and in older patients I do not think its results compare with those of surgery.

Regarding the basal metabolic rate, while it is always interesting to have information as complete as possible, I should not regard it as indispensable in a straightforward case. It is invaluable in the "formes frustes," in differential diagnosis, and in deciding whether an incomplete result is due to continuance of hyperthyroidism; but with private patients whose means are limited it should not be demanded as a routine if the clinical condition is clear or unless the information desired is actually necessary.

CONGENITAL PYLORIC STENOSIS

WITH OBSERVATIONS BASED ON 209
CONSECUTIVE CASES

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The clinical features of a typical case of congenital pyloric stenosis are well known. An infant suffering from this condition is usually healthy at birth: some authorities, indeed, maintain that it is unusually so, and will weigh nearer 8 than the average 7 lb. Typically, the infant is the son and heir, and for the first two weeks behaves normally, taking feeds well, gaining weight, not vomiting, and having normal motions. Then, in the third week, without evident cause, he begins to go downhill. First there is cessation of weight gain, then an occasional vomit, and less regularity of the bowels; soon there is actual weight loss, the vomiting becomes more frequent and copious and rapidly acquires projectile characteristics. At this time constipation is a definite feature, and the napkins are wet much less frequently than before.

Vomiting does not necessarily occur after each feed. One or more feeds may be retained, and then an unusually large vomit empties the stomach of the last and previous feeds together. The vomitus occasionally contains blood, either in the form of fine streaks or intimately mixed, giving a "coffee-grounds" effect. This has occasionally been observed for one or two days after operation. There is a distinct facies in this disease—the furrowed brow, pale face, prominent sucking-pads, over-ready lip reflex, and constant fist-gnawing, being readily recognized by anyone accustomed to seeing many cases. The consistently keen appetite, even after large vomits, and the absence of retching or evidence of indigestion are also helpful diagnostic points.

On physical examination the visible waves of peristalsis are perhaps the most striking feature. These may be seen at any time if the abdomen is examined in a good light—either spontaneously, usually after a feed, or elicited by flicking the skin with the forefinger. They appear as golf-ball-like waves of contraction, commencing beneath the left costal margin, and slowly progressing across the epigastrium towards the umbilicus, clearly outlining the shape and position of the stomach. The point where the waves cease is an indication of the locality of the pylorus, and here the tumour is to be palpated. The tumour is *always* palpable, but whether it is actually felt in any given case depends on a variety

of circumstances. It is sometimes tucked up under the liver and can only be appreciated when the stomach has either been emptied or filled, or is actively contracting. Several examinations may be necessary before the olive-like tumour is felt with certainty. There has to be complete relaxation of the abdominal wall, and this may not be readily obtained. The more often each case is examined the nearer will the number of tumours felt approximate to 100 per cent. One other striking feature on abdominal inspection is the marked hollowing of the lower half of the abdomen in comparison with the upper, which is usually distended by the dilated stomach. While the skin turgor is poor, as it is in marasmus, the striking difference between the upper and lower halves of the abdomen is only seen in pyloric stenosis.

Variations in the clinical history are frequent. First, in the time of onset of vomiting, which not infrequently occurs before the third week. In two of our cases it was first observed while the infants were still in the maternity hospital (that is, they were less than 10 days old), in one case, a doctor's child, it occurred on the fourth day: in two more it had quite certainly commenced in the first week. Bilderback has reported a case starting as early as the fourteenth hour after birth. At the other extreme we had three cases in which no vomiting occurred until the sixth week. Ibrahim¹⁴ found that out of 266 cases only five started as late as the eighth week, while Sauer¹ found that not more than 1 per cent. started after the eighth week. Secondly, while absolute constipation is the rule, diarrhoea may occur, and this may be due to one of two causes—(a) infection, or (b) hunger. The infective type of case occurs earlier—while there is still a fairly patent lumen—and does not differ from other infective diarrhoeas of infancy. The second type manifests itself in frequently passed, small greenish-brown stools, containing little faecal matter and consisting largely of mucus.

