THE PROPHYLACTIC REQUIREMENT AND THE TOXICITY OF VITAMIN D

It is now more than 40 years since Sir Edward Mellanby1 demonstrated that cod liver oil would prevent rickets. Since this discovery, rickets due to vitamin D deficiency, once a serious pediatric problem in temperate climates, has become a comparatively rare clinical entity throughout the civilized world. Nonetheless, cases of deficiency rickets still occur in the United States, Canada, Great Britain, and elsewhere.

In temperate climates, sunlight cannot be relied upon to provide year-round protection from rickets in infancy and early childhood, and vitamin D must be provided from other sources. Until recently, the intakes of vitamin D recommended by official organizations in a number of countries could only be achieved by administration of oral vitamin D supplements, since the normal diet (even one including butter, milk, and egg yolk) contained relatively little vitamin D. Today, however, the situation is greatly altered, at least in such countries as the United States, Canada, and Great Britain. Because the addition of supplemental vitamin D to various foods is sanctioned, individuals of all ages now receive variable and sometimes considerable amounts of vitamin D from pasteurized, evaporated, or powdered milk, margarine, certain ready-to-eat cereals, and a variety of other foodstuffs. Indeed, in the United States and Canada there is now a reasonable likelihood that the individual, even the small infant, may receive the total recommended allowance of vitamin D from an average diet; in some instances he will receive considerably more than the recommended intake even when no vitamin supplement is given.

It is well known that vitamin D produces serious toxic effects if consumed for a period in grossly excessive amounts. In addition, however, vitamin D, in amounts not much greater than the recommended allowance, has been incriminated as one of the factors in the pathogenesis of idiopathic hypercalcemia of infancy, and in this respect even small excesses of vitamin D may occasionally be injurious. Whereas in the past it was frequently the practice to administer doses of vitamin D in excess of the recommended allowance with the object of providing an extra measure of nutritional safety, it is now evident that all those concerned with the optimal nutrition of the population must bear in mind the possible untoward effects of vitamin D prescribed for prophylaxis. This, in turn, demands that closer attention be paid to the total intake of vitamin D, a task that is becoming increasingly difficult as each new "fortified" food is introduced onto the market.

In the report that follows, the Committee on Nutrition of the American Academy of Pediatrics summarizes the evidence regarding the prophylactic requirement and the toxicity of vitamin D, and presents certain recommendations for use of the vitamin.

THE REQUIREMENT OF VITAMIN D AT VARIOUS AGES

Vitamin D is believed to function in minute concentrations by regulating or potentiating certain complex biochemical reactions at various sites in the body. The amount necessary to achieve optimal physiologic function in a given individual is dependent upon a number of factors, among which are believed to be age, rate of growth, efficiency of intestinal absorption (especially of fat), and coexisting disease, but little is known concerning the influence of these factors.

From the sections that follow, it will be apparent that vitamin D is an essential fac-
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tor in the metabolism of the growing human being, and, indeed, probably at all ages. For the healthy premature and full-term infant, fairly reliable estimates of the minimal requirements have been made. This has been possible in part because the newborn infant develops evidence of vitamin D deficiency relatively rapidly, and in part because, by selecting for study infants born in the autumn, the otherwise undefinable amount of vitamin D contributed by sunlight can justifiably be neglected. The minimal requirements during later childhood, adolescence, adulthood, pregnancy, and lactation have been much more difficult to determine because sources of vitamin D become more accessible and more varied, because rickets rarely develops after infancy, and because other satisfactory criteria of minimal vitamin D deficiency have not yet been established.

