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Fat newborn
lingual lipase

A Review. Fat Digestion in the Newborn: Role of Lingual Lipase and Preduodenal Digestion

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The neonatal period represents one of the most vulnerable periods in human life, particularly with respect to nutrition. During this period of rapid growth and development, there is a high demand for essential nutrients as well as for an adequate energy supply. At birth, with the sudden transfer from the high carbohydrate diet of the fetus to the high fat diet of the newborn, fat becomes the major energy source for the growing infant. In human milk and in most infant formulas, 45–50% of the total calories are present as fat, although the fat content is only 3.5–4.0% (29, 71). The fat content varies widely in the milk of different species, from 1.9% in the horse to 12 and 17% in the rat or reindeer, respectively; the highest amounts of fat (as much as 50%) are found in the milk of aquatic mammals (29). More than 90% of milk fat is in the form of triglycerides (29) which contain saturated and unsaturated long-chain fatty acids esterified to glycerol (by definition long-chain fatty acids contain more than 14 carbon atoms). The overall process of fat digestion and absorption is dominated by the fact that dietary lipids, in contrast to other nutrients such as carbohydrates and protein, are nonpolar and, therefore, largely water insoluble. Digestion and absorption of dietary fat represents thus a process of transport of water-insoluble molecules from one water phase, the intestinal lumen, to another water phase, the lymph and plasma. During this process, the triglycerides are hydrolyzed to free fatty acids and 2-monoglycerides; these products of lipolysis are more polar than the triglycerides and can be solubilized within the aqueous environment of the intestine. Solubilization is achieved with the aid of bile acids through the formation of mixed micelles containing free fatty acids, monoglycerides, glycerol, and small amounts of nonpolar lipids such as diglycerides, cholesterol, and fat soluble vitamins. The products of lipolysis are taken up by the mucosal cells by passive absorption. Within the intestinal mucosa, long-chain fatty acids are bound by a special protein of low molecular weight (fatty acid binding protein) described recently by Ockner and Manning (59). After activation to acyl-CoA, the fatty acids are reesterified to form triglycerides. The newly synthesized triglycerides are assembled into chylomicrons where they form the nonpolar core of the particles, whereas polar lipids (phospholipid and cholesterol) and newly synthesized protein form the outer envelope. The chylomicrons enter the bloodstream primarily via the lymphatics. Fat digestion has been reviewed recently in several excellent articles (6, 47, 58, 78). This very short summary of the general steps involved in fat digestion and absorption outlined previously seems to stress the predominant role of the intestine in this process. Indeed, in a review on this subject, Johnston (47) stated in 1970 that "dietary triglycerides are not appreciably affected by any of the enzymatic processes involved in the gastrointestinal tract until the fat reaches the small intestine. In the duodenum, the two most important factors in the digestive process, are the intraluminal levels of pancreatic lipase (for fat hydrolysis) and of bile salts (for the solubilization of the lipids before and during lipolysis).

FAT DIGESTION IN THE NEWBORN

Whereas the absorption of dietary fat is very efficient in the adult and only as little as 4–5% of the ingested fat is excreted, this process is much less efficient in the newborn and especially in the premature infant. Fat absorption, measured either by the determination of the fat content of feces collected during 3 or more days on a standardized diet and expressed as a fraction of consumed fat (23, 79) or by determination of the increment in plasma triglycerides after an oral fat load (22), has been shown to be 65–75% in premature and under 85–90% in term newborns. The wide variations in the efficiency of fat absorption in the newborn depend on the type of dietary fat as well as on the functional maturity of the gastrointestinal tract at birth.

Inefficient fat absorption could be due to one or more of the following factors: impaired digestion, impaired solubilization of the products of lipolysis leading to lower uptake by the intestinal mucosa, and/or impaired reesterification within the mucosal cells.

The extensive studies of Koldovsky and his collaborators (48, 66) were among the first to point out the marked discrepancy between the high fat intake and the low activity of pancreatic and intestinal lipases in the newborn. A brief summary of their data (Table 1) shows that, whereas the fat intake is more than twice as high in 10-day-old rats, pancreatic lipase activity is only one-eighth of that in adults.