Pathology

The pathology of this condition is still unexplained. There have for long been three main theories: (1) that there is a congenital hypertrophy; (2) that there is a primary spasm, with hypertrophy occurring only secondarily; and (3) that there is in every case a combination of both hypertrophy and spasm. The third postulate is almost certainly correct, but the underlying cause has not been fully explained. That there may be a primary hypertrophy is undoubted, for cases have been reported in which a tumour has been present at birth, and even in premature babies. Hyperadrenalism, phimosis (Tyrrell Gray¹⁰), lack of vitamin B in the maternal diet during pregnancy (leading to a delayed myelination of the pyloric nerve), and many other theories have been propounded.

As regards the cause of the spasm there are even more interesting theories. Ernberg¹¹ holds that trauma is the basis of every case, the trauma usually arising from over-distension of the stomach. White¹² thinks all these infants are hypertonic, and that there is, in addition, an autonomic incoordination (John Thomson¹³) which leads to contraction of the pyloric sphincter, instead of relaxation, when food reaches the antrum; this continued incoordination rapidly increases the hypertrophy and causes dilatation of the stomach with consequent retention of food and mucous gastritis.

It is a fact that in every case there is dilatation of the stomach and a varying degree of gastritis with swelling of the pyloric mucosa. The swelling usually takes from two to three weeks to reach its maximum. It coincides with the *complete* obstruction of the pyloric lumen, and accounts for the fairly constant time of onset of acute symptoms of the condition. The pressure exerted on the pyloric capillaries may easily cause thromboses and

account for the occasional blood-stained vomitus which is seen. Relief from this pressure by operation causes a rapid return of the mucous membrane to normal. Possibly, in those cases which progress slowly to a spontaneous cure this result is brought about by the gradual atrophy of the pyloric mucous membrane with its consequent shrinkage and gradually increasing patency. If this were indeed so, ephedrine might produce a similar result—particularly if used in combination with atropine.

The chief objection to the second theory is that pyloric tumours have repeatedly been found at birth. The probable sequence is that there is a primary hypertrophy and a secondary spasm, but during the first week of life little food is taken, insufficient to reach the vomiting threshold and bring about that gastric retention, with its associated gastritis, that culminates in pyloric obstruction.

Pathological Anatomy

At operation the appearance of the pylorus is remarkably constant in all well-developed cases. It is white, densely hard, olive-shaped, and in dimensions about one and a half inches long and three-quarters of an inch in diameter. The hypertrophy is mainly confined to the circular coat, which is often three times its normal thickness. The mucous membrane is plicated and oedematous. Sections through the pylorus examined microscopically confirm that the hypertrophy is mainly limited to the circular muscle fibres. Wollstein² has shown that post-operative healing occurs by contraction of the fibrous tissue of the serous and submucous coats, and that the stomach and pylorus return to their normal size after about three months. Occasionally the oesophagus is dilated as well as the stomach, though not to such a pronounced extent.

Aetiology

Boys are much more frequently affected than girls. In a large series Feer³ found 80 per cent. were in boys. In this series we found 91.4 per cent. in boys. First children, too, seem to be more susceptible—in this series 69.8 per cent. It is rare for more than one infant in a family to be affected, though two cases of ours gave a similar history in siblings. Bilderback⁴ has reported the condition in twins, and Tribble⁵ recorded multiple cases in the same family. In one family which came under our notice there were only two children, both girls: they were operated on for pyloric stenosis, whilst a cousin, the only child, a girl, had also been operated on for the same complaint. In another family there were only two boys, both of whom had pyloric stenosis, whilst in four other families a history was obtained of older members of the family dying in early life from what appeared to have been the same condition.

Diagnosis

The four cardinal diagnostic features are: *vomiting*, *constipation*, *visible gastric peristalsis*, and a *palpable tumour*. In a typical case they are all present, and there is no difficulty in diagnosis. Ancillary aids to diagnosis are as follows: (1) The history—first child, male, onset of symptoms in second to third week. (2) The facies (see above). (3) The progressive weight loss at an age when weight gain is normally most rapid. (4) Urinary examination: oliguria and little or no chloride present. (5) An *x-ray* after an opaque meal showing gastrostasis and delayed emptying of the stomach.