In early years there was much disagreement regarding the relative efficacies of the various forms of vitamin D. It is now believed that, microgram for microgram, vitamin D₂ (calciferol) and vitamin D₃ (irradiated 7-dehydrocholesterol) have equal potencies in the human.² Ordinarily, vitamin D is almost completely absorbed by the intestine, and the vehicle in which the vitamin is administered (be it oil, aqueous suspension, milk, or other food) is believed not to affect absorption unless the intestinal absorption of fat is impaired. In children with steatorrhea, the finely dispersed, water-miscible preparations are thought to be preferable on the basis of indirect evidence obtained from vitamin A absorption studies.⁶,⁹

The Normal Full-term Infant

Numerous studies, most of them conducted some 20 or 30 years ago, have concerned the efficacy of various amounts of vitamin D in preventing rickets,⁷,¹⁰-¹² in promoting intestinal absorption of calcium,¹³,¹⁴ and in promoting linear growth.¹¹,¹⁵,¹⁶

On the basis of the above criteria, estimates of minimal vitamin D requirement range from approximately 100 U.S.P. units⁷,¹¹,¹² to approximately 400 U.S.P. units per day¹⁰,¹⁶ (1 U.S.P. unit = 1 I.U.). Doses of vitamin D greater than 400 I.U. per day did not result in a greater degree of protection against rickets⁷,¹⁰,¹¹ and did not further increase retention of calcium.¹³,¹⁴ Although there is not complete agreement on the minimal requirement of vitamin D to promote maximal linear growth (or even whether vitamin D effects linear growth), it would appear that intakes of 250 I.U. daily are at least as effective as greater intakes.¹²,¹⁶

Many of these early studies are now open to question from the standpoint of modern experimental design. However, the observation that intakes of 300 to 500 I.U. of vitamin D per day resulted in rapid healing of severe rickets⁵,¹⁰ provides strong evidence concerning the probable effectiveness of the doses proposed for prophylaxis.

The formerly high incidence of rickets among Negro infants living in the large metropolitan areas of the northern United States gave rise to the impression that sunshine was less effective in preventing rickets in individuals with deeply-pigmented skins; however, sociologic factors made this difficult to prove. On the other hand, data in the American literature supports the opinion that the amount of ingested vitamin D required to prevent¹⁰,¹¹ or to cure¹⁰ rickets in Negro infants does not differ from the requirements of white infants.

The manner in which other factors, such as chronic infection, metabolic disease, and rapid skeletal growth influence vitamin D requirement is not yet accurately known. In particular, there has been argument regarding the relation between calcium intake and vitamin D requirement. Clearly, it is necessary to provide sufficient dietary calcium to meet the requirements of the growing skeleton. Similarly, sufficient vitamin D must be provided to prevent rickets and to promote satisfactory calcium retention. However, having satisfied the minimum needs in these two respects, there is no reason to postulate any specific relation between D requirement and calcium intake.
This principle is of special importance in considering the vitamin dosage of the breast-fed infant, since, per calorie, the calcium content of human milk is approximately one-third to one-quarter that of a cow's milk formula. However, both from theoretical considerations and practical observation, the calcium requirements of the normal full-term infant are satisfactorily met by human milk, and there is no reason to increase the prophylactic dose of vitamin D to more than 400 I.U. per day for the breast-fed infant.

In many parts of Europe, the custom of giving daily vitamin supplements to babies has never been established. In these regions, it is the practice to administer to infants, usually under direct medical supervision, single large oral or intramuscular doses (Stossen) of vitamin D at intervals. Individual doses of 300,000 I.U. at intervals of 1½ to 3 months have been suggested. The Committee endorses the view of Lightwood and Stapleton that such administration of vitamin D is unphysiologic and has no useful place in countries where daily vitamin D prophylaxis has become established practice.

The Premature Infant

Although the various techniques used to determine the vitamin D requirement of full-term infants have been applied to premature infants, it has been more difficult to establish the requirement. In part at least, this has been because of the relatively greater requirement for calcium. The skeleton of the infant born 6 weeks prematurely contains approximately half as much calcium as that of the full-term infant. Clearly, it is axiomatic that the premature infant should be given sufficient calcium to satisfy the needs of the rapidly growing skeleton. Since the average accretion of calcium during the last 2 months of fetal life has been estimated at approximately 200 mg per day, an intake of calcium that will permit retention of this amount must be provided. The relatively low calcium content of human milk makes such retention unlikely, even when the intake of vitamin D is sufficient to permit maximal intestinal absorption. Disregard of this principle by early investigators may explain the statement that premature infants frequently developed rickets when receiving intakes of vitamin D as great as 5,000 I.U. per day.