In more recent studies, Snook (74) and Deschodt-Lankman *et al.* (17) have shown that in the rat, pancreatic lipase activity decreases after birth and rises markedly only after weaning. Similar findings have been reported in human studies. Although zymogen granules and lipase activity have been detected in the fetal pancreas at 4–5 month of gestation (49), pancreatic lipase activity is low in newborns, especially in prematures (16, 28, 57, 83).

In addition to low pancreatic lipase activity, the newborn is unable to maintain adequate bile acid levels. In a series of elegant studies, using nonradioactive deuterium-labeled bile acid, Watkins *et al.* (81) have measured the total body pool of bile acid by an isotope dilution technique. Their studies, summarized in Table 2, have shown that the bile acid pool is reduced in the newborn infant to approximately one-half of the adult values when compared on the basis of body surface area. Values for premature infants between 32–36 wk of gestation were further reduced to approximately one-half to one-third those of the full-term infants (80) (Table 2). The rate of synthesis of bile acids is lower in prematures than in term infants, who in turn have lower synthesis rates than adults (Table 2).

The low pancreatic lipase activity coupled with relative lack of bile acids would indicate a severe inability of the newborn to digest the high amount of dietary fat.

We have at present no information on the capacity of the jejunum of the newborn or premature infant to absorb the products of lipolysis; studies in rats have shown, however, that the absorptive capacity of fatty acids is much higher in the ileum of newborn than of adult rats (45).

In a detailed study of the mucosal phase of fat absorption, Holtzapple *et al.* (45) have investigated the esterifying capacity of the small intestine by evaluating the activity of microsomal enzymes as well as by measuring the capacity of whole slices to convert oleic acid to triglyceride. Their *in vitro* studies have shown that the uptake and rate of esterification of oleic acid by jejunal

Table 1. *Relationship between pancreatic lipase activity and fat intake in newborn and adult rats (66)*

Age	Pancreatic lipase[1]	Fat intake[2]
Suckling, 10 days old	200	6.08
Adult	1700	2.52

[1] U/g pancreas (wet weight).
[2] Cal/100 g body wt/24 hr.

Table 2. *Bile salt synthesis in premature and newborn infants, cholic acid pool size and synthetic rate (80)*[1]

Age	Cholic acid pool (mg/m^2)	Cholic acid synthesis (mg/m^2/day)
Premature[2]	85.5 ± 20.8	34.6 ± 6.4
Full-term	290 ± 36	110 ± 20
Adult	600 ± 20	190 ± 25

[1] Data are mean ± SE.
[2] 32–36 wk gestation.

Table 3. *Fatty acid absorption in the jejunum of newborn rats (45)*[1]

Experiment	6 Days	11 Days	Adult
Fatty acid binding protein,[2] (% of total protein)	16.4 ± 0.9		15.0 ± 2.1
Oleic acid binding (%)[2]	13.9 ± 4.0		10.2 ± 1.0
Oleic acid uptake (nmole/g)[3]	1920	1216	448
Oleic acid esterification[3] (nmole/g)	1100	920	340
Oleyl-Co A synthetase[4] (nmole/mg protein/min)	150 ± 60	150 ± 17	190 ± 53
Acyl-Co A-monoglyceride[4] acyl transferase (nmole/mg protein/min)	150 ± 30	210 ± 66	115 ± 26

[1] The data are mean ± SE.
[2] Measured in the cytosol of jejunal mucosa.
[3] Measured in jejunal slices.
[4] Measured in microsomal preparations of jejunal mucosa.

slices is 3–5-fold higher in suckling than in adult rats (Table 3). The activity of acyl-CoA: monoglyceride acyltransferase was 40–50% higher in microsomal preparations from suckling rats, while the activity of oleyl-CoA synthetase and the amount of fatty acid binding protein was similar in suckling and adult rats.

Because high fatty acid uptake and esterification is directly related to high levels of free fatty acids (72) and monoglycerides (53) within the intestine, it is very difficult to reconcile the marked discrepancy between low intraluminal lipolysis (17, 48, 66, 74) and increased mucosal reesterifying capacity (45) (Table 3). This apparent discrepancy led Henning and Kretchmer (41) to ask whether there is an alternative mechanism for fat digestion in the neonate. Indeed, our studies in rat (34) and man (33, 37), as well as previous studies in ruminants (20, 25–27, 60, 64, 65, 76, 82), have shown that the digestion of dietary fat is initiated in the stomach by a potent lipase secreted from serous glands (von Ebner, 77) located at the base of the tongue. The enzyme probably plays a major role in lipid digestion in the newborn by compensating for the low activity of pancreatic lipase.

