way and may be a useful guide to treatment provided that it is possible to collect timed urine samples. In the untreated child with phenylketonuria the presence of phenyllactic acid in the urine gives a falsely high value for phenylalanine, since the lactobacilli used in the biological assay are able to metabolize some phenyllactic acid. The use of paper chromatography of the urine has also been advocated as a method of control of the diet, but it is necessary to have either timed samples or a constant fluid intake at the time at which urine collections are made. At plasma levels of phenylalanine of 4–7 mg./100 ml., phenylalanine can be detected in the urine only in concentrated samples, on paper, and the method is therefore less precise than any technique that employs measurement of plasma levels. It has been our practice to make weekly estimations of the plasma phenylalanine when the diet is first started and thereafter to estimate levels only at monthly intervals unless the child's gain in weight and progress were not satisfactory.



CASE 1



CASE 2

Details of clinical and biochemical progress of Cases 1 and 2. (The thick stippled lines represent the limits of normal plasma phenylalanine values, using the method of microbiological assay.)

Mental Development

It is not the purpose of this paper to review critically all the reported cases of phenylketonuria treated from early infancy. It can be said, however, that of all the 10 cases that we have been able to discover in which treatment has been begun by the age of 6 weeks, and in which the dietary control of phenylalanine has been satisfactory, there is no example of mental deficiency.

We wish to record briefly the cases of two further infants in whom treatment was started at the age of 3 and 6 weeks respectively, and in whom difficulties arose from excessive restriction of phenylalanine during the first year of life (see Fig.).

Case 1.—A male child born on July 4, 1959 (no consanguinity between parents), was found to have phenylketonuria by routine examination of the urine with phenistix at the age of 17 days. The diagnosis was confirmed by urinary chromatography and by the finding of a plasma phenylalanine level of 45.4 mg./100 ml. on the 18th day of life. Dietary treatment was started on the 21st day and has been continued without intermission up to the time of writing. Between the ages of 6 and 9 months the infant's plasma phenylalanine fell to a level of 0.52 mg./100 ml. During this period he became anorexic and lethargic, vomited, and developed an eczematous rash. There was loss of weight and the development quotient fell. The deficiency of phenylalanine was at first overcorrected and the plasma level rose to 11.8 mg./100 ml. during the subsequent three months. A satisfactory balance was finally achieved, and by the age of 18 months the weight had risen to 24 lb. (10.9 kg.) and the infant was walking and beginning to talk. The development quotient (Griffith's scale) is now 82. This child's untreated phenylketonuric brother has an I.Q. of 18%, while those of his parents and two normal siblings range from 65 to 90%.

Case 2.—This patient, a male born on June 4, 1959, is the second child of healthy parents. The first child, also a male, was found to be suffering from phenylketonuria at the age of 18 months. The patient's urine was tested at 2 weeks of age and found to be negative to ferric chloride, but at 6 weeks was strongly positive. He was put on the diet immediately, the phenylalanine level in the blood before treatment being 47.5 mg./100 ml. At first he was maintained on a diet containing 70 mg. (14 mg./kg.) of phenylalanine a day, and this kept his blood level at between 0.3 and 0.7 mg./100 ml. From 2½ months of age his gain in weight fell off and he remained stationary at approximately 11 lb. (5 kg.) until 6½ months of age, despite an increase in his phenylalanine ration to 130 mg. (26 mg./kg.) a day at 4 months and a satisfactory calorie and vitamin intake. It was not until his phenylalanine was increased to 200 mg. (40 mg./kg.) a day that he began to put on weight at the normal rate and his plasma level rose to 1.42 mg./100 ml. At the time of writing he was well maintained on a diet

of 300 mg. (30 mg./kg.) of phenylalanine a day, had a Griffith quotient of 77% at the age of just over a year, and weighed 21 lb. (9.5 kg.).

Observations on these two patients and others under our care thus show that in the first year of life, while growth is rapid, the basic requirements of phenylalanine are relatively higher in mg./kg. body weight than at older ages. Excessive restriction of phenylalanine intake at this stage may lead to subnormal levels of plasma phenylalanine, with loss of weight, vomiting, listlessness, and a generalized eczematous rash. Mental development is also retarded during these episodes.