More recent studies in which large groups of formula-fed premature infants were observed clinically, roentgenographically, and biochemically indicate that rickets could usually be prevented and normal calcium and phosphorus homeostasis maintained with vitamin D intakes as low as 100 to 200 I.U. per day. Rates of growth in body length are reported to have been as rapid with intakes of 100 to 200 I.U. daily as with intakes of 400 to 1,200 I.U. daily. Recent studies re-emphasize the necessity of commencing vitamin D prophylaxis within the first 2 weeks of life.

The Pre-school and School Child

There is no doubt that vitamin D is required beyond infancy, since nutritional rickets occurs occasionally in older children. However, the requirement of vitamin D is more difficult to ascertain at this age than in infancy because of the slower rate of skeletal growth, the greater opportunity to ingest foods fortified with vitamin D, and the tendency to receive more exposure to sunlight. Because clear-cut evidence of rickets occurs so rarely beyond infancy, this manifestation cannot be employed as a dependable index by which to determine vitamin D requirement in this age group. On the basis of unpublished calcium retention studies, Stearns estimated that the requirement of growing children is of the order of 400 I.U. per day. There is no question that this intake provides an ample supply of vitamin D for normal children. However, it should be recalled that before the current trend toward widespread vitamin D enrichment of food, a balanced diet and outdoor play practically always provided sufficient vitamin D to prevent detectable evidence of vitamin D deficiency even though, in a great many instances, the
youngsters had not received any vitamin supplements, and the computed intake of vitamin D was considerably less than the figure recommended above.

Obviously, additional data are needed to delineate the minimal requirement in this age group.

The Adolescent

The determination of the minimal vitamin D requirement of the adolescent presents the same problems as those met for children. Some years ago, it was considered that rapid skeletal growth during this period necessitated a considerably greater intake of vitamin D (up to 3,900 I. U. per day). However, when studies were made in healthy adolescents under conditions of optimal calcium and phosphorus intake, maximal calcium retention was achieved with intakes of 400 I. U. per day.

The Adult

Calcium retentions have been measured in a number of healthy adults consuming average unfortified diets with standardized intakes of calcium and varying supplemental intakes of vitamin D. In none of these studies was a consistent difference in calcium retention detected before and during the administration of vitamin D supplements. For this reason it has sometimes been implied that healthy adults do not require vitamin D, and no allowances are recommended by the various national committees (Table I).

From physiologic considerations, this is probably not strictly correct. It is more likely that the amount of vitamin D needed for the maintenance of normal calcium and phosphorus metabolism in adults is so low that the requirement is readily met by the average diet and by casual exposure to sunlight. The hypothesis of a small requirement is strengthened by a number of reports of adults with osteomalacia attributed to vitamin D deficiency. One report mentions 15 nuns who developed radiographic and clinical signs of osteomalacia during World War II while confined to a convent and clinical signs of osteomalacia during.

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evidence that these states impose physiologic stresses upon the normal calcium and phosphorus metabolism of the adult. Although the calcium content of the diets of the women was poor, the osteomalacia responded to vitamin D rather than to extra calcium. These studies have therefore been taken to indicate that amounts of vitamin D greater than those needed by the normal adult are required for optimal nutrition during the last trimester of pregnancy and during lactation. However, data regarding the actual requirements are lacking.

In addition, provision should be made in the diet for the extra calcium required by the growing fetus (approximately 200 mg are deposited per day during the last 2 months of pregnancy) and by lactation (approximately 200 to 300 mg are excreted per day).18

Summary: Recommended Allowances at Various Ages

Allowances currently recommended in the United States, Great Britain, and Canada are shown in Table I. The recommendations are seen to be in reasonably close agreement. As indicated, there are minor differences in the terms of reference. However, it should be noted that in all instances the figures are intended to be taken as representing the total recommended daily intake of vitamin D from all ingested sources, assuming no exposure to ultraviolet radiation, assuming the consumption of adequate quantities of calcium and phosphorus (values about which, incidentally, there is still much argument44) and incorporating a safety factor beyond the minimum daily requirement of the normal individual.

