Nucleotides may have a role in nutrition of young pigs[1]

Hans H. Stein[2] and Christopher D. Mateo[3]

South Dakota State University, Brookings SD 57007
Department of Animal and Range Sciences

[1] The manuscript was presented at Alltech's 20th Annual Symposium, May 24-26, 2004, Lexinton, KY, and is adapted from an article published in the proceedings from that symposium.
[2] Hans H Stein is an associate professor in monogastric nutrition at South Dakota State University.
[3] Christopher D. Mateo is a PhD. Student in the Department of Animal and Range Sciences at South Daktota State University.

Introduction.

Research in human nutrition has demonstrated that the inclusion of nucleotides in parenteral formulas and infant milk formulas improve intestinal health and the development of the immune system in infants. In contrast, limited information about the need for nucleotides and about the role of nucleotides in the development of the immune system and the intestinal tissue in young animals exist. The objective of the present contribution is to review current knowledge of the roles and functions of nucleotides in young animal feeding.

Nucleotide biochemistry and nomenclature.

Nucleotides are ubiquitous molecules with considerable structural diversity. They are composed of a nitrogenous base linked to a pentose sugar to which at least one phosphate group is attached (Figure 1). The pentose sugar may be a ribose for a ribonucleic acid (RNA) or a 2'-deoxyribose for a deoxyribonucleic acid (DNA). The nitrogenous base can be a purine or a pyrimidine. Pyrimidine bases are composed of six membered rings and comprise uridine, cytosine, and thymine (Table 1). Purine bases have an additional five membered ring and comprise adenine, guanine, and hypoxanthine. The phosphate group may be in a mono, di, or tri phosphate form, and is commonly esterified to the C-5' hydroxyl group of the pentose sugar (Rudolph, 1994).

When the phosphate group is absent, the compound is known as a nucleoside. A chain of nucleotides attached together via a phosphodiester linkage at the 3' and 5'

positions of neighboring ribose units are called polynucleotides or nucleic acids. Nucleic acids conjugated to proteins are called nucleoproteins.

Sources of nucleotides in feed

Nucleotides, particularly IMP, are mainly found in feed rich in protein (Carver and Walker, 1995). Generally, feed ingredients containing cellular elements are potential dietary sources of nucleotides in the form of nucleoproteins. Organ meats, poultry, and seafood are good sources of nucleoproteins (Kojima, 1974; Clifford and Story, 1976; Barness, 1994). Single cell proteins, bakers and brewers yeast, and yeast extract are ingredients that have a relatively high concentration of nucleotides (Maloney, 1998; Ingledew, 1999; Tibbets, 2002). Feed ingredients are not routinely analyzed for their concentrations of nucleotides, but data are available for a few ingredients (Table 2). Most commonly used feed ingredients contain relatively low amounts of nucleotides.

The nucleotide concentration in the milk of lactating mammals is species specific and the concentration of most nucleotides changes during the lactation period (Johke, 1963; Gil and Sanchez-Medina, 1981; Gil and Sanchez-Medina, 1982; Mateo et al., 2004b). Because of these species differences in milk nucleotide concentration, it is possible that the nucleotide requirement may also vary among species, but at this point there are no data available on the nucleotide requirement of animals. The demand for nucleotides increases during periods of stress and rapid growth. Therefore, the requirement may be elevated during the immediate post-weaning period of livestock species. Current research in our laboratory is addressing this hypothesis.

Digestion, absorption, and metabolism of nucleotides.

Dietary nucleoproteins, nucleic acids, and nucleotides need to be enzymatically hydrolyzed prior to absorption because only nucleosides, bases, and small amounts of nucleotides are absorbed. This process takes place in the small intestine. Endonucleases, phosphodiesterases, and nucleoside phosphorylase are the major enzymes involved in this process (Figure 2). These enzymes originate from the brush border epithelium (Markiewicz, 1983; Morley et al., 1987), pancreatic juice (Weickman et al., 1981), and bile (Holdsworth and Coleman, 1975).