INTRAGASTRIC LIPOLYSIS

It is thought that the only role of the stomach in fat digestion is to mix the ingested fat by "churning, kneading, and squirting movements" (5) and, thereby, to help the process of emulsification.

Hydrolysis of fat in the stomach has been observed, however, by a number of investigators dating back to the end of the 19th century (for excellent reviews of the early studies, see References 14 and 48). While the early studies could not exclude contamination by pancreatic lipase as a contributing factor, later studies have definitely established the presence of lipolytic activity within the stomach (Tables 4 and 5).

The importance of the stomach in fat digestion became apparent in studies on the effect of gastrectomy on lipid absorption (52). Although the steatorrhea associated with this condition has been attributed mainly to the faster passage of food through the intestine, the facilitating action of partial fat digestion within the stomach on the further action of pancreatic lipase should not be overlooked (20, 63, 67). The elegant studies of Borgstrom *et al.* (8) in 1957 have shown that considerable lipolysis (10–22%) occurred

Table 4. *Lipolytic activity in gastric contents*[1]

Species	Sample	Age	Reference	Amount hydrolyzed	pH optimum	Reaction products[2] DG	MG	Glycerol	FFA
						% of total glycerides			% TFA
Man[3]	Gastric aspirate	Premature[4]	(37)	56 ± 12	5.0–6.0	30.3	26.3	43	38
	Gastric aspirate	Adult	(33)	240 ± 25	5.4	67.3	25.5	7.2	47
Rat[5]	Gastric contents	Suckling[6]	(34)	830 ± 90	5.4	84.6	19.3	3.8	24
	Gastric contents	Adult	(34)	1850 ± 150	5.4	86.0	14.0		9
Cow[3]	Gastric aspirate	Suckling	(25)	1300 ± 360	6.0				
Dog[7]	Gastric contents	Adult	(18)	5550 ± 1100	4.2–5.5				

[1] Data are mean ± SE.
[2] DG, diglyceride; MG, monoglyceride; TFA, total fatty acids.
[3] Data are nmole/min/ml aspirate.
[4] Premature infants, 30–34 wk of gestation.
[5] Data are nmole/min/g stomach contents.
[6] 3- to 6-day-old suckling rats.
[7] The amount of fatty acids produced was identical in normal dogs and in dogs deprived of pancreatic juice.

Table 5. *Intragastric digestion of dietary fat in man*

Age group	Substrate	pH	Time after feeding	% Hydrolysis FFA % of TFA	Reference
Children	Tributyrin	4.9–5.4	30–60 min	42–67	(70)
	Triolein	4.9–5.4	30–60 min	2.0–2.5	(70)
Adults	Tributyrin	2.2–2.6	30–60 min	47–53	(70)
	Triolein	2.2–2.6	30–60 min	0.2–0.3	(70)
	Corn oil	4.0–5.0	1–4 hr	10–20	(8)
	Human milk fat		60 min	11–26	(19)
	Trioctanoin	4.0–7.0	[1]	21–33	(14)
	Triolein	4.0–7.0	[1]	1–16	(14)
Children	Long-chain triglyceride			50	(55)
Premature infants, 30–34 wk gestation	Isomil 20[2]	4.0–5.5	7 min	10–15	(37)
Adults	Milk fat	4.5–5.5	1–3 min	11–15	(33)
	Corn oil	4.5–5.5	1–3 min	8–10	(33)

[1] Gastric aspirates were incubated *in vitro* 60 min.