The Committee on Nutrition believes that available data support the view that for full-term infants fed cow's milk formulas or human milk a total intake of 400 I.U. vitamin D per day from all dietary sources is a suitable allowance to prevent rickets and to promote optimal calcium and phosphorus metabolism. The same dose, preferably provided as a water miscible suspension,37 is considered to be suitable for premature infants fed commonly employed formulas of cow's milk. The higher recommendation of the British authorities (Table I) is intended to provide an additional safety factor, but there does not appear to be scientific proof that the extra amount is actually more effective. For both full-term and premature infants the range of individual variation has been well investigated. It may be assumed that this dose provides a moderate safety factor, and that few, if any, normal infants will develop rickets while receiving such an intake. Vitamin D prophylaxis should be commenced within the first 2 weeks of life.

There is no question that in certain locales and under proper conditions prophylactic amounts of vitamin D can be acquired from sunlight during the summer months. However, to cover all contingencies, the Committee considers that an attempt should be made to ensure the provision of the 400 I.U. allowance from ingestible sources on a year-round basis.

Available data do not provide accurate estimates of the minimum requirement beyond the period of infancy. For children and adolescents, the Committee recommends a total dietary intake of 400 I.U. of vitamin D per day from all sources as a safe allowance. As indicated below, in the United States such an intake will ordinarily be acquired from fortified foods without administration of a vitamin supplement. In Canada, the same situation frequently obtains in individual cases, but cannot be so generally relied upon.

The small requirement of the healthy adult is satisfactorily met by casual exposure to sunlight and by the consumption of usual unenriched foods, and no vitamin D supplementation is necessary unless specifically indicated by reason of occupation or other unusual circumstance. A total daily intake of 400 I.U. of vitamin D is considered adequate to provide for added demands during the second half of pregnancy and during lactation.

It is the opinion of the Committee that there is no necessity to exceed the recom-
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Recommended allowance during convalescence from acute infections. Similarly, for most chronic conditions, the recommended allowance is probably adequate.

The Dangers of Vitamin D

Notwithstanding lack of knowledge concerning minimal requirements, the Committee believes a daily intake of 400 I.U. of vitamin D can be expected to prevent detectable vitamin D deficiency in the normal infant or child consuming adequate amounts of calcium. Furthermore, there is no evidence to indicate that larger amounts of vitamin D would be more effective in any way. On the other hand, because nowadays many infants and children undoubtedly receive more than 400 I.U. of vitamin D daily, and because there is incontrovertible evidence that prolonged intake of vitamin D in large doses produces hypercalcemia with its numerous sequelae, it has become imperative to define the safe upper limits of vitamin D intake.

Many years ago Hess and Lewis demonstrated that very large doses of vitamin D would produce hypercalcemia. Since that time hypervitaminosis D has been reported in many individuals, a considerable number of whom were infants and children. There appears to be a fairly wide range of susceptibility to the toxic actions of vitamin D and it has been estimated that approximately 20% of normal adults who receive 100,000 I.U. of vitamin D daily for several weeks or months will develop hypercalcemia. Hypercalcemia is accompanied by anorexia, nausea, weight loss, polyuria, constipation, and reversible azotemia. If hypercalcemia continues generalized vascular calcification, nephrocalcinosis and irreversible renal insufficiency eventually supervene. In terms of unit body weight, dosages in the region of 1,000 to 3,000 I.U./kg/day for several weeks or months are toxic in the adult, and evidence suggests that this unit dose manifests approximately the same degree of toxicity in infants under 2 years of age.

For a 1-year-old infant, this amount of vitamin D would represent a total dose of between 10,000 and 30,000 I.U. per day.

The Risk of Vitamin D Toxicity in Infancy

The dosages mentioned above are at least 25 times greater than the prophylactic requirement. On the other hand, Jeans & Stearns suggested in 1938 that daily intakes of vitamin D in the range of 1,800 to 6,300 I.U. inhibited linear growth of normal infants and were therefore undesirable. Because the series of infants was small, and because considerable variability was observed in the individual growth patterns of experimental and control subjects, the data are difficult to interpret. The study has not been confirmed by other workers, and there has been little concern until relatively recently about administering prophylactic doses of vitamin D in the order of 2,000 I.U. daily.

