Critical Review

D-Lactate in Human and Ruminant Metabolism

Julia B. Ewaschuk,* Jonathan M. Naylor,† and Gordon A. Zello*[1]

*College of Pharmacy and Nutrition and †Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, SK, Canada S7K 5C9

ABSTRACT D-Lactate is normally present in the blood of mammals at nanomolar concentrations due to methylglyoxal metabolism; millimolar D-lactate concentrations can arise due to excess gastrointestinal microbial production. Grain overload in ruminants, short-bowel syndrome in humans, and diarrhea in calves can all result in profound D-lactic acidemia, with remarkably similar neurological manifestations. In the past, D-lactate was thought to be excreted mainly in the urine, and metabolized slowly by the enzyme D-α-hydroxy acid dehydrogenase. More recent studies reported that mammals have a relatively high capacity for D-lactate metabolism and identified a putative mammalian D-lactate dehydrogenase. A growing body of literature is also emerging describing subclinical elevation of D-lactate as an indicator of sepsis and trauma. This article describes advances in the understanding of D-lactate metabolism, D-lactic acidosis in ruminants and humans, and subclinical elevation of D-lactate. J. Nutr. 135: 1619–1625, 2005.

KEY WORDS: • *D-lactate* • *metabolism* • *acidosis* • *ruminants* • *humans* • *diarrhea*

New developments in the understanding of mammalian D-lactate metabolism and D-lactic acidosis, along with several recent articles suggesting the use of plasma D-lactate concentration as a clinical diagnostic tool, indicate the need for a comprehensive review of D-lactate biochemistry.

Lactate, or 2-hydroxypropanoate, was discovered in 1780 by a Swedish chemist, Scheele, who isolated it from sour milk (1). Lactate is the simplest hydroxycarboxylic acid and exists as 2 stereoisomers, or enantiomers, due to its asymmetric C2 atom (**Fig. 1**). Typically, an enantiomer that rotates light in the clockwise direction is called D, for dextrorotary, and the enantiomer that rotates light counterclockwise is called L, for levorotary. An alternative classification uses + and − based on the similarity of the molecule to the 2 chiral forms of glyceraldehyde. Usually the (+) and D categorizations are the same for a chiral molecule; however, lactate is an exception to these rules, with a levorotary D-isomer and a dextrorotary L-isomer. Both enantiomers have similar physical and chemical properties (2). Lactate has a p*K* of 3.86 and dissociates freely at physiological pH, yielding a lactate ion:lactic acid ratio of 3000:1.

Normal serum lactate concentration is ~1–2 mmol/L and is considered entirely L-lactate because lactate produced by mammalian cells is nearly all of this form, with the exception of D-lactate formed in nanomolar concentrations via the methylglyoxal pathway. Exogenous sources of D- and L-lactate include fermented foods such as sauerkraut, yogurt, and pickles, and microbial fermentation in the colon, which typically do not pose an acid-base threat (3–5).

L-Lactic acidosis is relatively common, occurring primarily as a result of tissue hypoxia, but also due to drugs and toxins, inborn errors of metabolism, and underlying disease states (6). D-Lactic acidosis is a less common occurrence; however, there are several circumstances in which D-lactate can become elevated in the blood in both ruminants and humans. This review discusses these scenarios and describes the recent studies of subclinical D-lactate elevation in diabetes and as a marker of sepsis, ischemia, and trauma.

Biochemistry and metabolism of D-lactate

Metabolism and excretion. Serum D-lactate concentration in healthy adults ranges from 11 to 70 nmol/L (5,7–9). Urine excretion is ~0.1 μmol/h (10). D-Lactate excretion is highest in y 1 of life and decreases by age 4 y (11).

L-Lactate is rapidly metabolized to pyruvate by L-lactate dehydrogenase in the liver, but mammals were reported to lack D-lactate dehydrogenase (10,12,13). D-Lactate is thought to be metabolized to pyruvate instead by the enzyme D-α-hydroxy acid dehydrogenase (EC 1.1.99.6), which metabolizes D-lactate at about one-fifth the rate that L-lactate dehydrogenase metabolizes L-lactate (14). Until recently, D-lactate dehydrogenases had been isolated only in lower organisms (15,16), but new studies identified putative human and murine mitochondrial D-lactate dehydrogenases (EC 1.1.1.28) (17,18). Bovine and rat tissues possess considerable D-lactate utilization in vitro (19,20). In humans, parenteral infusion of DL-lactate (3.0 mmol/kg) causes increases in pyruvate, alanine, 3-hydroxybutyrate, and acetoacetate (10).

