Infant Formulas and the Use of Vegetable Protein

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ABSTRACT

Soy-based formulas and meat-based formulas are used as successful replacements for milk in the nutritional management of infants who are, or are suspected to be allergic to milk. Used most widely are soy-based formulas which eliminate the symptoms and ensure normal growth and well being of the infant. Soy-based formulas are made in both powdered and liquid forms, and the trend during the past decade has been to use a soy protein isolate to reduce or eliminate the presence of carbohydrates which cause flatulence and abnormal stooling. Details of the nutritional composition of soy-based infant formulas are discussed together with the selection and processing of protein in order to minimize the presence of antinutritional factors.

INFANT FORMULAS AND THE USE OF VEGETABLE PROTEIN

Because of the wide variety of associated symptoms and the lack of a simple means for establishing diagnosis or immunologic pathogenisis, allergy to cow's milk in infants and children continues to be a perplexing problem for the physician. Perpetuation of the allergic syndromes can lead to general failure to thrive, slow or even retarded growth and other health problems. Consequently, implementation of a dietary management program that ensures both adequate nutrition and the elimination of symptoms becomes an important concern.

TABLE I

Symptoms and Signs of Cow Milk Allergy

Vascular	Respiratory
Shock	[a]Rhinitis
	[a]Bronchitis
	[a]Asthma
Dermatologic	[a]Sneezing
	[a]Coughing
[a]Eczema	[a]Chronic nasal discharge
Urticaria	Rattly respiration
Hives	Excessive mucus in throat
Angioneurotic Edema	Recurrent croup
Perianal Dermatitis	
Gastrointestinal	Central Nervous (Behavioral)
[a]Diarrhea	
[a]Vomiting	Refuses milk
[a]Colic	Excessive crying
[a]Abdomical pain	Excessive sweating
Malabsorption	Headache
Enteropathy	Hyperirritability
Constipation	Hyperkinesis
Stomach spasms	Listlessness
	Constitutional
	Failure to thrive
	Retarded growth
	Malnutrition

[a]Most common indicators.

Incidence of allergy to cow's milk has been estimated to be from 0.3% (1) to 7% (2) in general infant and children groups and from 14% (3) to 30% (4) in "suspected alergic" infants and children. And, in general, cow's milk has been designated the food allergen most commonly affecting children (5).

Some of the symptoms and signs of cow milk allergy are shown in Table I. The wide range of determined incidence is attributed to differences in diagnostic criteria, the groups studied, and the statistical methodology employed. Variances notwithstanding, the figures are considered sufficient to show that allergy to cow's milk is a very real problem in clinical medicine (6,7).

Soy-based formulas and meat-based formulas are used as successful replacements for milk in the nutritional management of infants who are allergic to milk or are suspected of milk allergy. Used most widely are soy-based formulas which eliminate the symptoms and ensure normal growth and well being of the infant.

Soy-based formulas are supplied in both powdered and liquid forms and Table II shows many of the formulas commercially available in the world today. The products can be obtained in powder form which require reconstitution with water and in two fluid forms, i.e., a ready-to-feed form and a concentrated liquid form, the latter usually requiring dilution with an equal volume of water prior to feeding.

For some children the formula is the sole source of nutrition for many days and perhaps several months of their lives. It is, therefore, imperative that the formula supply adequate and balanced nutrition, that it be microbiologically safe, and that it be free from toxic or antinutritional factors.

Several governments have standards for infant formulas, while the standards of the Codex Committee on Foods for Special Dietary Use (8) are generally used for those coun-

TABLE II

Soy-based Infant Formulas

Name	Product form[a]	Manufacturer
Bon Lact	P	Wakado Pharmaceuticals, Japan
Espelin	P	Med-Nim (Pty) Ltd., South Africa
Isomil	R,C,P	Abbott Laboratories (Ross), USA
Lactopriv	P	Topfer, West Germany
Mull-Soy	C	Syntex Laboratories, USA
Multilac	P	Carlo Erbe S.p.A., Italy
Neo-Mull-Soy	R,C	Syntex Laboratories, USA
Nursoy	R,C	Wyeth Laboratories, USA
Nutri-Soja	C,P	N.V. Nutricia, The Netherlands
Prosobee	R,C	Mead Johnson, USA
Sobee	P	Mead Johnson, USA
Soja Semp	C	Semper, Sweden
Soyalac	R,C,P	Loma Linda Foods, USA
i-Soyalac	C	Loma Linda Foods, USA
Vegebaby	R	Laboratoire Sopharga, France

[a]Where P = powder, R = ready to feed, and C = concentrated liquid.