[2] Isomil 20, a product of Ross Laboratories, Columbus, Ohio contains 2.1% coconut and 1.4% soy oil; both oils contain more than 80% of the lipid in the form of long-chain triglycerides.

in the stomach content of man (Table 5). Although the authors attributed the lipolytic activity to regurgitated intestinal contents, later studies on gastric aspirates obtained free of duodenal contamination confirmed the presence of lipase activity (1, 14, 55) (Tables 4 and 5). Evidence of marked intragastric lipolysis is present also in other species: in the stomach of the normal dog 30% of the fat was found hydrolyzed 4 hr after feeding (18); because the same level of lipolysis was observed after pancreatic diversion, the lipolytic enzyme was clearly of preduodenal origin (Table 4).

The lipolytic activity in gastric contents differs markedly from pancreatic lipase (4, 6, 7, 10): the pH optimum is lower, in the range of 4.0–7.0 (11, 14, 19, 33, 34, 44, 70), the activity is not stimulated by bile salts, which are sometimes inhibitory (11, 14, 33), is higher on short and medium-chain triglycerides than on long-chain triglycerides (11, 14, 70), and produces mainly partial glycerides and free fatty acids (1, 14, 33, 34) (Tables 4 and 5).

A gastric lipase, demonstrated by histochemical techniques within the mucosa (3) and by lipase assay in whole homogenates of the stomach wall (11), was thought to be the source of the activity in gastric contents. However, the fact that the lipase in gastric mucosa was specific for short-chain triglycerides and had almost no activity on long-chain triglycerides (3, 11), contrasts sharply with the marked hydrolysis of corn oil within the stomach (8, 33, 34) and with the breakdown of triolein in samples of gastric juice free of pancreatic contamination (14) (Tables 4 and 5). Because diversion of oral secretions from the stomach by means of esophageal fistula completely abolished intragastric lipolysis in the rat (34) we have proposed that hydrolysis of dietary fat in the stomach is catalyzed by a lipase secreted from lingual serous glands (77). This assumption is based on the following additional findings: more than 95% of the total lipolytic activity within the oral cavity of the rat was present in lingual serous glands (34), whereas no lipolytic activity was found in the major salivary glands in rat (34) or man (33); the lipolytic activity present in gastric and esophageal aspirates had characteristics similar to those of lingual lipase: low pH optimum (5.0–5.5), activity on long-chain triglycerides, and production of mainly partial glycerides and free fatty acids (31, 33, 34, 37, 69) (Table 6). Several of these characteristics such as maximal activity in the absence of bile salts (31, 33, 37) and sharp rise in enzyme activity immediately after birth (32) (Table 7) indicate that the enzyme might be ideally suited for activity in the newborn. The reaction products, monoglycerides and free fatty acids, are amphiphilic substances that stabilize lipid emulsions (73), and could, thus, help to overcome the partial lack of bile salts in the newborn.

ORIGIN OF ENZYME ACTIVITY

Lingual lipase is present in lingual serous glands (von Ebner, 77), a group of tubuloalveolar glands located beneath the single large circumvallate papilla of the rat (21), or the entire region of the circumvallate papillae (2–9) in man (5). The papillae are found on the proximal dorsal surface of the tongue; the glands are embedded in the underlying muscular tissue and their ducts open at the base of the papillae. Von Ebner's glands have been described in a large number of mammals (15). The fine structure of the glands, studied in the rat (38) and man (31), is similar to that of other exocrine glands (49, 75). The acinar cells are packed with numerous electron-dense, membrane bounded secretory granules that range in size from 400–1700 nm in diameter in the glands of man (31) or rat (38). Lipase activity is contained within the secretory granules (30), and is rapidly released after feeding, and sympathetic or parasympathetic stimulation (30). In ruminants, lipase activity was also present in extracts of glandular tissue from the back and root of the tongue and from the pharyngeal end of the esophagus (64).

Whether there is any connection between taste buds, present in the walls of the circumvallate papillae (5) and the activity of the lingual serous glands, where ducts open into the trough of the papillae (38, 54), is not known at present. A similar proximity of taste buds (54) and lipase (34) containing serous glands exists also in the soft palate (50). In addition, the appearance of taste buds (54) and of lipase activity (32) occurs at the same time in the fetal rat. It has originally been proposed that the function of the serous secretion of von Ebner's gland is to wash out the taste buds "in order to prepare them for new stimuli" (5). Furthermore, Baradi

Table 6. *Hydrolysis of long-chain triglyceride by lingual (oro-pharyngeal) lipase: characteristics of the lipolytic activity*[1]