With increasing age the growth rate decreases and the same patient requires less phenylalanine for growth requirements. Unless a corresponding decrease is made in the dietary phenylalanine, the plasma levels again rise to excessive levels, with an adverse effect upon mental development. The actual requirements, therefore, vary from patient to patient and at different ages in the same patient, and can be determined only by estimations of the plasma phenylalanine.

Where diagnosis is delayed beyond the age of 6 months the response to treatment is usually far less encouraging. One child originally diagnosed at the age of 9 months has, despite three years' intensive treatment, failed to increase his rate of development from the time of diagnosis, the development quotient (Griffith scale) remaining at 29%. Occasionally an older child, particularly those less severely affected, appears to respond very well to treatment (Woolf *et al.*, 1958), and it would certainly seem justifiable to give all phenylketonuric children diagnosed by the age of 3 years the opportunity of a trial on dietary treatment. It is the experience of both parents and those concerned with treatment that these children become less restless and fidgety and are more easily managed in the home while on treatment than while on normal diet, although formal developmental and intelligence tests may show little evidence of improvement.

There is thus continuing evidence in favour of the institution of comprehensive routine screening of all infants before the age of 6 weeks for the presence of phenylketonuria. The paper test is cheap (about a penny a test), and it has been shown (Boyd, 1961) that the organization of the test can be well fitted into the framework of the preventive health services as organized by the local health authorities.

Summary

The practical application of mass methods of detection of infants with phenylketonuria by public health authorities and increasing evidence of the value of dietary restriction have necessitated further simplification of low-phenylalanine diets.

Factors in the construction of these diets and the importance of biochemical control are discussed and the dangers of excessive phenylalanine restriction emphasized.

ADDENDUM.—Since this paper was written several cases of skin rash, weight loss, and a failure to thrive have occurred in small infants on "minafen," similar to the cases reported due to excessive phenylalanine restriction. Preliminary investigations suggest that in some cases this may be due to vitamin deficiency. It is therefore recommended that an extra vitamin supplement, including vitamin E, should be added to the diet of all children on artificial protein supplements.

APPENDIX. QUANTITIES OF FOOD CONTAINING KNOWN AMOUNTS OF PHENYLALANINE

I. Phenylalanine = 200 mg.

Dairy Products

Cheese, Cheddar	12 g.	Milk, dried, skimmed	11 g.
Egg, raw, boiled	31 g.	Milk, dried, whole	14 g.
Egg, fried	26 g.	Trufood (reconstituted 1 part in 8 water)	222 g.
Milk, fresh	116 ml.		

II. Phenylalanine = 100 mg.

1. *Dairy Products*

Milk, double cream	107 ml.	Milk, dry, whole	7 g.
Milk, fresh	58 ml.	Trufood (1 part in 8)	111 g.
Milk, dry, skimmed	5 g.		

2. *Meat*

Bacon, fried	13 g.	Lamb chop, grilled	10 g.
Beef, boiled	7 g.	Lamb chop, fried	12 g.
Beef, corned	10 g.	Liver, ox, fried	6 g.
Beef, roast, lean	8 g.	Mutton, leg, boiled	10 g.
Beef, steak, fried	11 g.	Mutton, leg, roast	11 g.
Beef, steak, grilled	9 g.	Mutton, leg, stewed	11 g.
Beef, steak, stewed	7 g.	Pork, fresh, roast	10 g.
Brain	16 g.	Pork, salt, smoked	10 g.
Chicken, boiled	9 g.	Pork chop, grilled	9 g.
Chicken, roast	8 g.	Rabbit, stewed	6 g.
Duck, roast	11 g.	Tongue, ox, boiled	13 g.
Ham, boiled, lean	11 g.	Turkey, roast	12 g.
Heart, sheep, roast	7 g.	Veal cutlet, fried	7 g.
Kidney, stewed or fried	8 g.	Veal, roast	7 g.