TABLE III

Approximate Analysis of a Typical Soy Protein Infant Formula[a]

Approximate analysis (wt./liter)			Vitamins per liter:		
Protein	20.0	g	Vitamin A	2500	I.U.
Fat	36.0	g	Vitamin D	400	I.U.
Carbohydrate	68.0	g	Vitamin E	15	I.U.
Minerals	3.8	g	Vitamin C	55	mg
Calcium	0.70	g	Vitamin B_1	0.04	mg
Phosphorus	0.50	g			
Sodium	0.30	g	Vitamin B_2	0.60	mg
Potassium	0.71	g			
Chloride	0.53	g	Vitamin B_6	0.40	mg
Magnesium	50	mg			
Iron[b]	12	mg	Niacin (mg. equiv.)	9.0	mg
Zinc	5.0	mg			
Copper	0.50	mg	Folic acid	0.10	mg
Maganese	0.20	mg			
Iodine	0.15	mg	Vitamin B_{12}	3.0	mcg
Water	901.6	g	Pantothenic acid	5.0	mg
Calories per fl. oz. 20			Biotin	0.15	mg
Calories per 100 ml. 68			Vitamin K_1	0.15	mg

[a]Isomil, Ross Laboratories, U.S.A.

[b]The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

tries lacking their own specific regulations. In the United States, the standards of the Food and Drug Administration (9) must be adhered to. The latter are based on various recommendations of the Committee on Nutrition of the American Academy of Pediatrics (10). The modern infant formula, therefore, meets the requirements of the growing child not only for protein, fat and carbohydrate, but for many vitamins and minerals as well. Table III shows the approximate analysis of a typical soy protein infant formula available in the United States. The values shown are for a 20 Kcal/fl. oz. formula, which is the strength most commonly used in the U.S. for the full term infant. Since a refined soy protein isolate is used in this formula, many minerals, in addition to vitamins, must be added during manufacture to ensure that the formula consistently contains the composition shown in Table III.

All common vegetable proteins are deficient in one or more of the amino acids essential to man. Soy proteins are deficient in methionine. Infant formula regulations require that nutritional adequacy be demonstrated, and usually this takes the form of exceeding a specific protein efficiency ration (PER) value. The Codex and Canadian standards are such that the PER value must be at least 85% of casein, while in the USA the FDA standard is 70% of casein. L-Methionine is therefore included in soy-based infant formulas to meet the PER requirement. Table IV shows a comparison of the essential amino acid requirment for the human infant (11) and levels found in a typical formula containing soy protein and methionine. Levels of essential amino acids in the formula exceed estimated requirements.

A consideration of other vegetable proteins for infant feeding must, therefore, include an assessment of the required fortification with essential amino acids to meet the requirements of the infant and demonstration of nutritional adequacy in the PER assay.

Extensive clinical testing of a new infant formula is very desirable, and all reputable companies have their products tested in animals and then extensively in humans under strict supervision before the product is marketed.

Infant formulas containing soy protein have been commercially available for almost 50 years. The first formulas contained full-fat soy flours and, as a consequence, were dark in color and had a beany flavor. The presence of soluble carbohydrates from the soybean were the cause of flatus in the infant and also yielded foul smelling stools.

TABLE IV

Essential Amino Acid Requirement of the Infant and Analysis of a Typical Soy Protein Infant Formula

Amino acid	Estimated amino acid requirement mg/100 Kcal	Levels in infant formula[a] mg/100 Kcal
Histidine	26	73
Isoleucine	66	132
Leucine	132	235
Lysine	101	173
Methionine	24	59
Phenylanine	57	154
Threonine	59	106
Tryptophan	16	31
Valine	83	135
Cystine	23	28

[a]Isomil, Ross Laboratories, USA.

With the development of more refined soy proteins, i.e., soy protein isolates, the manufacture of today's high quality soy infant formula is possible. Today's formulas are almost white or milk-like in color, are fairly bland tasting, and yield normal stools. Apart from nutritional concerns discussed earlier, commercial soy proteins for use in infant formulas should satisfy several other requirements. The protein content should preferably be greater than 90% of the dry weight. In this way the ash value is kept low, and it facilitates the addition of minerals to the formula so that nutritional requirements can be met while not allowing any mineral to reach harmful or toxic levels. The soluble carbohydrate content from the soybean should be low to prevent subsequent abnormal flatus and stool condition. The viscosity of an aqueous solution of the soy protein should be low so as to decrease the heat requirements for sterilization of the formula and thus minimize nutritional losses during hot fluid processing and sterilization. Soy protein should remain in solution during processing and sterilization. The protein should be white or very light tan in color and be bland tasting to permit manufacture of a formula that is as close to milk in aesthetic properties as possible.