The duodenum has the greatest absorptive capacity (Bronk and Hastewell, 1987). Under physiological conditions, nucleotides have a limited capacity to pass through the microvillous membrane of the enterocytes (Sanderson and Youping, 1994). This may be due to the absence of a nucleotide transport system. Nucleotides also have a high negatively charged phosphate group that hinders absorption. Therefore, the nucleoside form is the major vehicle for the entry of purines and pyrimidines into the enterocytes. Nucleoside transport into the enterocyte occurs by facilitated diffusion and by specific Na^+-dependent carrier mediated mechanisms (Bronk and Hastewell, 1987). This is a relatively efficient process and it is believed that more than 90% of dietary nucleosides and bases are absorbed into the enterocyte (Salati et al., 1984; Uauy, 1989). From the enterocyte, partial metabolic products of dietary and endogenous nucleotides and nucleosides enter the hepatic portal vein. These molecules are carried to the hepatocytes for further metabolism. From the liver, partial metabolic products of dietary and endogenous nucleotides and nucleosides are released into the circulations and enter the

muscle tissues. If these products are not reutilized for nucleotide production or not absorbed in a specific tissue, the purine and pyrimidine bases are catabolized into uric acid and ß-alanine or ß-aminoisobutyrate (Rudolph, 1994; Carver and Walker, 1995; Thorell et al., 1996). In avians and in primates, uric acid is excreted in the urine, but in mammals other than primates, uric acid is further catabolized into allantoin via the enzyme uricase. Allantoin is then excreted via the urine. The products of pyrimidine catabolism are ß-alanine and ß-aminoisobutyrate. They are further metabolized into NH_3, CO_2, and Acetyl CoA.

Synthesis of nucleotides.

Humans and animals can synthesize nucleotides de novo via the De Novo Pathway provided that the required precursors are available. This process takes place in the cytocol of hepatocytes where all the enzymes for purine and pyrimidine synthesis are available. The purine IMP is synthesized from α-D-ribose-5-phosphate via a process involving 11 reactions. Glutamine is the N-donor in this proces. Glycine, aspartate, and tetrahydrofolate derivatives are other precursors needed in the synthesis of IMP. Both AMP and GMP are subsequently formed from IMP via adenylosuccinate and xanthosine monophoshate, respectively (Rodwell, 2000). The precursors for pyrimidine synthesis are carbamoyl phosphate and aspartate. The pyrimidine UMP is formed in a process involving 6 reactions. A dephosphorylation of UMP yields UDP which is subsequently turned into CMP or TMP. Glutamine and N^5N^{10}-methylene-folate are needed in the synthesis of CMP and TMP, respectively (Rodwell, 2000). The de novo synthesis of both purine and pyrimidine nucleotides synthesis is a metabolically costly process requiring a

significant amount of energy in the form of ATP. In addition, both reactions require glutamine.

Synthesis of a nucleotide from a nucleoside and an inorganic phosphate group is accomplished via the Salvage Pathway. The nucleosides used in the Salvage Pathway may originate from dietary sources because most dietary nucleotides are changed to nucleosides prior to absorption. The Salvage Pathway may also be used to re-synthesize nucleotides via phosphoribosylation of purines and pyrimidines formed during the catabolism of nucleotides. This pathway may spare energy and allow cells that are incapable of de novo synthesis (i. e., leukocytes, erythrocytes, bone marrow cells, intestinal mucosal cells, and lymphocytes) to maintain their nucleotide pools (Sanderson and Youping, 1994).

Physiological roles of nucleotides.

The concentration of ribonucleotides is relatively constant in all cells, while the concentration of deoxyribonucleotides varies with the stage of the cell cycle (Barness, 1994). Nucleotides are the building blocks for nucleic acids (DNA and RNA). However, nucleotides also have physiological roles in the body such as being a source of energy (i. e., ATP and GTP), cofactors in oxidation and reduction reactions (i. e., FAD, NAD^+, and $NADP^+$), serve as physiological regulators (i. e., cAMP and cGMP), and carry activated intermediates (i. e., UDP-glucose, CMP-sialic acid, and CDP-choline) and acyl groups (i. e., CoA). In addition, nucleotides have been shown to influence the development of the immune system, the microflora of the intestinal tract, and the integrity of the small intestine.

Effects of nucleotides on the immune system

Dietary nucleotide supplementation has been associated with both humoral and cellular immunity, but the exact mechanism has not been elucidated. Dietary nucleotides contribute to the circulating pool of nucleosides available to stimulate leukocyte production (Kulkarni et al., 1994; Carver and Walker, 1995). Therefore, there is an elevated need for nucleotides during periods of immunological challenges.