The chief condition from which true pyloric stenosis has to be differentiated is *pylorospasm* (the gastro-enterospasm of hypertonic infants). In this connexion it will be remembered that the "position in family" and "sex" are not so pronounced in pylorospasm, but otherwise the symptoms may be very similar, both having

visible peristalsis, projectile vomiting, loss of weight, and constipation. The differentiation is made largely by the response to therapy. For this purpose either atropine or luminal works excellently. When fully under the influence of one or other of these drugs the pylorospasm begins to recover; such is not the case with true pyloric stenosis. Luminal may be given in doses of 1/8 or 1/6 grain, according to weight, before each feed, until drowsiness occurs, and is suitable for out-patient treatment. The atropine treatment is more satisfactorily confined to in-patient cases. Starting with $m\ iij$ of a 1 in 1,000 solution of atropine sulphate—that is, 1/2 grain to 1 oz.—the dosage is increased by $m\ i$ before each feed until a definite "atropine flush" is noticed. This may occur at any point up to a dosage of $m\ x$. The flush, which commences a few minutes after the ingestion of the atropine, is always readily observable. The correct dosage for any case is $m\ i$ less than the "flush-producing" dose. It is an interesting fact that cases of pylorospasm seem to tolerate considerably higher doses than do the stenotics—itsself a helpful point in differential diagnosis. An important practical point is that solutions of atropine do not retain their potency and should be freshly prepared each week. It is usually stated that the differential diagnosis between these two conditions is of paramount importance because operation is contraindicated in pylorospasm and is dangerous. Actually this is not a fact, and mechanically and theoretically it should not be. One case (not included in this series) on which an operation was performed proved to be an instance of spasm only, but freeing of the pyloric mucous membrane (as in the Fredet-Rammstedt operation) brought about immediate and permanent cure. Nevertheless, pylorospasm probably exists more frequently in the mind of the clinician than in the abdomen of the child.

Another condition which may simulate pyloric stenosis is *congenital duodenal stenosis* (atresia). This rare anomaly is distinguished by the time of the onset of the symptoms—usually within twenty-four hours of birth—by the fact that the vomit contains bile, and by the absence of a palpable tumour. A barium meal may help, and exploration will definitely settle the problem.

Finally, a severe case of *gastritis* may, by the loss of weight and continued vomiting, give rise to a similar picture. Here, however, the vomiting is quite different: it consists of small amounts of food brought up at frequent intervals; it is not projectile in character, is sour, possibly containing bile, is unaccompanied by visible gastric peristalsis, and there is no palpable tumour. Further, diarrhoea is commoner than constipation, and the urine contains abundant chlorides; the appetite is impaired, in definite contrast to the voracity of the true pyloric stenosis.

Choice of Treatment

The best results have been obtained by medical treatment, with, in each individual case, the relief by the surgeon of the mechanical obstruction at the pylorus at the moment of choice. If the case is a mild one, in which the symptoms have been present for only a short time, medical treatment should be commenced immediately. If it is a severe one it should be operated on at once—in fact, treated as a surgical emergency. Between the above-mentioned mild and severe types there comes a third and most important one; in this the symptoms are not such as to make the case appear urgent, and though many of them can be, and are, cured by medical measures, quite a number of them will ultimately become severe and require operation at a time when they will be far less able to stand it. These are the cases in which opinions differ as to the line of treatment to be adopted, and from which the majority of failures in both the medical and surgical treatment arise.

If all these cases are treated medically, quite a number will show a definite and progressive improvement, and will completely recover. They will, however, require to undergo continued treatment and close observation for from six to sixteen weeks, during which time they must be considered as weakly children liable to all intercurrent affections to which ailing children are heirs—enteritis, bronchopneumonia, etc. A further number will alternately improve and decline over a period of weeks or even months. Ultimately some of these, having successfully run the gauntlet of intercurrent affections, recover, whilst others will require operation. A third variety will show little or no sustained improvement, and will quickly or slowly develop into the severe type which demands operation.