Clearly the technology that yielded the high quality soy protein isolate of today enabled the infant formula industry to make great improvements over the formulas made from soy flours.

Although the details of manufacture of infant formulas is proprietary information, it is probably true to say that most formulas are made by first preparing the aqueous portion containing protein source, carbohydrate and minerals, and a separate fat portion, usually containing an emulsifier. These two portions are then mixed, homogenized, analyzed, and formulation adjustments are made if necessary. Ingredients which are most heat and oxygen sensitive (e.g., vitamin C and the B vitamins) are then added together with the required amount of water to standardize the formula. The product is then either heat treated and spray dried to yield a powder, or filled into glass or metal containers and sterilized to yield ready-to-feed or concentrated liquid products. The finished products are then subjected to chemical and microbiological analyses and must satisfy the manufacturer's product specifications for release.

Although this paper is addressed to the use of vegetable proteins in infant formulas, some mention should be made of the carbohydrates used. Milk-based formulas contain lactose as the carbohydrate source. In a soy protein infant formula, the source of carbohydrate is usually sucrose, corn syrup (hydrolyzed corn starch), or a mixture of sucrose and corn syrup. Therefore, not only are soy protein formulas recommended for infants who are allergic to milk protein, but they are appropriate for feeding infants who exhibit

TABLE V

Vegetable Protein and Potential Contaminants Considered to be Undesirable in Infant Formulas

Protein source	Potential contaminant
Cottonseed	Gossypol
Cereal grains	Gluten
Peanut	Aflatoxin
Rapeseed	Erucic acid

lactose intolerance or have lactase deficiency.

Of constant concern to the infant formula manufacturer is the possibility that toxic or antinutritional factors might enter the formula. Such undesirable agents might not only come with the protein, but might also come from other ingredients or the process water. The manufacturer therefore must subject all ingredients to stringent analyses before acceptance for use in the formula.

The ingredients must satisfy the specifications set for such items as heavy metals, pesticides and herbicides, as well as microbiological specifications which usually include total standard plate count, aerobic and anerobic thermophile content, yeasts and molds and pathogens.

Soy protein contains factors which are of concern to the formula manufacturer; for example, trypsin inhibitor. If the formula is made from soy protein isolate, the inhibitor content of the formula will be low, and analysis has shown that over 90% of the original trypsin inhibitor is destroyed during the aqueous heat processing of the formula. Furthermore, when a soy protein formula was incorporated in a rat diet, no incidence of pancreatic hypertrophy or hyperplasia was observed histologically, and weight gain was equivalent to rats on a diet containing casein as the source of protein (12).

Soy protein isolates contain ca. 20 mg. of phytic acid/g, and therefore the effect of this phytic acid on mineral availability from the formula must be determined and shown to be adequate for the infant. Approximately 90% of the phytic acid of one such soy protein was removed by ultrafiltration. Three formulas, each containing a different calcium and phosphorus level but with similar calcium/phosphorus ratios and similar zinc, iron, copper and magnesium levels, were prepared from the phytate-reduced soy protein isolate and three formulas from phytate containing isolate. Weanling male rats, ten per diet group, received these formulas as their sole source of diet for four weeks. The protein and calorie efficiencies, bone and carcass ash, calcium, phosphorus and zinc of rats receiving the phytate-containing formulas were not significantly different from the rats receiving corresponding phytate-reduced formulas. The results suggest that, regardless of the calcium and phosphorus levels of the formulas, phytate does not interfere with calcium, phosphorus and zinc utilization from a soy formula for the rat (13).

The relative zinc availability in human milk, infant formulas and cow's milk was recently studied in the rat, and the authors concluded that a soy protein formula such as that shown in Table III could be expected to provide adequate quantities of zinc for infants (14).

The soybean is also known to contain hemagglutinins, compounds that have the ability to agglutinate red blood cells. In a recent study it was shown that soy flakes have measurable hemagglutinating activity, but that soy protein isolates have very little or no activity and that infant formulas prepared from soy protein isolates exhibit no activity (15).

In consideration of vegetable proteins for use in infant formulas, we must be extremely concerned about potential harmful effects to the child resulting from the ingestion of undesirable materials. For example, Table V shows some compounds that might be present, even in trace quantities, in commercial vegetable protein preparations that would be of concern to the infant formula manufacturer and to the pediatrician.

I have tried in a very concise way to call attention to the great detail and thoroughness with which a source of protein for potential use in an infant formula must be examined. The infant formula manufacturer must obviously prepare formulas that comply with regulations, but over and above that, these formulas by analytical and clinical testing must assure an adequate supply of balanced nutrition to the growing child while simultaneously not exposing the child to potentially harmful substances.

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