D-Lactate is anaplerotic because its transport into the mitochondrial membrane results in the shuttling of oxaloacetate and malate to the cytosol (17). The transport of D-lactate from the cytosol to the mitochondrial matrix allows D-lactate to be oxidized by the putative D-lactate dehydrogenase, which is

[1] To whom correspondence should be addressed.
E-mail: Gordon.Zello@usask.ca.

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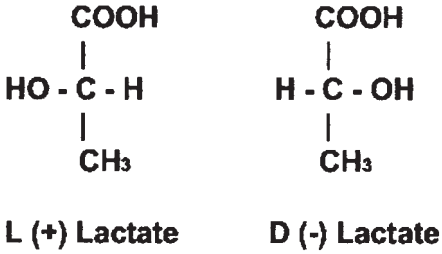

FIGURE 1 Lactate enantiomers.

located on the inner face of the inner mitochondrial membrane (17). Three novel transporters have been identified that shuttle D-lactate across the mitochondrial membrane: the D-lactate/H^+ symporter, the D-lactate/oxoacid antiporter, and the D-lactate/malate antiporter (17).

Controversy regarding the metabolism and excretion of D-lactate in mammals exists in the literature. Conventional opinion is that D-lactate is not well metabolized by mammals and is excreted mainly in the urine (11,13,21–25). This is based largely on Cori's experiments in the late 1920s (26), confirmed 40 y later (27), demonstrating that D-lactate is poorly metabolized and 30–40% of ingested D-lactate is excreted in the urine, compared with none of the L-isomer. Experiments in the 1980s and 1990s, using either D-lactate or ^{14}C-labeled D-lactate, refuted the earlier results and established that D-lactate is indeed readily metabolized (12,28–30), although the former results continue to be quoted frequently and pervade the current literature.

In humans (n = 10) infused with 1.0–1.3 mmol sodium DL-lactate/(kg · h), ~90% of D-lactate was metabolized, and 10% excreted in the urine (12). At higher infusion rates of 3.0–4.6 mmol/(kg · h), metabolism decreased to ~75% of overall clearance (12). de Vrese et al. (28) determined a half-life of 21 min for D-lactate in the blood of healthy humans given an oral load of 6.4 mmol/kg. Doubling this dosage increased the half-life of D-lactate to 40 min, most likely reflecting the saturation of D-lactate metabolism. Contrary to earlier studies, only 2% of administered D-lactate in that experiment was excreted in the urine in the 24 h after ingestion (28). In rats administered ^{14}C-labeled D-lactate, 3.7% of the total dose was excreted renally, with exhalation of $^{14}CO_2$ accounting for 85% of excretion (29). The dosage in that study (300 μmol sodium D-lactate/rat) was lower than in Cori's experiment (19 mmol/kg body weight), and was administered both orally and i.p., rather than by gavage, making comparison difficult. Nevertheless, when the dosage (13.4 mmol/kg) and method of administration (i.g.) were accounted for in an ensuing experiment, still only 0.9% of the total dose was excreted renally and 2.4% excreted as metabolites, with exhalation of $^{14}CO_2$ accounting for 30–45% of excretion (30); 54–68% of administered ^{14}C was not recovered, likely representing D-lactate metabolized to pyruvate or acetyl CoA and unabsorbed D-lactate, which was excreted in the feces or metabolized by microbes (30). The method of administration accounted for considerable differences in metabolism and excretion, with parenteral infusion resulting in much less unrecovered ^{14}C (8%) than enteral administration (54–68%) (30).