Species	Source	Age	Reference	Amount hydrolyzed	pH optimum	Reaction products[2] DG	MG	Glycerol	FFA
						% of total glycerides			% TFA
Man	Esophageal aspirate[3]	Newborn[4]	(69)	13.24 ± 10.6	5.4	26.25	28.4	45	36
	Esophageal aspirate[3]	Adult	(33)	53.5 ± 10.3	5.4	75.9	21.0	3.1	43
	Tongue[5]	Adult[6]	(31)	0.30 ± 0.08	4.5–5.5	58.0	7.0	31.6	44
Rat	Tongue[5]	Newborn[7]	(34)	15.0 ± 1.2	4.5–5.5	70.0	18.6	11.6	20
	Tongue[5]	Adult	(34)	66.4 ± 6.0	5.0–5.5	69.0	25.6	5.2	25
Cow	Esophageal aspirate	Newborn[8]	(25)	35.6 ± 6.6	4.5–6.0	67.6	32.4		18

[1] Data are mean ± SE.
[2] DG, diglyceride; MG, monoglyceride; TFA, total fatty acids.
[3] Data are nmole/min/ml aspirate.
[4] Aspirates from the esophageal pouch were obtained from three infants with congenital esophageal atresia.
[5] Data are nmole/min/mg tissue.
[6] Tongue homogenate of post mortem specimens of glandular tissue from the region of the vallate papillae.
[7] 3- to 6-day-old suckling rats.
[8] The aspirate was obtained via esophageal fistula in 2- to 3-wk-old calves; data are μmole/min/ml. Substrate tributyrin.

Table 7. *Characteristics of lingual lipase*

1. Secreted from lingual serous glands (von Ebner); absent from secretions of major salivary glands (parotid, sublingual, mandibular).
2. Site of action: stomach.
3. pH optimum 4.5–5.5.
4. Substrate long-chain triglyceride.[1]
5. Reaction products: diglyceride, monoglyceride, FFA, glycerol.
6. Bile salts not needed for activity.
7. Enzyme activity high in newborns.
8. Sucking and high fat diet stimulate enzyme activity.

[1] In rat and human preparations (31, 34); in the ruminant activity is highest on short-chain triglyceride (27, 64).

and Bourne (2) have suggested that the secretion could be of importance to the sense of taste. Lipase activity is completely absent from the major salivary glands of all species studied (27, 34) including man (33).

LINGUAL SEROUS GLANDS DURING DEVELOPMENT

The structural development of the serous glands of the tongue and of lingual lipase have recently been investigated in the rat (32). The lingual serous glands were initiated in 19- to 20-day fetuses as epithelial ingrowths from the vallate and foliate papillae (gestation in the rat is 22 days). Lipase activity was first detected in 20-day-old fetuses and increased 14-fold by birth. The only serous cells containing appreciable numbers of secretory granules and exhibiting signs of exocytosis were the demilune cells of the lingual mucous glands (Fig. 1). The data suggest that lipase activity detectable in the tongues of 20-day-old fetuses originates predominantly in the demilune cells of the mucous glands. During the first suckling period, lipase activity decreased by 50%, presumably due to the release of stored enzyme, because no decrease in enzyme activity was noted in animals removed from the mother immediately after birth. By the second postnatal day, the activity had returned to birth levels and continued to rise exponentially thereafter.

Beginning at 3–4 days postnatally, synthesis and storage of enzyme by the differentiating lingual serous glands probably contributes to the rapid rise in lipase levels. The developmental pattern of lingual lipase thus differs markedly from that of pancreatic lipase. Although both enzymes are present in the fetus (9, 32, 49, 69), pancreatic lipase activity decreases sharply after birth and remains low until weaning (16, 17, 74), whereas lingual lipase activity rises rapidly after birth (32), reaching adult activity levels at 17 days (before weaning).