However, in 1952 reports from Great Britain and Switzerland drew attention to a small group of infants with unexplained hypercalcemia. Shortly after the initial reports were published, cases of infantile hypercalcemia commenced to be diagnosed in increasing numbers throughout the British Isles. In its rare severe form hypercalcemia was associated with mental retardation, osteosclerosis, severe azotemia and other bizarre features. In its relatively more common mild form, which typically commenced between the second and tenth month of life, there was fairly sudden onset of anorexia, vomiting, polydipsia, weight loss, and failure to thrive, and the serum calcium was elevated above 12 mg/100 ml (often to 15 mg/100 ml or higher). Mild, usually reversible azotemia frequently developed.

Because many of the features resembled those of hypervitaminosis D, it was logical that attention should be focused upon the possibility that vitamin D was implicated in the pathogenesis of this new and important health problem. It was found that the hypercalcemia was controlled when all sources of vitamin D were withheld and a very low...
calcium intake instituted, although the additional features of the severe form did not disappear.

In 1953 and 1954 at a time when approximately 100 new cases of hypercalcemia were being diagnosed annually in Great Britain, an extensive survey of infant feeding practices in Great Britain revealed that, as a result of the then liberal enrichment of national dried milk powder and infant cereals with vitamin D, a normal infant consuming an average diet plus the recommended daily supplement of vitamin D (at that time 700 to 800 I.U.) might readily ingest 4,000 I.U. of vitamin D per day.45

On the other hand, idiopathic hypercalcemia cannot be explained solely on the basis of excessive vitamin D intake. For one thing, it was noted that not all affected infants were ingesting as much as 4,000 I.U. of vitamin D per day. For instance, in a study of 38 cases from Glasgow, 26 (two-thirds) had received less than 2,000 I.U. per day, and 8 (one-fifth) had received less than 1,000 I.U. per day. Further, it should be recalled that, of the large number of British infants who during one period are presumed to have ingested 3,000 to 4,000 I.U. per day, relatively few suffered any detectable ill effects.

To account for some of the contradictory findings, it has been suggested that patients with idiopathic hypercalcemia may be hypersensitive to vitamin D or, alternatively, that they may have an inborn disturbance in cholesterol metabolism which causes the accumulation of vitamin D or of some abnormal metabolite with vitamin D-like action.47,48 The fact that none of the affected infants had been entirely breast-fed suggests that the higher calcium content or some other feature of cow’s milk may also be a factor.

Although it is obvious that infants who develop hypercalcemia differ in some fundamental way from normal infants, it is hard to escape the still-circumstantial evidence which appears to relate the condition with vitamin D. As a result of recommendations of the British Paediatric Association Committee on Hypercalcaemia49 and of the Joint Subcommittee on Welfare Foods,5 measures were taken to reduce the average intake of vitamin D of British infants by halving the potency of National Cod Liver Oil and by considerably reducing the amounts of vitamin D added to dried milk powders and to infant cereals. It has been estimated that the average intake of vitamin D has probably been reduced to between one-third and one-half the former quantity as a result of these measures.

Obviously, careful evaluation of the present incidence of idiopathic hypercalcemia in Britain is essential before conclusions can be drawn regarding the importance of vitamin D in the etiology of the condition. Unfortunately, this information is not yet accurately known. However, according to annotations in the British Medical Journal and in Lancet in 1960, many pediatricians believe that the incidence of the disease has fallen since the recommendations regarding vitamin D intake were carried out. It is very tempting therefore, to suggest that vitamin D and idiopathic hypercalcemia are causally related. On the other hand, because it is not yet possible to weigh the many complex factors, it seems unwarranted to draw final conclusions regarding the etiologic role of vitamin D until the results become available of a comprehensive study which is currently being undertaken by the British Paediatric Association Committee on Hypercalcaemia.