If surgical intervention is insisted on in all moderately severe cases there is no doubt that many which would have recovered under medical treatment will be included. This, however, would appear to be more than balanced by the knowledge that they are cured more quickly by these means, and that a great many who would eventually require operation will have this done while they are much better able to stand it. All will have eliminated an anxious period of several months, during which, starved and well-nigh exhausted, they are but too willing victims to any complaint that is going round. They will also, by a procedure occupying but a few minutes, be enabled to absorb nutriment in a natural manner, and have the causal factor of their inanition immediately removed.

Medical Treatment

It is a well-known fact that the condition of pyloric stenosis is one which tends to spontaneous recovery from the fourth to the sixth month of life, for although the hypertrophy does not disappear the pyloric lumen gradually increases and more and more food can pass through. Medical treatment aims at keeping the infant alive until this spontaneous improvement commences. The two most important points in the treatment are: (1) maintenance of body fluids, and (2) prevention of infection.

In view of the small quantity of food which can be utilized by oral ingestion, the bulk of the fluid will have to be given parenterally. To ensure the maximum absorption of such food as is given, however, the following methods may be employed.

First, feeding as infrequently as possible—preferably not more often than four-hourly, the food being therefore as concentrated as possible. Any infant fed four-hourly has less tendency to vomit than one fed three-hourly or less often. Having regard to the caloric requirements it will usually be found possible to give an adequate formula using whole lactic acid milk with 10 per cent. glucose added—caloric value 1 per c.cm. (30 per oz.)—if breast milk is not obtainable. The use of wet-nurses, though not so common now as formerly, finds its greatest value in cases of pyloric stenosis, and makes an enormous difference to the mortality of the medically treated cases.

Secondly, thickened foods are said to be vomited less easily, so that each feed may be boiled with 20 per cent. starch until it is of porridge-like consistency. It is fed from a "hygeia" or similar nipple with a wide orifice about the size of a lead pencil, being "basted" in with a spoon. The drawback to this method is that each feed takes about forty minutes to give.

Thirdly, taking advantage of the resting phase through which a stomach usually passes after emptying itself by vomiting, re-feeding may be employed, the approximate quantity vomited being re-fed immediately. This is often successfully retained.

Fourthly, luminal depresses the vomiting centre and may be used in conjunction with the foregoing methods

in dosage as described under "pylorospasm." The same applies to atropine.

Fifthly, once (or twice) daily gastric lavage is of particular value where the stomach is already dilated and there is considerable retention and mucous gastritis. Normal saline is a satisfactory fluid to use, or sodium bicarbonate followed by saline. In view of the tendency which exists in all cases of pyloric stenosis to tetany, it is inadvisable to use sodium bicarbonate alone, as its continued use for lavage may precipitate an attack of manifest tetany.

Lastly, parenteral fluid administration. The fluids employed are isotonic saline, dextrose solution 5 or 10 per cent. in distilled water or normal saline, Hartmann's solution,⁶ and blood. The routes by which fluids may be administered are subcutaneous, intravenous, and intraperitoneal. If the dextrose is prepared according to the method described by Schwentker⁷ fewer reactions will occur than if glucose solutions are used. Blood transfusions are particularly valuable, and may be repeated many times in amounts not exceeding 10 c.cm. per lb. of actual body weight; it is not advisable to use more than 10 c.cm. per lb. lest undue stress on the heart should lead to dilatation, or the increased right-sided pressure should even reopen one of the foetal septal communications, and give rise to signs of congenital morbus cordis.⁸ Subcutaneous salines, however, are the main form of this treatment, and are best given by a two-way set, one needle in each flank, pointing towards the umbilicus, and delivered by gravity. Either needle may be inserted into the peritoneum at will, and a combined subcutaneous and intraperitoneal injection given. This latter method has the following advantages: (1) it is quicker, and (2) it supplies both a rapidly and a slowly absorbed quantity of fluid.

If surgical treatment is imminent it is undesirable to give any intraperitoneal injections for the twenty-four hours preceding operation, nor should the subcutaneous fluid impinge on the area to be incised.