The secretion of a potent lipase in the proximal part of the oral cavity raised the question whether aspiration of saliva (a frequent occurence in the newborn) could lead to breakdown of lung surfactant, a complex phospholipid that lines the alveoli and is essential for normal lung function (12). Because lecithin is the major component of surfactant (12), we have tested whether it is a substrate for lingual lipase. The complete lack of activity on lecithin (Hamosh *et al.*, unpublished observations) agrees well with the studies of Paltauf *et al.* (61), who showed that lingual lipase attacks the Sn-3 position of triglycerides twice as fast as the Sn-1 position. The presence of the phosphoryl-choline group at the Sn-3 position probably completely prevents enzyme activity.

INTRAGASTRIC DIGESTION IN SUCKLING RUMINANTS

The most thorough studies of intragastric digestion of dietary fat have been conducted in ruminants. These studies have been addressed to the origin of the lipolytic enzyme (60, 64, 65, 76), the regulation of enzyme secretion by factors such as suckling (27, 51, 64, 82) and amount of fat in the diet (27), as well as the possible facilitating action of partial digestion by lingual lipase on further lipolysis by pancreatic lipase (20). In earlier studies, Ramsey and Young (65) and Otterby *et al.* (60) have compared the extent of lipolysis of whole-milk diets given orally or introduced directly into the abomasum (the equivalent of the stomach in nonruminants) and have concluded that a salivary lipase, which they called pregastric esterase was primarily responsible for the hydrolysis of milk fat. The techniques used in these studies did not, however, rule out the possibility that part of the lipolytic activity originated in secretions of the abomasal mucosa or from pancreatic lipase in regurgitated duodenal contents. Definite proof that the lipolytic activity originates in the oral cavity comes from recent studies of Toothill *et al.* (76) who found no lipolytic activity in secretions obtained from innervated pouches of the abomasum. Because in ruminants the only tissues containing lipase activity are those in and around the base of the tongue (64), one may conclude that they are the source of the lipase active in the abomasum of the preruminant calf.

The high lipolytic activity in suckling calves is probably a temporary adaptation to the high fat content of milk. Ruminants normally consume low fat diets and are not particularly well