3. *Fish*

Cod, steamed	14 g.	Lobster, boiled	16 g.
Cod, fried	12 g.	Mackerel, fried	13 g.
Cod, grilled	9 g.	Pollack, steamed	15 g.
Crab, boiled	14 g.	Pollack, fried	18 g.
Haddock, steamed	11 g.	Prawns, cooked	8 g.
Haddock, fried	12 g.	Salmon, fresh, steamed	13 g.
Haddock, smoked, steamed	11 g.	Salmon, tinned	13 g.
Halibut, steamed	11 g.	Sardines, tinned	12 g.
Herrings, fried	11 g.	Shrimps, cooked	11 g.
Herrings, soused	10 g.	Trout, steamed	10 g.
Herring roe, fried	8 g.	Turbot, steamed	27 g.

4. *Cereals*

All-bran	24 g.	Force	20 g.
Baby cereal (Cow & Gate)	9 g.	Grape-nuts	15 g.
Baby cereal, oats (Scott's)	19 g.	Groats (Robinson's)	12 g.
Baby cereal (Robinson's)	25 g.	Post toasties	30 g.
Barley, pearl, boiled	54 g.	Robrex	12 g.
Cornflakes	30 g.	Shredded wheat	22 g.
		Wheatflakes	20 g.

5. *Bread, Biscuits, etc.*

Bread, brown	24 g.	Rice, raw	28 g.
Bread, white	26 g.	Sago	100 g.
Ryvita	22 g.	Tapioca	50 g.
Vitawheat	24 g.	Oatmeal	12 g.

III. Phenylalanine = 20 mg.

1. *Fruit*

Apricot, fresh	66 g.	Melon, cantaloup	40 g.
Apricot, dried, stewed	20 g.	Melon, yellow	66 g.
Apricot, tinned	80 g.	Nectarines	44 g.
Banana	36 g.	Orange	45 g.
Blackberries, stewed	56 g.	Orange juice	66 g.
Cherries, raw	66 g.	Peach, fresh	66 g.
Currants, black, stewed	66 g.	Peach, dried, stewed	33 g.
Currants, red, stewed	50 g.	Peach, tinned	100 g.
Currants, dried, stewed	23 g.	Pear, tinned	100 g.
Dates	20 g.	Pineapple, fresh	80 g.
Figs, dried, stewed	20 g.	Plums, raw	66 g.
Gooseberries, raw	66 g.	Plums, stewed	100 g.
Gooseberries, stewed	66 g.	Prunes, stewed	44 g.
Grapes, black	66 g.	Raisins, dried	36 g.
Grapes, white	66 g.	Raspberries, raw	44 g.
Grapefruit	66 g.	Raspberries, stewed	66 g.
Greengage, raw	50 g.	Rhubarb, stewed	100 g.
Greengage, stewed	80 g.	Strawberries, raw	66 g.
Loganberries	36 g.	Sultanas, dried	23 g.
Loganberries, tinned	66 g.		

2. *Vegetables*

Artichokes, boiled	28 g.	Mustard and cress	25 g.
Asparagus, boiled	16 g.	Onions, fried	52 g.
Beans, broad	14 g.	Parsnips, raw	23 g.
Beans, French, boiled	76 g.	Parsnips, boiled	30 g.
Beans, runner, boiled	76 g.	Potatoes, raw	20 g.
Beetroot, boiled	58 g.	Potatoes, boiled	28 g.
Broccoli, boiled	14 g.	Potatoes, baked	17 g.
Cabbage, raw	30 g.	Potatoes, roast	15 g.
Cabbage, boiled	83 g.	Potatoes, chipped	11 g.
Carrots, raw	76 g.	Pumpkin, raw	74 g.
Carrots, boiled	35 g.	Seakale, boiled	28 g.
Cauliflower, boiled	38 g.	Spring greens	23 g.
Celery, raw	44 g.	Swedes, raw	36 g.
Celery, boiled	66 g.	Swedes, boiled	44 g.
Egg plant	56 g.	Sweet potatoes, boiled	36 g.
Leeks, boiled	22 g.	Tomatoes, raw	105 g.
Lettuce	36 g.	Tomatoes, fried	95 g.
Marrow, boiled	100 g.	Turnips, raw	50 g.
Mushrooms, raw	16 g.	Turnips, boiled	56 g.
Mushrooms, fried	14 g.		