ESTIMATES OF VITAMIN D INTAKES IN THE UNITED STATES AND CANADA AT VARIOUS AGES

The large number of vitamin preparations and of commonplace commercially-fortified foodstuffs on the North American market provide a variable and virtually unavoidable intake of vitamin D which, though difficult to estimate, may often be considerable. Table II gives information concerning some of the foods currently enriched with vitamin D in the United States and Canada. Because of frequent changes by the manufacturers, this information is
### TABLE II A

**VITAMIN D ADDED TO FOODS IN U.S.A.**

<table>
<thead>
<tr>
<th>Food</th>
<th>Product</th>
<th>Manufacturer and Trade Name</th>
<th>Approximate Vitamin D Content Claimed (I.U./unit measure)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Milks</strong></td>
<td>Dairy Milk</td>
<td>Fortified (approx 85% total sales)</td>
<td>1 U.S. quart</td>
</tr>
<tr>
<td></td>
<td>Evaporated Powdered</td>
<td>All brands</td>
<td>400</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Klim (whole) &amp; most powdered infant formulas</td>
<td>1 U.S. quart (reconstit.) 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Skim milks (powdered)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Milk flavorings</strong></td>
<td>Powders</td>
<td>Ovulant (plain or chocolate)</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hershey—Instant Cocoa Mix</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nestle—&quot;Quick&quot;</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>Syrups</td>
<td>Borden’s Dutch Chocolate</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Baker’s—Instant Choc. Mix</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bosco</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cocoa Marsh</td>
<td>50</td>
</tr>
<tr>
<td><strong>Margarine</strong></td>
<td>Parkay, Kraft</td>
<td>1 oz</td>
<td>250</td>
</tr>
<tr>
<td></td>
<td>All-Sweet, Blue Bonnet’s, Good Luck, Imperial, Mazola</td>
<td>1 oz</td>
<td>155</td>
</tr>
<tr>
<td><strong>Breakfast cereals</strong></td>
<td>Kellogg—All Bran</td>
<td>1 oz</td>
<td>400</td>
</tr>
<tr>
<td></td>
<td>Cornflakes</td>
<td>1 oz</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>Special K</td>
<td>1 oz</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>Sugar Pops</td>
<td>1 oz</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>Pep</td>
<td>1 oz</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>Concentrate</td>
<td>1 oz</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>General Mills—Hi-Pro</td>
<td>1 oz</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>Quaker—Life</td>
<td>1 oz</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>Coco-Wheats</td>
<td>1 oz</td>
<td>80</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td>Bread</td>
<td>Special Sunbeam Bread (a premium product only)</td>
<td>1 slice</td>
</tr>
<tr>
<td></td>
<td>Candy</td>
<td>Swiss Bar</td>
<td>1 oz</td>
</tr>
<tr>
<td></td>
<td>Beverage</td>
<td>Stuart’s Instant Vita Drink</td>
<td>1 glass</td>
</tr>
</tbody>
</table>

*Only approximate. The recorded figures are computed from the manufacturers' label claims and represent minimum values, since it is customary manufacturing practice to add an "overage" to allow for possible deterioration, etc. Overage may constitute as much as 100% or more of the label claim in the United States. In Canada, regulations prescribe that a given food may contain not less than 400 or more than 800 I.U. of vitamin D in a reasonable daily intake of that food, but despite the regulations, the overage permitted within the limits of good manufacturing practice undoubtedly remains a factor to be considered.

There are certain differences between the United States and Canadian figures. In the United States, vitamin D is added to virtually all evaporated milk in a concentration of 400 I.U. per reconstituted U.S. quart, and a similar amount is added to 85% of all dairy milk marketed in the United States (although the latter figure may decrease as a result of the recent re-introduction of unfortified dairy milk by certain supermarkets). In Canada, all brands of evaporated milk contain approximately 600 to 800 I.U. vitamin D per reconstituted Imperial quart (i.e., 500 to 700 I.U. per reconstituted U.S. quart). However, in contrast to custom in the United States, less than 1% of dairy milk on the Canadian market is enriched.*
with vitamin D. For this reason, a considerable number of Canadian babies will fail to receive sufficient amounts of vitamin D in their food, and in a certain proportion of these, rickets may be expected to develop unless vitamin D is given as a supplement or by exposure to sunlight.