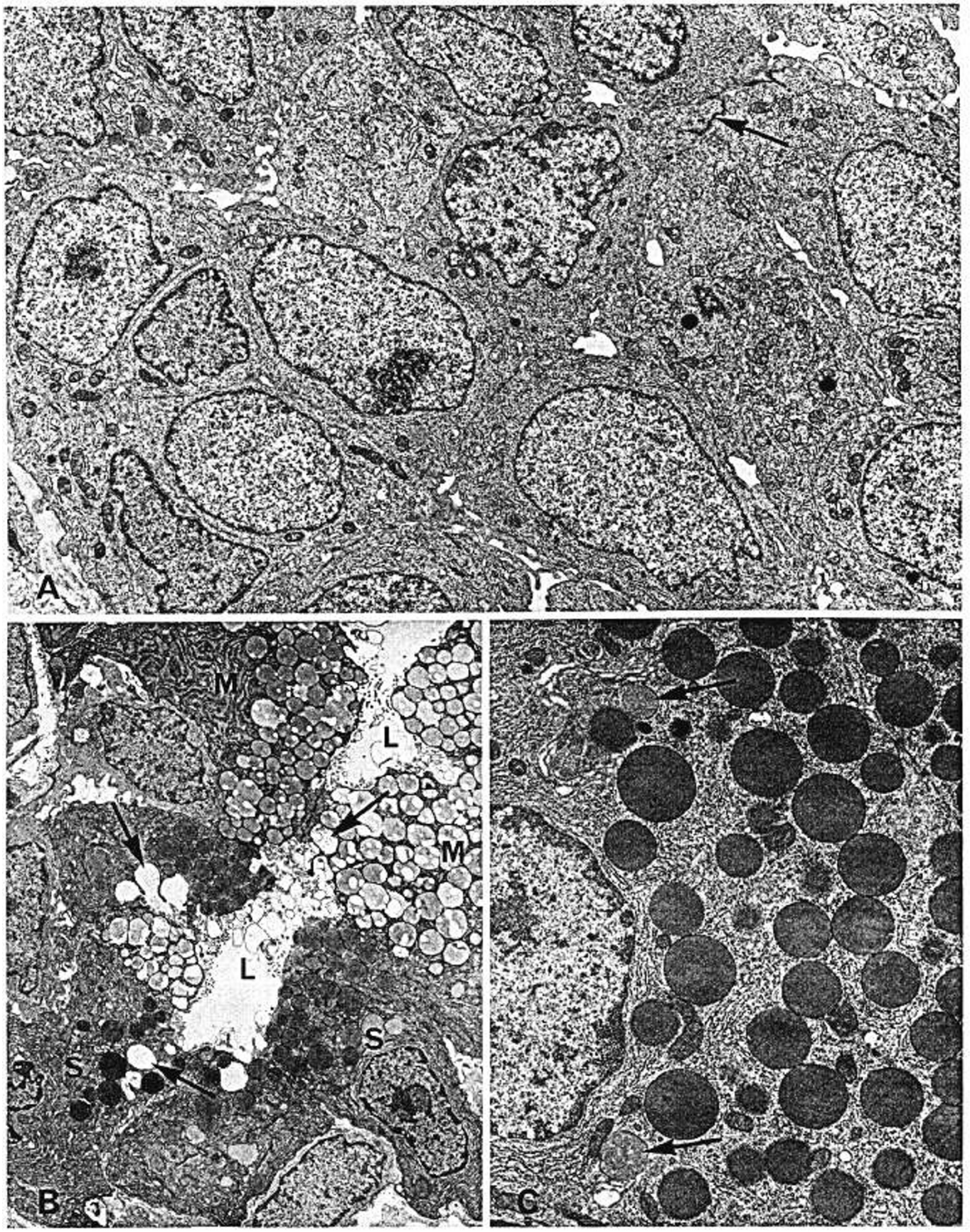

Fig. 1. *A.* Epithelial cells of the developing lingual serous glands of a newborn rat. The cells are filled with free polyribosomes, but have little rough endoplasmic reticulum, a small Golgi apparatus, and no secretory granules. A lumen is just beginning to form (*arrow*). ×5700. *B.* Mucous (M) and serous (S) cells from the posterior lingual mucous glands of a 1-day-old rat. Both cell types have numerous secretory granules, abundant rough endoplasmic reticulum, and a well-developed Golgi apparatus. The lumina (L) are large and filled with discharged secretory material and membranous debris. Both cell types show evidence of exocytosis (*arrows*). ×3900. *C.* Lingual serous gland acinar cell from a 6-wk-old rat. The cytoplasm is filled with rough endoplasmic reticulum and dense homogenous secretory granules. Immature granules (*arrows*) are present in the Golgi region. ×10000. The electronmicrographs are courtesy of Dr. Arthur R. Hand.

Table 8. *Lipid digestion in the absence of pancreatic lipase in calves*[1,2] *(26)*

Pancreatic juice	Lipid fractions in jejunal contents of milk-fed calves (% of total lipids)			
	Triglyceride	Diglyceride	Monoglyceride	Free fatty acids
Absent	53.0 ± 1.7	15.4 ± 0.7	12.8 ± 0.5	18.8 ± 0.7
Present	39.8 ± 1.6	18.4 ± 0.9	14.2 ± 1.2	27.6 ± 1.1

[1] The data are mean ± SE.

[2] Lipid digestion was studied in four calves fitted with a shunt between the pancreatic duct and duodenum and an additional cannula in the upper jejunum approximately 1 m distal to the entrance of the pancreatic duct.

Table 9. *Lipid absorption in the absence of pancreatic lipase in calves*[1,2] *(26)*

	Pancreatic juice	
	Absent	Present
Long-chain TG-FA[3] fed (g)	66.8 ± 3.8	72.4 ± 5.9
Dietary long-chain fatty acid absorbed (g)	46.0 ± 2.1	69.9 ± 6.3
Efficiency (%)	69.1 ± 3.3	96.5 ± 3.1

[1] Data are mean ± SE.

[2] The quantity of lipid absorbed into lymph during normal flow of pancreatic juice and during pancreatic deprivation was studied in six calves with shunts established between the thoracic duct and the left common jugular vein as well as between the pancreatic duct and the duodenum.