IV. Phenylalanine=10 mg.

1. *Fruit*

Apple, raw	100 g.	Loganberries	18 g.
Apple, baked	100 g.	Loganberries, tinned	33 g.
Apricot, fresh	33 g.	Melon, cantaloup	20 g.
Apricot, dried, stewed	10 g.	Melon, yellow	33 g.
Apricot, tinned	40 g.	Nectarines	22 g.
Banana	18 g.	Oranges	22 g.
Blackberries, raw	15 g.	Orange juice	33 g.
Blackberries, stewed	28 g.	Peach, fresh	33 g.
Cherries, raw	33 g.	Peach, dried, stewed	16 g.
Cherries, stewed	100 g.	Peach, tinned	50 g.
Currants, black, stewed	33 g.	Pear, raw	66 g.
Currants, red, stewed	25 g.	Pear, stewed	100 g.
Currants, dried, stewed	11 g.	Pear, tinned	50 g.
Damson, stewed	16 g.	Pineapple, fresh	40 g.
Dates	10 g.	Pineapple, tinned	66 g.
Figs, dried, stewed	10 g.	Plums, raw	33 g.
Fruit salad, tinned	66 g.	Plums, stewed	50 g.
Gooseberries, raw	33 g.	Prunes, stewed	22 g.
Gooseberries, stewed	33 g.	Raisins, dried	18 g.
Grapes, black	33 g.	Raspberries, raw	22 g.
Grapes, white	33 g.	Raspberries, stewed	33 g.
Grapefruit	33 g.	Rhubarb, stewed	50 g.
Greengage, raw	25 g.	Strawberries, raw	33 g.
Greengage, stewed	40 g.	Sultanas, dried	11 g.
		Tangerines	22 g.

2. *Preserves*

Blackcurrant purée	50 g.	Jam—fruit with stones	50 g.
Cherries, glacé	33 g.	Marmalade	200 g.
Honey, comb	33 g.	Mincemeat	33 g.
Honey in jars	50 g.	Syrup, golden	33 g.
Jam—fruit with seeds	33 g.	Treacle	16 g.

REFERENCES

Armstrong, M. D., and Low, N. L. (1957). *Proc. soc. exp. Biol. (N.Y.)*, **94**, 142.
—— and Tyler, F. H. (1955). *J. clin. Invest.*, **34**, 565.
Baird, H. W. (1958). *J. Pediat.*, **52**, 715.
Blainey, J. D., and Gulliford, R. (1956). *Arch. Dis. Childh.*, **31**, 452.
—— and Leyton, G. B. (1961). To be published.
Block, R. J., and Weiss, K. W. (1956). *Amino Acid Handbook*. Thomas, Springfield, Illinois.
Boyd, M. M. M. (1961). *Brit. med. J.*, **1**, 771.
Brimblecombe, F. S. W., Stoneman, M. E. R., and Maliphant, R. (1959). *Lancet*, **1**, 609.
Commonwealth Agricultural Bureaux (1956). Tables of the Amino Acids in Foods and Feedingstuffs. Tech. Comm. No. 19.
Gibbs, N. K., and Woolf, L. I. (1959). *Brit. med. J.*, **2**, 532.
Henderson, L. M., and Snell, E. E. (1948). *J. biol. Chem.* **172**, 15.
Horner, F A., and Streamer, C. W. (1956). *J. Amer. med. Ass.*, **161**, 1628.
Hsai, D. Y-Y., Knox, W. E., Quinn, K. V., and Paine, R. S. (1958). *Pediatrics*, **21**, 178.
Hughes, B. P. (1958). *Brit. J. Nutr.* **12**, 188.
Knox, W. E. (1960). *Pediatrics*, **26**, 1.
La Du, B. N. (1959). *Ann. intern. Med.*, **51**, 1427.
—— and Michael, P. J. (1960). *J. Lab. clin. Med.*, **55**, 491.
McCance, R. A., and Widdowson, E. M. (1946). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 235.
Rose, W. C., Coon, M. J., and Lambert, G. F. (1954). *J. biol. Chem.*, **210**, 331.
Stoneman, M. E. R. (1959). M.D. Thesis, University of Manchester.
Woolf, L. I., Griffiths, R., Coates, S., and Dillistone, F. (1958). *Arch. Dis. Childh.*, **33**, 31.

