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these vacuoles. Clinically, CALP may be used as a serum indicator of the severity of steroid hepatopathy.

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Studies on clinical application of endoscopic ultrasonography in the dog.

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Endoscopic ultrasonography (EUS) is widely used as a technique for diagnostic imaging of the pancreas in human medicine. The author performed EUS on the normal pancreas and for experimentally induced pancreatic disorders in dogs to investigate the efficacy of this modality in diagnosis of pancreatic disorders in the dog. The EUS device used in the present study was a Hitachi/Pentax FG-32UA echoendoscope with a curved-array ultrasonic transducer, mounted in front of the objective lens. The EUS device was connected to a Hitachi EUB-565A ultrasound scanner. Dogs were placed in dorsal recumbency under general anesthesia, the tip of the ultrasonic endoscope was inserted into the stomach, and all examinations of the pancreas were performed from within the stomach.

The first chapter describes EUS performed on 12 normal adult dogs to establish the procedure for imaging the pancreas using anatomical landmarks, and to collect EUS images of the canine normal pancreas. EUS provided good images of most of the pancreas except for the edges of each pancreatic lobe. Useful information on the pancreatic parenchyma, including the pancreatic lobular structure, pancreatic duct and vessels of the pancreas was obtained by EUS. Blood flow in the vessels was detected by color

Doppler and pulsed-wave Doppler examination. These results suggested that EUS is available as an effective diagnostic modality for the canine pancreas.

The second chapter describes EUS examination, gray-scale histogram analysis of EUS images and transcutaneous ultrasonography (TUS) done in seven dogs with caerulein-induced pancreatitis. One dog was subjected to laparotomy and biopsy specimen collection for histopathology. By EUS, the pancreatic lesions were first detected at 60 minutes after the start of caerulein infusion. This was earlier than when they were first detected using TUS. EUS findings included swelling, subcapsular hypoechoic areas and anechoic stripes through the pancreatic parenchyma. No marked change of histogram analysis was seen until 30 minutes. From 30 to 60 minutes, a decrease of the mean brightness (mean data of brightness : MD) of the pancreatic parenchyma was first observed. These changes of the MD reflected histopathological findings, including vacuolization of acinar cells and interstitial edema of the pancreas. These findings indicated that EUS can detect delicate and diffuse changes of the pancreatic parenchyma. Furthermore, gray-scale histogram analysis reflected histopathological changes more sensitively than

endoscopic ultrasonic B-mode images.

The third chapter describes endoscopic ultrasonographic evaluation and gray-scale histogram analysis of the pancreatic atrophic lesion after pancreatic duct ligation performed in four normal adult dogs. EUS revealed that the pancreatic ducts were markedly dilated and the pancreas gradually atrophied with a hyperechoic parenchyma. In gray scale histogram analysis of the pancreas, the MD increased gradually until eight weeks, then decreased temporarily. The standard deviation (SD) of the histogram increased markedly and then fluctuated up and down until the fourth week, after which the MD and SD became stable. At four weeks postoper-

atively, collapse of most pancreatic acinar structures was observed and each atrophic lobule was associated with a significantly large amount of interstitial fibrous tissue histopathologically. This was similar to naturally occurring chronic pancreatitis. At 12 weeks postoperatively, most exocrine tissue had decreased and was partly replaced by fibrous and fatty tissue. The changes of MD and SD reflected these histological changes. These findings indicated that EUS is a useful device to image atrophic disorders of the pancreas in dogs. Furthermore, gray-scale histogram analysis provides helpful information for ultrasonic tissue characterization of the pancreas.

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Molecular basis of drug oxidation polymorphism in the Dark Agouti rat : importance of cytochrome P450 2D2

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The Dark Agouti (DA) rat has been proposed as a poor metabolizer model for the human debrisoquine 4-hydroxylase polymorphism. Earlier studies suggested that the poor metabolizer phenotype in the DA rat is due to the absence of the expression of CYP2D1 mRNA. Although cytochrome P450 2D1 (CYP2D1) catalyzes debrisoquine 4-hydroxylation, other reports have indicated the involvement of another CYP2D, purified from rat hepatic microsomes and presumed to be CYP2D2, which also exhibits this activity. The levels of CYP2D1 and CYP2D2 mRNAs were markedly lower in DA as compared to Sprague Dawley (SD) rats. Using a baculo-

virus expression system, recombinant CYP2D1 and CYP2D2 from *Spodoptera frugiperda* (Sf9) insect cells were examined and found that both forms catalyze debrisoquine 4-hydroxylase activity. These results suggest that reduced debrisoquine 4-hydroxylase activity in the DA rat is due to the low level expression not only of CYP2D1 but also of CYP2D2.

Interestingly bunitrolol 4-hydroxylation was catalyzed by recombinant CYP2D2, While CYP2D1 was inactive toward to this substrate. Thus the low bunitrolol 4-hydroxylation in DA rats was due to the low level of CYP2D2 expression in this rat strain.