By constructing hypothetic menus, and using the information contained in Table II, an estimate has been made in Table III of the amounts of vitamin D that might be ingested under present-day living conditions in the United States and Canada. Two diets have been constructed for each of three age groups, one selected to represent an arbitrarily average situation, the other to represent a situation in which the intake is unquestionably, but not unrealistically high.

In computing the total intakes of vitamin D the amount administered as a vitamin supplement must be included. For several concentrated drop preparations, the daily amount recommended by the manufacturer contains from 800 to 1,000 I.U., but most products now contain 400 I.U. per recommended dose. Most of the candy-type multiple vitamin preparations available for older children in both the United States and Canada contain 400 I.U. per lozenge. Most multiple vitamin capsules intended primarily for adults contain 1,000 I.U. vitamin D or more per capsule.

A glance at Table III will indicate that the well-cared-for infant, receiving an
evaporated milk formula and vitamin supplement (as is customary in North America) will automatically ingest two to four times the recommended daily allowance of vitamin D without taking the question of overage into account. However, it seems unlikely, under present circumstances, that a significant proportion of the infant population in either the United States or Canada would obtain as much vitamin D as many British babies were estimated to have received before the present restrictive measures were implemented. On the other hand, the well-cared-for toddler in North America, still receiving a vitamin supplement, is likely to receive at least three times the recommended allowance and the daily intake might reasonably exceed 2,000 or even 3,000 I.U. For the older child, even higher intakes can be envisaged, especially if he regularly receives one of the candy-like vitamin preparations or has access to a vitaminized candy bar or beverage.

Admittedly these hypothetic examples have no validity as estimates of the national vitamin D intake. They were selected merely to emphasize the diversity of foods that are artificially enriched, and the unexpected ease with which vitamin D can now be acquired in both the United States and Canada.

**COMMENT**

From the foregoing discussions, it is evident that vitamin D is essential for the maintenance of normal calcium and phosphorus metabolism in humans. On the basis of present evidence, it is considered that a total intake of 400 I.U. of vitamin D per day provides an adequate margin of safety.

### TABLE III

**Hypothetic Total Daily Intakes of Vitamin D**

<table>
<thead>
<tr>
<th>Age of Child</th>
<th>Intake</th>
<th>Amount of Vitamin D Contributed by Individual Food</th>
<th>Total Intake ( \text{I}.U./\text{day} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Average ( 400 )</td>
<td>( 1,400 )</td>
</tr>
<tr>
<td>6 mo</td>
<td>Average</td>
<td>( 800 )</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>( 1,000 )</td>
<td></td>
</tr>
<tr>
<td>8 yr</td>
<td>Average</td>
<td>( 600 )</td>
<td>( 1,600 )</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>( 1,000 )</td>
<td>( 2,000 )</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td>( 800 )</td>
<td>( 2,000 )</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>( 1,000 )</td>
<td>( 3,000 )</td>
</tr>
<tr>
<td></td>
<td></td>
<td>( )</td>
<td></td>
</tr>
</tbody>
</table>

A. Children in United States

B. Children in Canada

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* When values appear in parentheses, total intake of vitamin D has been calculated twice; once including and once excluding these values.
to protect substantially all normal growing individuals from detectable evidence of vitamin D deficiency.

At the same time, it is known that excessive amounts of vitamin D are toxic. The low limit of toxicity is not clearly defined, but British experience with the problem of idiopathic hypercalcemia suggests that this toxic level may, on rare occasions, be as low as 3,000 to 4,000 I.U. per day for susceptible individuals in the infant age group, and sometimes considerably lower.