Infants fed milk formula fortified with nucleotides had better responses to immunization as evidenced by an increase in humoral antibody response (Fanslow et al., 1988; Pickering et al., 1998) and increased cytokine production (Carver et al., 1991). Similar responses to nucleotide supplementation were reported from in vivo experiments with mice (Jyonouchi et al., 1993; Jyonouchi, 1994). Dietary supplementation of purified nucleotides to milk replacers of newborn bull calves challenged with lipopolysaccharide, resulted in calves that tended to have higher mean IgG levels compared to the unsupplemented control calves (Oliver et al., 2002). Nucleotide supplementation also increased lymphocyte stimulation to phytohaemagglutinin and concanavalin-A challenges in weanling piglets by 50 and 30%, respectively (Zomborsky-Kovacs et al., 1998). Results of these studies suggest that dietary sources of nucleotides play a role in developing, maintaining, and enhancing the immune system.

Effects of nucleotides on intestinal microflora

Dietary nucleotides enhance intestinal absorption of iron, affect lipoprotein and long chain polyunsaturated fatty acid metabolism, have trophic effects on the intestinal mucosa and liver, and reduce the incidence of diarrhea (Cosgrove, 1998; Schlimme et al., 2000). The fecal flora of infants fed a nucleotide-supplemented commercial milk formula

had a predominance of bifidobacteria (Tanaka and Mutai, 1980), while enterobacteria dominated in the fecal flora of infants fed a commercial formula without nucleotide supplementation (Uauy, 1994). These studies suggest that nucleotide supplementation may positively influence the microflora in the gastrointestinal tract which leads to a lowering of gastric pH and hinders the proliferation of pathogenic bacterial species as evidenced by a lower rate of diarrhea (Yu, 1998). Recent results from our laboratory suggest that newly weaned pigs fed a nucleotide deficient diet supplemented with nucleosides had elevated quantities of probiotic bacteria and reduced concentrations of *Cl. perfringens* compared to control pigs fed non-supplemented diets (Mateo et al., 2004a).

Effects of nucleotides on intestinal development

Dietary nucleosides may enhance the growth and maturation of intestinal epithelial cells as evidenced by an increased formation of mucosal protein, DNA, taller villi in the small intestine and increased maltase to lactase enzyme ratio (Uauy et al., 1990; Carver, 1994). Dietary nucleotides may also stimulate enterocyte differentiation (Sanderson and Youping, 1994). Parenteral supplementation of nucleic acids supports mucosal cell proliferation and function as demonstrated by increased mucosal wet weight, protein and DNA contents, villous height, but not crypt depth, and narrower tight junctions of the jejunal mucosa width (Kishibuchi et al., 1997; Tsujinaka et al., 1999).

Are dietary nucleotides needed in diets for weanling pigs?

The need for nucleotides is elevated during periods of rapid growth, during periods of stress, and in immuno-compromised animals. In newly weaned pigs, all of

these factors are present – therefore, it is expected that they have a high requirement for nucleotides during the immediate post-weaning period. Because nucleotide synthesis is an energy- and glutamine-requiring process and because newly weaned pigs are often deficient in both energy and glutamine, it is possible that pigs are not able to synthesize sufficient quantities of nucleotides during this period. If this is correct, dietary nucleotides would be expected to have a growth promoting and/or health enhancing effect on newly weaned pigs. In a typical starter diet for weanling pigs, the concentration of 5'CMP is close to the concentration found in the DM of sow's milk during the last half of lactation, but the concentration of 5'AMP, 5'GMP, 5'IMP, and 5'UMP is much lower than in sow's milk (Table 3). Assuming that the concentration of nucleotides in sow's milk represents the requirement of the pigs, it is easily concluded that a starter diet for young pigs is deficient in four of the five nucleotides. It may, therefore, be beneficial to add additional nucleotides to such diets. The results from in vivo as well as in vitro experiments in our laboratory indicate that nucleoside supplementation during the immediate post-weaning period may positively influence the gastrointestinal microflora by decreasing *Cl. perfringens* and increasing *L. acidophilus* and *Bifidobacterium spp.* The implication of this finding is that pigs fed diets supplemented with nucleosides may have improved intestinal health and improved performance.