One explanation for the disparities between the very early experiments and the more recent ones is advances in methodologies available for D-lactate analysis, from early nonstereoselective colorimetric assays with low sensitivity (31,32), to more current stereospecific HPLC and capillary electrophoretic methods (33–36). Furthermore, species differences in D-lactate metabolism have been observed. Renal reabsorption of D-lactate in humans is not as efficient as it is in dogs (12,37). D-Lactate is considered a physiological isomer in coprophagous animals because high rates of gastric D-lactate production were reported in rats and rabbits (29). Even between these 2 species, differences were observed in oxidation rate and renal excretion of D-lactate (29). Rats were used in numerous studies defining D-lactate metabolism (17,20,26,29,30,38), and perhaps have less relevance to other species than expected. Stable isotopic investigations could clarify human metabolism of D-lactate.

D- and L-Lactate mutually interfere in renal absorption (12). Even at high doses, L-lactate reabsorption always exceeds 70%, and D-lactate reabsorption never exceeds 50%, even at very low dosages (12). At D-lactate plasma concentrations higher than 3.0 mmol/L, renal tubular reabsorption of D-lactate decreases by as much as 30% (12). Reabsorption of lactate occurs against an electrochemical gradient, which indicates active reabsorption (9). Both L- and D-lactate appear to use the same sodium cotransport system, which may contribute to the mutual interference between L- and D-lactate reabsorption (12). Renal tubular reabsorption of lactate is reduced by increased urine volume (39). Oh et al. (12) proposed that D-lactic acidosis may be more prevalent in volume depletion.

D-Lactate is transported into and out of various tissues via the proton-dependent monocarboxylate transporters (MCT-1 to MCT-8)[2] (40). MCTs are expressed in most tissues, were identified in retina, muscle, kidney, brain capillary endothelial cells, cardiac myocytes, enterocytes, hepatocytes, erythrocytes, thymocytes, placenta, and nervous tissue, and have been reviewed extensively (40,41). D-Lactate is absorbed by the small intestinal and colonic epithelial cells (42,43) by MCT-1, which exhibits an uptake coefficient for L-lactate twice that for D-lactate and mutual inhibitory effects (44). Both saturable and nonsaturable absorptive processes are present in rat jejunum (45). The saturable process has a higher affinity for L-lactate than D-lactate, whereas no difference is present between the isomers for the nonsaturable process (45).

D-Lactate may be implicated in the development of metabolic bone disease in patients administered long-term parenteral nutrition for malabsorption. In a study of patients administered total parenteral nutrition for a mean of 74 mo, 2 of 27 subjects had elevated blood D-lactate (1.1 and 2.8 mmol/L). Only those 2 subjects had evidence of osteomalacia; vitamin D, phosphate, aluminum and calcium concentrations were normal (46). Further studies are required to confirm this association and identify the mechanism involved.

Methylglyoxal pathway. Methylglyoxal is produced in small amounts from carbohydrate, fat, and protein metabolism (**Fig. 2**). Due to its reactive and toxic nature, methylglyoxal must be eliminated from the body (47). The glyoxalase pathway is a biochemical process that catalyzes the conversion of methylglyoxal to D-lactate and glutathione via the intermediate *S*-D-lactoylglutathione by 2 enzymes: glyoxalase I and glyoxalase II (48,49) (Fig. 2). It is a ubiquitous reaction in biological life, taking place in the cytosol of cells and organelles, especially the mitochondria (49). D-Lactate can be used as an indicator of methylglyoxal and is much easier to measure than the unstable methylglyoxal (50).

Serum D-lactate values reported in studies of the methylglyoxal pathway are typically micro- or nanomolar, and generally do not contribute to acidemia. However, after high-dose

[2] Abbreviations used: MCT, monocarboxylate transporters; $PgCO_2$, gastric intramucosal CO_2 partial pressure; SBS, short-bowel syndrome.