Until relatively recently, the average diet contained very little vitamin D and could not necessarily be relied upon to prevent vitamin D deficiency during growth, particularly during infancy. The use of vitamin D supplements was therefore promoted, and there was widespread acceptance of this public health measure throughout North America. However, when it became evident that rickets had not been entirely eliminated by this measure, the decision was made to enrich commercial milks with vitamin D, and the outstanding success of this program gave impetus for the addition of this and other vitamins to a variety of foods. At the present time, a wide range of common foodstuffs contain added vitamin D, and it is obvious that the over-all vitamin D intake of all ages of the population has risen appreciably in the United States and Canada. Calculations indicate that the amount of vitamin D now acquired from the diet alone may readily exceed the recommended daily allowance, sometimes by a considerable amount.

Although the exact cause of idiopathic hypercalcemia of infancy remains to be established, there is now a large amount of evidence which incriminates vitamin D as an important etiologic factor. Despite the fact that infantile hypercalcemia has, until now, been much less common on this continent than in Great Britain, more than 30 cases have already been reported in North America since 1954 and existence of a number of unpublished cases is known to members of the Committee.

Thus, in the face of existing evidence, the Committee on Nutrition considers that practitioners and public health authorities should strive to ensure that the total vitamin D intake of all infants reaches the recommended allowance of 400 I.U. per day, but at the same time, they should make concerted efforts to restrict the upper limit of intake for all sources to an amount as close to this figure as is practicable. This demands that cognizance be taken of the amount of vitamin D contributed by the formula and other components of the diet before prescribing a vitamin D supplement, and that attention be paid to the amount of vitamin D provided by the supplement chosen.

It demands, also, that efforts be intensified to dispel from the minds of parents the concept of vitamins as tonics, with the hope of reducing the all-too-prevalent practice of vitamin D “over-insurance” in the home. Although there is no specific evidence that daily intakes of vitamin D in the order of 2,000 to 3,000 I.U. produce deleterious effects on individuals beyond infancy, it should be realized that the present trend in nutrition is imposing a new situation upon the children and adults of North America, the long-term effects of which are entirely unknown.

The addition of vitamin D to practically all commercial milk supplies in the United States has been amply justified by the dramatic reduction which it brought about in the incidence of rickets. By inference, similar benefits would presumably be observed in Canada by broadening the present milk-fortification program to include dairy milk. On the other hand, the milk consumption habits of North American children ensure a uniformity and dependability of intake which does not apply to other foodstuffs. Hence, the enrichment of a large variety of additional foods with vitamin D cannot be similarly justified.

**SUMMARY AND RECOMMENDATIONS**

Despite inadequacies in information concerning the minimum prophylactic requirement of vitamin D for all age groups be-
beyond infancy, there is no doubt that a total intake of 400 I.U. per day is adequate to prevent vitamin D deficiency in substantially all normal children from birth through adolescence.

Evidence derived from the study of idiopathic hypercalcemia suggests that certain infants excessively sensitive to the toxic action of vitamin D may, on rare occasions, be adversely affected by daily intakes of 3,000 to 4,000 I.U. and sometimes considerably less. Because of the prevalent practice of food fortification in the United States and Canada, there is now a definite possibility that the individual, even the young infant, may ingest considerably more than the recommended vitamin D allowance, and intakes of 2,000 to 3,500 I.U. per day are possible, particularly beyond infancy. Although there has been no specific evidence that intakes of this order produce deleterious effects beyond infancy, it is pointed out that the long-term consequences of this new nutritional situation on older children or adults are entirely unknown.

In view of these considerations the Committee on Nutrition recommends that efforts be taken to ensure a total vitamin D intake of 400 I.U. per day by all infants and children. At the same time, an attempt should be made to restrict the intake from all sources to an amount not greatly in excess of this figure.

The value of carefully planned enrichment of commercial milk supplies with vitamin D has been clearly demonstrated. However, the present practice of enriching foods other than milk and infant formula products is not justified, and discontinuation of this practice is to be recommended. Under the present circumstances, cognizance should be taken of the amount of vitamin D acquired by the individual from food sources before prescribing a vitamin D supplement.

In keeping with present concepts regarding vitamin D requirement, commercial vitamin D supplements should be adjusted to contain not more than 400 I.U. per dose.

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