Conclusion

Nucleotides are molecules with considerable structural diversity. They are composed of a nitrogenous base linked to a pentose sugar to which at least one phosphate

group is attached. Feed or food ingredients containing cellular elements are potential sources of nucleotides. Nucleotides have many important physiological, gastrointestinal, and immunological functions in the body. The exact metabolism of nucleic acids ingested by young animals is unknown. Synthesizing nucleotides de novo is metabolically costly compared to synthesis via the Salvage pathway and requires glutamine. During periods of rapid growth and development, disease challenges, injury or stress, dietary nucleotide supplementation may be beneficial because of the role of nucleotides in developing and enhancing immunity, maintaining intestinal health, and preserving energy. Diets fed to newly weaned pigs and possibly also to other young animals are deficient in nucleotides. At the same time, the intake of glutamine and energy which is required for De Novo Synthesis of nucleotides is low. Therefore, newly weaned animals are in a nucleotide dilemma because they have an elevated requirement for nucleotides, but a low intake of both nucleotides and the precursors needed to synthesize nucleotides. Future research is needed to elucidate if dietary supplementation with nucleotides or nucleosides can enable young animals to overcome this dilemma.

References

Barness, L. 1994. Dietary source of nucleotides-from breast milk to weaning. J. Nutr. 124:128-130.

Bronk, J. R., and J. G. Hastewell. 1987. The transport of pyrimidines into tissue rings cut from rat small intestine. J. Physiol. 382:475-488.

Carver, J. D., B. Pimentel, W. I. Cox, and L. A. Barness. 1991. Dietary nucleotide effects upon immune function in infants. Pediatrics. 88:359-363.

Carver, J. D. 1994. Dietary nucleotides: cellular immune, intestinal and hepatic system effects. J. Nutr. 124: 144-148.

Carver, J. D., and W. A. Walker 1995. The role of nucleotides in human nutrition. Nutr. Biochem. 6:58-72.

Clifford, A. J., and D. L. Story. 1976. Levels of purines in foods and their metabolic effect in rats. J. Nutr. 106:435-442.

Cosgrove, M. 1998. Perinatal and infant nutrition. Nucleotides. Nutr. 14:748-51.

Fanslow, W. C., A. D. Kulkarni, C. T. Van Buren, F. B. Rudolph. 1988. Effect of nucleotide restriction and supplementation on resistance to experimental murine candidiasis. J. Parenter. Enteral. Nutr. 12:49-52.

Gil, A., and F. Sanchez-Medina. 1981. Acid soluble nucleotides of cow's, goat's and sheep's milks at different stages of lactation. J. Dairy Sci. 48:35-44.

Gil, A., and F. Sanchez-Medina. 1982. Acid soluble nucleotides of human milk at different stages of lactation. J. Dairy Res. 49:301-307.

Holdsworth G., and R. Coleman. 1975. Enzyme profiles of mammalian bile. Biochem. Biophys. Acta 389:47-50.

Ingledew, W. M. 1999. Yeast-could you base a business on this bug? Pages 27-47 in Biotechnology in the Feed Industry. Proc. of Alltech's 15th Annual Symposium. T. P. Lyons and K. A. Jacques, eds. Nottingham University Press, Nottingham, UK.

Johke, T. 1963. Acid soluble nucleotides of colostrum, milk, and mammary gland. J. Biochem. 54:388-397.

Jyonouchi, H., L. Zhang, and Y. Tomita. 1993. Immunomodulating actions of RNA and nucleotides on murine lymphocytes in vitro. Augmentation of antibody production to T-dependent antigens and expansion of T-helper cells. J. Nutri. Immunol. 22:5-24.

Jyonouchi, H. 1994. Nucleotide actions on humoral immune responses. J. Nutr. 124:138-143.

Kishibuchi, M., T. Tsujinaka, M. Yano, T. Morimoto, S. Iijima, A. Ogawa, H. Shiozaki, and M. Monden. 1997. Effects of nucleoside and a nucleotide mixture on gut mucosal barrier function on parenteral nutrition in rats. J. Parenter. Enteral Nutr. 21:104-111.

Kojima, K. 1974. Safety evaluation of disodium 5'-inosinate, disodium 5'-guanylate and disodium 5'-ribonucleate. Toxicology 2:185-206.

Kulkarni, A. D., F. B. Rudolph, and C. T. Van Buren. 1994. The role of dietary sources of nucleotides in immune function: a review. J. Nutri. 124:1442-1446.

Maloney, D. 1998. Yeasts. Pages 761-788 in Kirk-Othmer Encyclopedia of Chemical Technology. 4th, ed. J. I. Kroschwitz and M. Howe-Grant, eds. John Wiley and Sons, Inc., New York, NY.