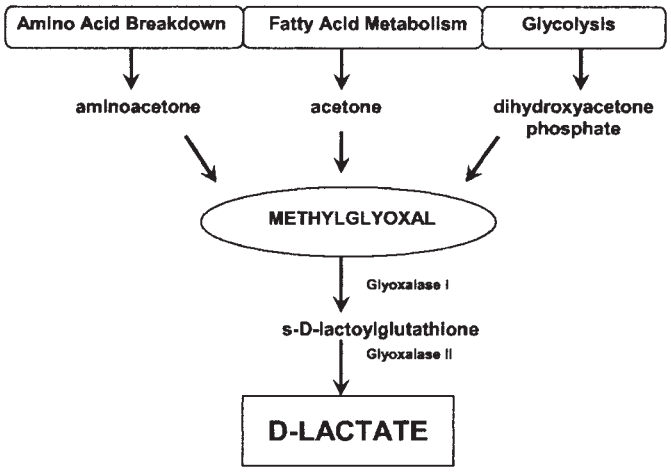

FIGURE 2 Methylglyoxal pathway.

(8 g/kg), long-term (22 d) ingestion of propylene glycol in cats, serum D-lactate concentrations reached 7 mmol/L, demonstrating that methylglyoxal metabolism, under extreme conditions, can result in D-lactic acidosis (51) (**Fig. 3**).

Gastrointestinal production. D-Lactate is normally produced in the fermentative organs of the gastrointestinal tract (rumen, cecum, colon), mainly by lactobacilli and bifidobacteria. Under normal circumstances, lactate does not pose an acid-base threat because it is converted by other microbes to acetate and other SCFAs (13). The major benefit of these organic acids in the gastrointestinal tract is to provide a fuel for oxidative metabolism and ion pumping for mucosal cells of the colon (13). Absorbed propionate is cleared by the liver and is converted to glucose, triglycerides, or carbon dioxide, and butyrate is oxidized by colonic mucosal cells for ATP production (4). The colon is protected from large influxes of carbohydrate by regulation of gastric emptying and effective small intestinal digestion and absorption.

D-Lactic acidosis

D-Lactic acidosis is a rare metabolic occurrence in humans, but is occasionally observed as a consequence of short-bowel syndrome (SBS). It also occurs in ruminants after grain overfeeding, inappropriate ruminal fermentation of milk, and as a sequela to diarrhea in neonatal calves. Recently we identified severe D-lactic acidosis in a cat with pancreatic insufficiency, a finding which is particularly interesting because cats are true carnivores (52). D-Lactic acidosis has been defined as metabolic acidosis accompanied by an increase in serum D-lactate $\geq$ 3 mmol/L (53). D-Lactate production, accumulation, and acidosis are caused by excessive gastrointestinal fermentation of carbohydrate by lactobacilli, or by endogenous production from ingested ethylene glycol, and the subsequent inability of the body to adequately clear D-lactate.

Short-bowel syndrome. A variety of disorders require surgical intervention, including congenital defects, necrotizing enterocolitis, morbid obesity, midgut volvulus, gangrene, and trauma. Patients who have had extensive resectioning of the small bowel, leaving behind a bowel $<$ 150 cm in length are at risk for various metabolic and nutritional disturbances and are classified as having SBS (54). SBS causes impairment of digestion of protein, fat, carbohydrate, vitamins, fluid, electrolytes, and minerals (54). Diarrhea, dehydration, acid/base disturbances, and nutrient deficiencies are common, and often necessitate total parenteral nutrition (54). D-Lactic acidosis in SBS was first described in 1979 (55).

D-Lactic acidosis is associated with neurotoxic effects, and symptoms manifest at serum concentrations $>$ 2.5–3 mmol/L (53). Patients with D-lactic acidosis have neurological dysfunction characterized by ataxia, slurred speech, and confusion, in association with a high anion gap metabolic acidosis (54,56). Patients may also have episodes of somnolence, hallucinations, clumsiness, nystagmus, blurred vision, ophthalmoplegia, disorientation, dizziness, lethargy, excessive irritability, and abusive behavior, which may last from a few hours to several days (53). In one study, 16 of 33 patients who had jejunoileal by-pass reported symptoms consistent with D-lactate encephalopathy after surgery (57). Jejunoileal by-pass is no longer widely practiced as a bariatric surgery, due to severe metabolic and nutritional consequences (58).