Surgical Treatment

The pre-operative treatment consists of: (1) restoration of body fluids, as above, especially blood transfusions in bad cases; and (2) a stomach wash-out immediately before operation.

OPERATION

Fredet's modification of Rammstedt's method⁹ is recommended.

The abdomen is opened by an incision one and a half inches long, high up over the inner half of the right rectus, thus obviating the possibility of intestinal prolapse and the needless waste of time in controlling it. The stomach is delivered by pressure on each side of the incision. The pylorus is incised longitudinally, care being exercised to avoid wounding any small vessels plainly seen beneath the serous coat. (If this point is not borne in mind much valuable time will be spent, either at the operation, or again later, looking for and ligaturing small vessels that are difficult to control.) The incision should be carried right on to the stomach: if it falls short of this very little benefit will accrue from the operation, for it will merely permit the lower gastric mucosa more effectively to plug up the exit from the stomach, and the infant may be denied even that little nourishment he enjoyed prior to the operation. The incision is deepened by blunt dissection until the mucosa is completely freed and pouts up into and along the whole of its length. Normal saline is introduced into the peritoneal cavity at the close of the operation; usually about four to six ounces may be left in. The whole operation should not take more than five to seven minutes.

Ethyl chloride and ether, open ether, gas and oxygen, or novocain may satisfactorily be employed. The majority of our cases had open ether, about twelve "bad risks" having local anaesthesia only. At the close of the

operation inhalation of carbon dioxide for half a dozen breaths is a good prophylactic measure against post-operative bronchitis or bronchopneumonia and collapse of the lung.

POST-OPERATIVE TREATMENT

The post-operative feeding schedule is the most important factor in bringing about a satisfactory result. The schedule used in all the later cases in this series is as follows.

Two hours after operation the infant receives 2 drachms of sterile water, two hours later 2 drachms of "formula." The latter has been either whole lactic acid milk with 10 per cent. glucose, or Cow & Gate (1 in 8) "full cream" in those infants who are not breast-fed; if they are still on the breast milk is expressed and given in these quantities. Feeds continue at two-hourly intervals, water and "formula" alternating, increasing by 2 drachms every four hours, until after forty-eight hours the infant is returned to the breast, or is taking 3-ounce feeds four-hourly. If at any time during the forty-eight hours vomiting occurs the schedule is put back to the preceding feed and started off from there again—for example, if vomiting occurs after eighteen hours, when $1\frac{1}{2}$ ounces of "formula" have been given, at twenty hours $1\frac{1}{2}$ ounces of water are given, and at twenty-two hours $1\frac{1}{2}$ ounces of "formula" again, and so on.

Since the introduction of this schedule post-operative complications have been very considerably reduced.

POST-OPERATIVE COMPLICATIONS

These can be classified into two groups: (a) surgical—comprising sepsis, hernia, haemorrhage, incomplete operation, and collapse; and (b) medical—gastro-enteritis, otitis, pyelonephritis, bronchopneumonia, and "ward infection."

Surgical Complications.—These include any of the sequelae of an abdominal operation—namely, sepsis and breaking down of the wound (due to sepsis or faulty closure), which may be followed by an early or late incisional hernia. Haemorrhage may also occur at the site of the pyloric incision; this can be obviated by exercising greater care in making the incision, and by perfect haemostasis—for example, by underpinning the vessels involved at the time of the operation. An incomplete operation soon makes itself manifest by an early and persistent recurrence of the original projectile vomiting, a condition which requires prompt intervention in the form of a second operation carried out right on to the distal portion of the stomach, as the original incision should have been made. By the severity of its symptoms this condition is readily differentiated from that of occa-

dioxide, as previously mentioned, is probably the best prophylactic for this complication.