Markiewicz A., M. Kaminski, W. Chocilowski, T. Gomoluch, H. Boldys, and B. Skrzypek. 1983. Circadian rhythms of four marker enzymes activity of the jejunal villi in man. Acta Histochem. 72:91-99.

Mateo, C. D., R. Dave, and H. H. Stein. 2004a. Effects of supplemental nucleosides for newly weaned pigs. J. Anim. Sci. 82(Suppl. 2):42

Mateo, C. D., D. N. Peters, and H. H. Stein. 2004b. Nucleotides in sow colostrum and milk at different stages of. J. Anim. Sci. 82:1339-1342.

Morley, D. J., D. M. Hawley, T. M. Ulbright, L. G. Butler, J. S. Culp, and M. E. Hodes. 1987. Distribution of phosphodiesterase I in normal human tissues. J. Histochem. Cytochem. 35:75-82.

Navarro, J., A. R. Barvo, M. J. Valera, and A. Gil 1996. Modulation of antibody-forming cell and mitogen-driven lymphoproliferative responses by dietary nucleotides in mice. Immunology Letters 53:141-145.

Oliver, C. E., M. L. Bauer, J. W. Schroeder, W. L. Keller, and C. S. Park. 2002. Dietary nucleotides enhance calf immune function. FASEB J. 16:5. (Abstr.)

Pickering, L. K., D. M. Granoff, J. R. Erickson, M. L. Masor, C. T. Cordle, J. P. Schaller, T. R. Winship, C. L. Paule, and M. D. Hilty. 1998. Modulation of the immune system by human milk and infant formula containing nucleotides. Pediatrics. 101:242-249.

Rodwell, V. W. 2000. Metabolism of purine and pyrimidine nucleotides. P. 386-401 in Harpers Biochemistry, 25th edition. Murray, R. K., D. K. Granner, P. A. Mayes, and V. W. Rodwell (Eds.). Appleton and Lange, Stanford, CT.

Rudolph, F. B. 1994. The biochemistry and physiology of nucleotides. J. Nutr. 124:124-127.

Salati, L. M., C. J. Gross, L. M. Henderson, and D. A. Saviano. 1984. Absorption and metabolism of adenine, adenosine-5'-mono-phosphate, adenosine and hypoxanthine by the isolated vascularly perfused rat small intestine. J. Nutr.114:753-760.

Sanderson, I. R., and H. E. Youping. 1994. Nucleotide uptake and metabolism by intestinal epithelial cells. J. Nutr. 124:131-137.

Schlimme, E., D. Martin, and H. Meisel. 2000. Nucleosides and nucleotides: natural bioactive substances in milk and colostrum. Br. J. Nutr. 84:59-68.

Tanaka, R., and M. Mutai. 1980. Improved medium for selective isolation and enumeration of Bifidobacterium. Appl. Environ. Microbiol. 40:866-869

Thorell, L., Sjoberg, L. B., and O. Hernell. 1996. Nucleotides in human milk: sources and metabolism by the newborn infant. Pediatr. Res. 40:845-852.

Tibbets, G. W. 2002. Nucleotides from yeast extract: potential to replace animal protein sources in food animal diets. Pages 435-443 in Nutritional Biotechnology in the Food and Feed Industries. Proc. Alltech's 18th Annual Symposium. T. P. Lyons and K. A. Jacques, eds. Nottingham University Press, Nottingham, UK.

Tsujinaka, T., M. Kishibuchi, S. Iijima, M. Yano, and M. Monden. 1999. Nucleotides and intestine. J. Parenter. Enteral Nutr. 23:74-77.

Uauy, R. 1989. Dietary nucleotides and requirements in early life. Pages 265-280 in Textbook of Gastroenterology and Nutrition in Infancy. E. Lebenthal, ed. Raven Press, Ltd. New York, NY.

Uauy, R. 1994. Nonimmune system responses to dietary nucleotides. J. Nutr. 124:157-159.

Uauy, R., G. Stringel, R. Thomas, and R. Quan. 1990. Effect of dietary nucleosides of growth and maturation of the developing gut in rat. J. Pediatr. Gastroenterology Nutr. 10:497-503.

Weickman, J. L., M. Elson, and D. G. Glitz. 1981. Purification and characterization of human pancreatic ribonuclease. Biochem. 20:1272-1278.