The pathogenesis of D-lactic acidosis in SBS is well elucidated (59). A short or bypassed small intestine causes poor digestion of carbohydrate, which leads to the delivery of sugars to the colon. Initially, increased organic acid production results, reducing pH in the colonic lumen. This acidic environment permits acid-resistant lactobacilli to grow preferentially, with the fermentative production of both D- and L-lactate. D-Lactate accumulates systemically, following the absorption of both enantiomers (59). When the rate of D-lactate production exceeds the body's capacity for metabolism and excretion, D-lactic acid accumulates in the blood and acidemia and metabolic acidosis result. Some lactobacilli also produce the enzyme DL-lactate racemase, which further contributes to excess D-lactate by converting L-lactate to D-lactate (23,59).

Treatment of D-lactic acidosis in SBS involves bicarbonate and fluid infusion, avoidance of carbohydrates, and administration of oral nonabsorbable antibiotics. Although widely used, antibiotics can induce D-lactic acidosis in SBS patients by promoting overgrowth of resistant D-lactate–producing microbes (60). Rapid resolution is possible with abrupt cessation of oral intake (22,61). Long-term parenteral nutrition is often administered, until adaptation of the residual small intestine allows enteral nutrition (22). Avoiding consumption of *Lac-*

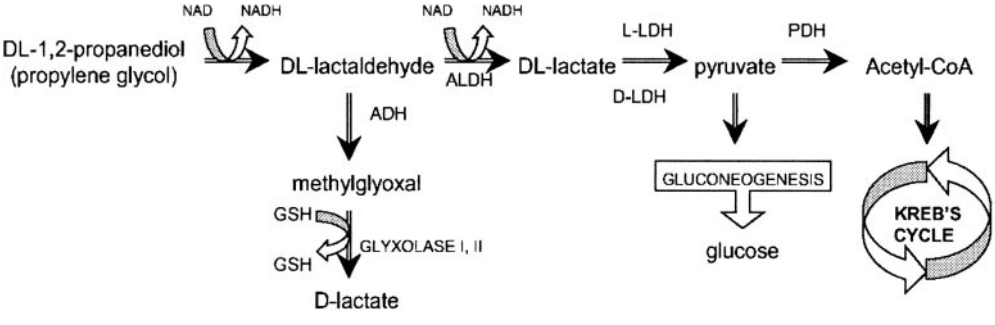

FIGURE 3 Propylene glycol metabolism. ADH, alcohol dehydrogenase; ALDH, aldehyde dehydrogenase; GSH, reduced glutathione; PDH, pyruvate dehydrogenase, L-LDH, L-lactate dehydrogenase; D-LDH, putative D-lactate dehydrogenase.

tobacillus acidophilus has been recommended (55), and replacing existing lactobacilli with probiotic species that produce only L-lactate was successful recently (62,63). Although no data exist at this time on this subject, it may also be prudent for SBS patients to avoid prebiotics.

The neurological symptoms observed in D-lactic acidosis are not well understood, and further research is required in this area. Other types of acidosis, including L-lactic acidosis, do not present with such symptoms, suggesting that D-lactate itself may be neurotoxic. D-Lactate is capable of crossing the blood-brain barrier (64), and was shown to be present in the cerebrospinal fluid of a patient with D-lactic acidosis (65). Entry into the brain is via diffusion through a nonsaturable mechanism (66). Alternatively, other products of excess microbial fermentation may yield these symptoms; possibilities include formate, succinate, histamine, tyramine, endotoxins, and ethanol, although the latter was not found in the blood of SBS patients (53,57,67). The origin of D-lactic acidosis–associated encephalopathy remains dubious.

Ruminal acidosis. The colon and the rumen are both fermentative organs, with comparable pH, flora, and redox potential (68). Much like D-lactic acidosis in SBS, ruminal acidosis results from excessive fermentation of carbohydrates by anaerobic microbes in the rumen and is reported extensively in cattle (67,69–71), and also in sheep, goats, camelids, and buffalo (67,72–74).

Deliberate or accidental overfeeding of grain or sugar-containing feeds to ruminants results in severe D-lactic acidosis, which may be either acute or chronic. Acute ruminal acidosis causes damage to the ruminal and intestinal epithelia with subsequent dehydration. Chronic acidosis causes a reduction in intake, nutrient absorption, and performance (70). An overload of easily digestible carbohydrates in the rumen and subsequent overfermentation results in increased production of SCFAs and DL-lactate (8,71). Ruminal DL-lactate concentrations may exceed 300 mmol/L, and result in serum DL-lactate concentrations of up to 25 mmol/L (71). High serum D-lactate concentrations are associated with neurotoxicity and typical symptoms of ataxia, lethargy, and nystagmus (67,71). Colonic fermentation may also contribute to acidemia in overfed ruminants (75).