[3] Triglyceride - fatty acid.

adapted to digest fat. In addition, continuous suckling is probably an important stimulus for high enzyme activity. Lipolytic activity in oral tissues (64) and in salivary secretions, collected either via an esophageal fistula or directly from the mouth (27, 65), was higher in young calves and declined sharply as the animals became older. Moreover, feeding of milk via a nipple maintained high lipase activity in 4-yr-old steers (51). The importance of intragastric lipolysis to the overall digestion and absorption of dietary fat in the preruminant calf is stressed by the careful studies of Gooden and Lascelles (26) who found that after the diversion of pancreatic secretions, 47% of milk fat entered the ileum digested to partial glycerides and free fatty acids, compared to 60% in intact calves (Table 8). Furthermore, 70% of long-chain triglyceride-fatty acids were absorbed in the absence of pancreatic juice (Table 9). The very efficient digestion and absorption of dietary fat (96.5%) in normal calves is probably the result of the combined action of lingual and pancreatic lipase. Recent *in vitro* studies have shown that the release of fatty acids by pancreatic lipase was enhanced by preincubation of milk fat with salivary lipase (20). The combined action of the two lipases may be of considerable importance to the very young calf, because the level of pancreatic lipase activity is low at this age (46).

FAT DIGESTION IN THE NEWBORN

Considerable hydrolysis of milk triglyceride to partial glycerides and free fatty acids occurs in the stomach of suckling rats (36, 40) and of newborn premature and term infants (37, 69) (Table 5). Information on the mechanism of fat digestion in the stomach of the newborn is based mainly on studies in rats. In young (3- to 10-days-old), fed rats, the stomach is distended by a milk clot that is solid in the fundic region and semisolid in the anthral part of the stomach (62). The pH within this milk clot is usually 5–6, dropping in the pyloric region to 3.5–4.5 (34, 39). This suggests that there is very little peptic activity (pH optimum 2–3) within the milk clot. One may assume, therefore, that lingual lipase, mixed with the ingested milk before swallowing, has optimal lipolytic conditions within the stomach. Sucking probably facilitates enzyme secretion from lingual serous glands. The intermittent changes in pressure (negative during suck and positive during swallow) probably enhance the emptying of the serous secretion, whereas bolus accumulation in this area facilitates mixing of milk and enzyme. Initial digestion by lingual lipase could markedly enhance the hydrolysis of milk fat because milk fat droplets are not a good substrate for human pancreatic lipase (14). Indeed, our recent studies have shown that after exclusion of lingual lipase, there is marked reduction of intragastric hydrolysis of milk fat in rats, leading in turn to lower lipolysis in the duodenum and jejunum (63). In addition, our initial assumption that partial hydrolysis within the stomach is essential to proper emulsification of dietary fat (33) has recently been confirmed by Roy *et al.* (67) who showed that fat absorption dropped from 88.5 ± 7.5% in normal to 59.7 ± 7% in rats with esophageal fistula. The difference between the two groups was almost abolished when the fat meal was presented as a fine emulsion.

A recent study confirms the importance of intragastric lipolysis in fat digestion of premature infants (68). A comparison of fat absorption in two groups of infants of 30 wk gestational age showed much lower fat excretion (14.9 ± 1.7% of ingested fat) in nasogastric fed infants than in a nasojejunal fed group (23.0 ± 2.9% ingested fat). Very high intragastric lipolysis and absorption of more than 50% of dietary fat have recently been described in a case of congenital pancreatic lipase deficiency (55). The observations suggest that in the absence of pancreatic lipase, intragastric lipolysis can compensate efficiently in the digestion and absorption of dietary fat.

The presence of lipase activity in esophageal pouches of infants with congential esophageal atresia indicates that enzyme activity in infants as in adults probably originates in the lingual serous glands; lipase activity in gastric aspirates of these children indicates, however, that lipolytic activity probably originates, concomitantly also within the stomach (69). Whether fat digestion in the newborn could, in addition, be aided by lipases in the intestinal mucosa or in milk is unknown at present. The intestinal mucosa contains several lipases (13, 56) among them an "acid lipase" that is substantially higher in suckling than in adult rats (13); however, the physiologic significance of these enzymes has not been defined. Although milk contains two lipases, lipoprotein lipase (35, 43) and bile salt-stimulated lipase (24, 42), it is doubtful that the former participates in the digestive process because it is inactive in the absence of serum proteins, whereas the role of the latter remains to be tested.

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