Yu, V. Y. 1998. The role of dietary nucleotides in neonatal and infant nutrition. Sing. Med. J. 39:145-150.

Zomborsky-Kovacs, M., S. Tuboly, H. Biro, L. Bardos, P. Soos, A. Toth, G. Tornyos. 1998. The effect of b-carotene and nucleotide base supplementation on haematological, biochemical and certain immunological parameters in weaned pigs. J. Anim. and Feed Sci. 7:245-251.

Table 1. Nucleotide nomenclature

Base	Product: Nucleoside	Ribo-nucleotide[a]	Deoxyribo-nucleotide[b]	Diphosphate nucleotide[c]	Triphosphate nucleotide[d]
Purines					
Adenine	Adenosine	AMP	dAMP	ADP/ dADP	ATP/ dATP
Guanine	Guanosine	GMP	dGMP	GDP/ dGDP	GTP/ dGTP
Hypoxanthine	Inosine	IMP	-	-	-
Pyrimidines					
Cytosine	Cytidine	CMP	dCMP	CDP/ dCDP	CTP/ dCTP
Uracil	Uridine	UMP	dUMP	UDP/ dUDP	UTP
Thymine	Thymidine		dTMP	dTDP	dTTP

[a]AMP = adenosine 5'-monophosphate; GMP = guanosine 5'-monophosphate; IMP = inosine 5'-monophosphate; CMP = cytidine 5'-monophosphate; UMP = uridine 5'-monophosphate

[b]dAMP = deoxyadenosine 5'-monophosphate; dGMP = deoxyguanosine 5'-monophosphate; dCMP = deoxycytidine 5'-monophosphate; dUMP = deoxyuridine 5'-monophosphate; dTMP = deoxythymidine 5'-monophosphate

[c]ADP = adenosine 5'-diphosphate; dADP = deoxyadenosine 5'-diphosphate; GDP = guanosine 5'-diphosphate; dGDP = deoxyguanosine 5'-diphosphate; CDP = cytidine 5'-diphosphate; dCDP = deoxycytidine 5'-diphosphate; UDP = uridine 5'-diphosphate; dUDP = deoxyuridine 5'-diphosphate; dTDP = deoxythymidine 5'diphosphate

[d]ATP = adenosine 5’-triphosphate; dATP = deoxyadenosine 5’-triphosphate; GTP = guanosine 5’-triphosphate; dGTP = deoxyguanosine 5’-triphosphate; CTP = cytidine 5’-triphosphate; dCTP = deoxycytidine 5’-triphosphate; UTP = uridine 5’-triphosphate; dTTP = deoxythymidine 5’-triphosphate

Table 2. Nucleotide concentration in some commonly used feed ingredients (as is basis)[a]

		Nucleotide (mg/g)				
Ingredient	Nucleotide:	5'CMP	5'AMP	5'GMP	5'UMP	5'IMP
Barley		0.002	0.001	0.001	0.000	0.001
Casein		0.001	0.000	0.000	0.000	0.000
Corn		0.003	0.002	0.003	0.000	0.001
Fish meal		0.026	0.011	0.002	0.001	0.035
Naked oats		0.003	0.003	0.003	0.001	0.001
Plasma		0.002	0.002	0.002	0.000	0.001
Protein plasma, spray dried		0.016	0.008	0.003	0.009	0.002
Red blood cells, spray dried		0.000	0.044	0.003	0.002	0.006
Soybean meal, 44 %		0.016	0.008	0.003	0.009	0.002
Whey, dried		0.270	0.019	0.000	0.001	0.004

[a] Data from Mateo et al. (2004a).

Table 3. Calculated nucleotide concentration of a starter diet for weanling pigs [a]

Item	Nucleotide:	Nucleotide (ppm)				
		CMP	AMP	GMP	UMP	IMP
Total in starter diet [b]		58.99	6.46	2.03	1.00	4.33
Sows milk [c]		56.00	117.50	185.5	2334.50	23.5
Difference		2.99	-111.04	-183.47	-2333.50	-19.17

[a] Adapted from Mateo et al. (2004a).

[b] Diet formulated to contain the following feed ingredients: Corn, 49.32%; Whey powder, 20%, Soybean meal, 8%; Fish meal, 8%; spray dried protein plasma, 7.5%, vitamins, minerals, oil, and crystalline amino acids, 7.18%.

[c] Data from Mateo et al. (2004b).