Treatment of ruminal acidosis generally involves withholding of feed. Inhibiting lactate-producing microbes, or enhancing those that consume lactate using probiotic strains are strategies gaining popularity (70,76).

Neonatal calves, like adult ruminants, have a 4-chambered stomach, consisting of the rumen, reticulum, omasum, and abomasum. The reticulorumen of the calf is generally nonfunctional until ~28 d of age, and liquid food passes directly into the abomasum via the esophageal groove. D-Lactic acidosis is a major component of acidemia in calves diagnosed as ruminal drinkers (77,78). It is postulated that pooling of milk in the rumen, either as the result of excessive intake or malfunction of the esophageal groove, leads to ruminal fermentation of lactose and D-lactic acidosis. Recently, severe systemic D-lactic acidosis was demonstrated to occur in young calves administered 3 L/d of milk intraruminally (79).

Controversy exists regarding the capacity of the rumen to absorb lactate. Both in vitro and in vivo studies indicate a high concentration of D- and L-lactate absorption from the rumen (43,67,71). The ruminal epithelium expresses MCT-1 on both the apical and basement membranes, which remove lactate and protons from the rumen to the cytosol and into the blood (80). However, other studies found that neither L- nor D-lactate is absorbed from the cecum or rumen of sheep (81), but rather in the small intestine (42). It was postulated that lactate cannot be absorbed through the rumen at pH < 4.0 (82), but this was not substantiated in a further investigation that found no impedance of ruminal D-lactate absorption by decreased pH (83).

D-Lactic acidosis in diarrheic calves. Historically, acidosis in diarrheic calves was reported to be caused by the loss of bicarbonate in the feces and the accumulation of L-lactate in the blood (84). It was theorized that diarrhea-induced dehydration resulted in tissue hypoxia and consequently, anaerobic respiration. Until recently, L-lactate was assumed to be the major organic acid present in the blood of diarrheic calves (85). The documented occurrence of acidemia in well-hydrated calves led to investigation of other potential organic acid production (84,86). It is now known that D-lactate accounts for ~64% of the total increase in organic acids, as measured by anion gap (87,88). Calves can have extremely high D-lactate concentrations, up to 25 mmol/L (87,88). Furthermore, D-lactate production occurs mainly in the large intestine of diarrheic calves, with some calves also producing excess D-lactate in the rumen (88). The mechanism is likely similar to that documented for D-lactic acidosis in SBS in humans except the etiology of the malabsorption is viral infection–induced villous atrophy rather than surgical removal of the small intestine. Failure of the esophageal groove may occur in those calves with excess rumen fermentation; further study is required to clarify this possibility. The absorption of D-lactate from the intestinal lumen, via proton-dependent MCT-1, may be enhanced due to the high concentration of protons produced from excess bacterial fermentation. This, along with decreased barrier function from pathogen invasion and inflammatory processes, may lead to enhanced absorption of D-lactate and the extremely high blood D-lactate present in some diarrheic calves. Dehydration is also common in diarrheic calves and may impair renal removal of hydrogen ions from the blood, exacerbating acidemia.

There is a possibility, although it has not been described, that a similar scenario could occur in diarrheic monogastrics, including humans. Villous atrophy and malabsorption certainly occur in humans suffering from viral diarrhea, but whether there is sufficient fermentation to cause excess D-lactate to accumulate is not known. Metabolic acidosis was identified in human rotaviral diarrhea, and was attributed to carbohydrate malabsorption; however, the identity of the acids was not determined (89).