Medical Complications.—"Ward infection" is the most difficult of these complications to be guarded against, and represents the most potent argument in favour of surgical treatment. Infants suffering from pyloric stenosis are by nature weakly, and prone to infection, so that the sooner they are out of hospital the better. In fact, after the first forty-eight hours are successfully passed, and a four-hourly schedule started, the infant may well be discharged. Of the other complications, gastro-enteritis is prevented by the use of a clean, digestible feed in proper quantity; otitis by the daily inspection of the ear drums and prompt use of phenol in glycerin drops at the first sign of reddening of the drum, or myringotomy if necessary. In this series four cases required myringotomy and two antrum drainage. Frequent examination of the urine and the use of sodium bicarbonate (no longer contraindicated after operation) are measures to be taken against pyelonephritis, while bronchopneumonia may be averted by general nursing care.

Review of Cases and Conclusion

There were thirty-one private cases and 178 hospital cases in the series under observation. Of the private cases twenty-two were first-born children—that is, almost 79 per cent.—and thirty were males—that is, 96.8 per cent.

In the private cases there was one death—a mortality rate of 3.2 per cent.—the cause of death being gastro-enteritis, a condition that had been present for several weeks prior to operation, and had never cleared up. This patient died ten days after operation. In two of the cases the symptoms occurred in the first week; in three they arose in the second week; in fifteen, in the fourth week; and in one in the fifth week. The infant that died was operated on in the eleventh week, the condition having been present for eight weeks. It weighed 7 lb. 12 oz. at birth and only 5 lb. 8 oz. at operation.

Mortality and Date of Onset

	Hospital	Private	Total
Number of cases ...	178	31	209
Number of deaths ...	29	1	30
Percentage death rate ...	16.4	3.2	14.4
Average age at the onset of symptoms	2 weeks 4 days	2 weeks 6 days	

Detailed Analysis of Both Groups

	Cases that Lived		Cases that Died		Totals		All Cases
	Hospital	Private	Hospital	Private	Hospital	Private	Totals
Average weight at birth ...	8 lb. 4 oz.	7 lb. 12 oz.	7 lb. 1 oz.	7 lb. 12 oz.	8 lb. 4 oz.	7 lb. 12 oz.	8 lb. 2 oz.
Average weight at operation ...	6 lb. 15 oz.	6 lb. 13 oz.	6 lb. 13 oz.	5 lb. 8 oz.	6 lb. 15 oz.	6 lb. 13 oz.	6 lb. 14 oz.
Average age at operation ...	6 weeks 1 day	5 weeks 1 day	8 weeks 5 days	11 weeks	6 weeks 4 days	5 weeks 2 days	6 weeks 2 days
Proportion in which tumour was felt ...	76.6 %	96.8 %	79.2 %	100 %	77.2 %	96.9 %	80.1 %
Proportion in which vomiting projectile ...	100 %	100 %	100 %	100 %	100 %	100 %	100 %
Proportion in which peristalsis visible ...	100 %	100 %	100 %	100 %	100 %	100 %	100 %

sional vomiting, which in some cases occurs during the first two or three days. Another complication noticed in eight of the cases under review was a sudden and sometimes fatal collapse: four died. This was probably due to the collapse of the lung, and it is regretted that permission for a post-mortem examination was not granted in the cases where this occurred. Inhalation of carbon

An inquiry into the causes of death in the whole group was interesting if not very illuminating—interesting because of the definite tendency towards certain types, not very illuminating because of the impossibility of obtaining post-mortem examinations in a number of cases. It was seen that a number developed bronchopneumonia. Of these five died, even though the lung

involvement was not extensive. A further and greater number developed enteritis, some (particularly the older cases) were suffering from this complaint prior to operation; in all, six died from this disorder. Nine died within a few hours of the operation, apparently without ever recovering from it. Four collapsed and died two or three days after operation, apparently from collapse of the lung—they had been thriving well. Three slowly and steadily petered out, dying some ten to fourteen days after operation. Although they had ceased vomiting, they continued to lose weight, and steadily went downhill without showing any response to remedial measures. It was noticed that a few cases, apparently good operative risks, behaved in this manner; though now obtaining and retaining their feeds, they seemed totally incapable of absorbing them. Others, apparently bad operative risks, immediately and continuously improved from the time of their operation. In this connexion it was noticed that breast-fed children behaved well, but as the vast majority of these had been ill for a shorter period, this is a fact which is perhaps not so significant as might appear at first glance. One died in tetany four days after operation. In another case the stitches burst, and the child died two days later.