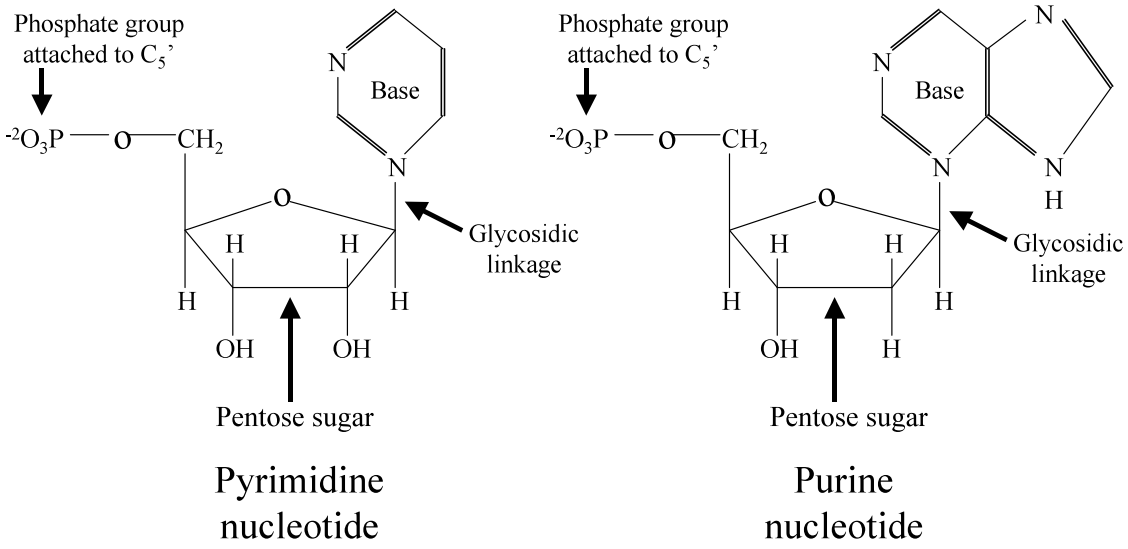

Figure 1. Structure of a nucleotide. C = carbon atom, H = hydrogen atom, O = oxygen atom, and N = nitrogen atom.

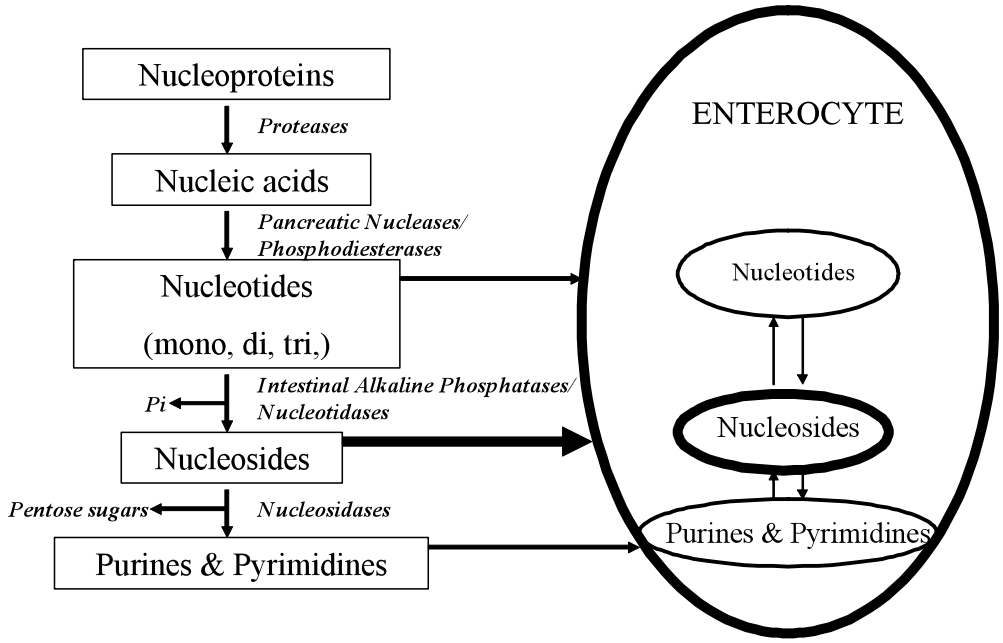

Figure 2**.** Digestion and absorption of nucleic acids and their related products. Adapted from Quan and Uauy, 1991