Subclinical elevation of D-lactate

Diabetes. In rats, the rate of D-lactate production in tissues with insulin-independent glucose uptake increases under hyperglycemic conditions (38). In that study, diabetic and starved rats had significantly higher concentrations of D-lactate in plasma, liver, and skeletal muscle compared with healthy rats (38). Methylglyoxal concentration was significantly elevated in plasma, but depressed in liver and muscle of starved and diabetic rats, compared with healthy rats. Christopher et al. (48) reported that increased serum D-lactate is associated with ketoacidosis rather than hyperglycemia, suggesting that ketone metabolism by hepatic cytochromes may be a major source of methylglyoxal in diabetic patients. Diabetic patients have roughly twice the blood D-lactate (28 μmol/L) concentrations of normal subjects (13 μmol/L) (50). Enzymes involved in the metabolism of methylglyoxal are elevated in diabetic patients, including aldose reductase, glyoxalase I, and glyoxalase II (90). Complications of diabetes, including retinopathy (91), nephropathy (92), and neuropathy (93) have been attributed to advanced glycation products,

including methylglyoxal. Clinically, D-lactate is unlikely to play an important role in diabetic patients because plasma concentrations appear to be subclinical in terms of neurotoxicity or acid-base imbalance.

Infection, ischemia, and traumatic shock. Infection, ischemia, and trauma all result in significantly elevated blood D-lactate concentrations. Most of these circumstances yield a D-lactate concentration that does not result in acidosis or neurological symptoms; typically, a concentration < 1 mmol/L is observed.

Various pathogenic bacteria produce D-lactate, including *Bacteroides fragilis*, *Escherichia coli*, *Klebsiella pneumonia*, and *Staphylococcus aureus* (94). The use of D-lactate as a marker for infection was proposed in 1986 (94). Indeed, venous blood D-lactate concentration as a predictor in the diagnosis of appendicitis has a lower false negative rate than C-reactive protein or leukocyte count (95). Plasma D-lactate is a sensitive marker for gut failure and endotoxemia in cirrhosis patients, likely due to impaired intestinal barrier function (96). Rats with experimentally induced *K. pneumonia* peritonitis develop a transient, but severe, D-lactic acidemia (25.6 mmol/L 6 h postinfection) (94). In bacterial meningitis, however, cerebrospinal fluid D-lactate was shown to be a poor indicator of infection, although slight elevations do occur (97).

In critically ill patients with septic shock, intestinal ischemia results in related increases in serum D-lactate concentrations and gastric intramucosal CO_2 partial pressure ($PgCO_2$) (98). No relation between $PgCO_2$ and L-lactate was evident in this population, although in a previous study in pigs, hemorrhagic shock and systemic L-lactate were related (99). Profound mucosal necrosis occurred early after resuscitation, implicating failure of the mucosal barrier as the likely cause of D-lactate absorption (100). Patients with mesenteric ischemia at laparotomy had significantly elevated D-lactate concentrations compared with patients operated on for an acute abdomen without intestinal ischemia (e.g., pancreatitis, diverticulitis, adhesions, gangrenous gallbladder); in these patients, D-lactate is a more reliable marker of ischemia than a physical exam (101).

Trauma can also result in elevated serum D-lactate. In pigs, nonvisceral gunshot injuries result in high plasma endotoxin and D-lactate concentrations and necrosis at the ileum villus, even in the absence of hemorrhagic shock (102). In rats, gut ischemia, severe burn injury (30% total body surface area), and acute necrotizing pancreatitis all result in elevated D-lactate (up to 0.65 mmol/L) (103).

The use of D-lactate as a diagnostic aid in clinical practice will require the availability of a D-lactate assay. Generally, this is not the case, and when available, techniques are often based on the D-lactate dehydrogenase enzymatic assay, which has numerous sources of error and is not adequately sensitive for the micromolar changes observed in infection or sepsis (35).

In conclusion, D-lactate, although generally considered the "nonphysiological" isomer of lactate, has an important role in numerous aspects of ruminant and monogastric metabolism, is clinically important in a variety of malabsorptive or gastrointestinal nutrient overload conditions, and may be important in some types of sepsis. Further elucidation of D-lactate metabolism is required, particularly to identify species differences. Probiotics may hold promise for use in prevention or treatment of D-lactic acidosis in SBS, and overfed or diarrheic ruminants. Clinical use of D-lactate as a diagnostic aid for ischemia or infection will depend on access to reliable D-lactate assays, currently not widely available in clinics and hospitals.

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