Two much stress cannot be laid on the importance of the following two factors. (1) Routine examination of the ears, particularly in cases of raised temperature, fretfulness, and disinclination for food—that is, cases not behaving according to plan. (2) Having a diet scheme and adhering to it: the stupid and malicious practice of eternally changing the diet at the slightest provocation causes both the infant and his attendants to become dizzy.

The early mortality was high (24 per cent. in the first sixty), but no case was ever denied operation, and many were moribund when subjected to it. Now that the cases are seen and operated upon early, most people realize that it is a simple, safe, and certain means of restoring the child to normal in the most rapid manner. In intelligent minds it is no longer the last desperate resort in a well-nigh hopeless condition. Generally speaking, the mortality in private cases is negligible; in hospital cases it is now about 5 per cent., and there is no reason why this should not be further reduced.

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Sir Kingsley Wood, the Minister of Health, has appointed the Central Housing Advisory Committee under the new Housing Act to advise him and local house management commissioners on specific questions which may be referred to it, and also to be available for consultation by the Minister on any questions connected with housing administration generally. The committee is also empowered to make representations to the Minister on any question of general concern in relation to housing. The chairman will be the Minister and the vice-chairman the Parliamentary Secretary to the Ministry, and the medical members are Sir Francis Fremantle, M.P., and Dr. J. Greenwood Wilson, medical officer of health for Cardiff. The secretary to the committee is Mr. H. H. George, M.C., to whom all communications should be addressed, at the Ministry of Health, Whitehall, S.W.1.

QUANTITATIVE ESTIMATION OF VITAMINS A AND D IN VARIOUS FOOD SUBSTANCES COOKED AND FRESH

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It was impossible to make quantitative estimations of vitamins before the international standards of reference became available, as there were no trustworthy units in which to express results. The *United States Pharmacopoeia* "rat unit" was devised to try to meet this want, but it was defined as "the amount of vitamin A required to produce an increase in weight of 2 to 3 grams per week for five weeks in rats which had ceased to grow on a diet deficient in vitamin A." It was not realized at the time that the animal response to any given dose of vitamin A fluctuates, with the result that the increase in weight of 2 to 3 grams per week could be brought about by different amounts of vitamin A at different times, and that the "unit" of vitamin A activity, therefore, varied accordingly.

Comparisons between different substances or between the products of different treatments of the same substance used to be made by determining the doses of the respective products which gave equal responses in small groups of animals. When the groups receiving the different doses were fed simultaneously the comparisons would be accurate provided the groups of animals were fairly big; but it has often happened that comparisons have been drawn between results obtained at different times, sometimes even after intervals of years, the variation in response of the whole stock of animals being unsuspected and therefore ignored. If a food was found to produce a smaller response in the test animals than it had produced some months previously, it was concluded that the food had lost in vitamin value during the interval. Quite recently an experiment was reported in which a sample of dried carrots had produced a bigger response in the test animals than part of the same sample had when examined three months before, and it was concluded that the vitamin A content had increased during storage. Without a simultaneous test on a standard of reference to estimate the sensitivity of the rats in each examination it is impossible to say whether the vitamin A (or carotene) had really increased in amount or not.

It has lately become possible to compare results obtained in the same laboratory at different times and in different laboratories at all times, because of the adoption of the international standards. Even now this can only be done when a simultaneous test of the standard is made whenever a vitamin estimation is carried out. It is completely misleading to determine the response of a group of animals to a dose of a standard once only and then to equate with that dose all doses of other substances which later produce a response equal to that originally produced by the standard. Coward, Key, and Morgan (1933) found that the response to a dose of vitamin A obtained at one time in their laboratory was five times the response to the same dose a year earlier. Coward and Key (1933) have found that the response to a dose of the international standard for vitamin D in the same laboratory fluctuated also, and at one time it was as much as ten times the response at another time. Similar fluctuations in response to doses of the international standard for vitamin D have also been reported