Humane methods of transporting by air various birds, animals, and reptiles are recommended in four new British Standards Institution publications (B.S.3149). Prepared at the request of the R.S.P.C.A., these recommendations were drawn up by B.S.I. technical committees, on which animal welfare organizations, the Medical Research Council, leading airlines, and packers and shippers of livestock were represented. These publications form Parts 3, 4, 5, and 6 of B.S.3149, "Carriage of Live Animals by Air." Each part is being issued separately. Part 1 (4s.), "Monkeys for Laboratory Use" was published in 1959; Part 2 (5s.), "Small and Medium-sized Seed-eating Birds," appeared in the early part of this year. The new parts are: Part 3 (5s.), "Rodents, Rabbits and Small Fur-bearing Animals"; Part 4 (5s.), "Dogs and Cats"; Part 5 (3s.), "Day-old Chicks and Turkey Poults"; and Part 6 (3s.), "Reptiles." Copies may be obtained from the British Standards Institution, Sales Branch, 2 Park Street, London W.1. (Postage extra to non-subscribers.)

STAPHYLOCOCCAL INFECTION IN A SURGICAL WARD

A THREE-MONTH STUDY

BY

I. F. McNEILL, M.B., B.S., F.R.C.S.

Senior Surgical Registrar, Royal Victoria Infirmary, Newcastle upon Tyne

I. A. PORTER, M.D.

Lecturer in Bacteriology, Medical School, King's College, Newcastle upon Tyne

AND

C. A. GREEN, M.D., Ph.D., D.P.H.

Professor of Bacteriology, Medical School, King's College, Newcastle upon Tyne

Despite the use of what are commonly thought to be adequate measures for the protection of the surgical patient, hospital cross-infection remains a disturbingly common condition. Examination of recently published accounts of non-epidemic sepsis in surgical wards reveals an incidence of from 1 to 41% (Williams *et al.*, 1960). Recent reports dealing with large numbers of cases have demonstrated the frequency with which clean incised surgical wounds become infected (P.H.L.S., 1960). Infections of the catheterized bladder (Miller *et al.*, 1960), the granulating burn (Lowbury, 1960), and the post-operative chest (Shooter *et al.*, 1958) are commonplace. Besides accentuating the difficulties and adding to the expense of surgical treatment such complications of hospitalization may greatly increase the morbidity of any surgical procedure.

Staphylococcal cross-infection in hospital is now an important and increasing part of this general problem. A staphylococcal wound infection may represent only a minor incident in a patient's convalescence. A serious wound infection, however, or an infection of the lung, the gastro-intestinal tract, or the site of amputation in a critically ischaemic limb may have a severe or even fatal outcome or at least jeopardize the results of surgical treatment.

In order to assess the extent of this problem in the Royal Victoria Infirmary a retrospective study was made of the number and type of staphylococcal infections occurring during an 18-month period in one male surgical ward (Table I). Of the 59 infections found, 48 were caused by hospital strains of staphylococci, and 11 were caused by strains not usually acquired in hospital. Of these infections, 48 were relatively minor post-operative complications and unimportant except as an index of technical failure, while 11 of the infections were of a more serious nature.

TABLE I.—*Retrospective Survey of Staphylococcal Infections During 18-month Period*

Total No. of infections	59
Minor infections	48
Major ,,	11
Infected amputation stumps	4
Subphrenic abscess	1
Pulmonary infections	3
Suppurative parotitis	1
Infected aortic graft	1
Septicaemia, lung, bone, and wound infection	1

48 infections were due to strains of "hospital" staphylococci.

As this small study indicated that staphylococcal cross-infection represented a serious problem, it was