Getting Acquainted With…. Bowzer's Digestive System, Part 3
Large intestine, Liver, and Pancreas

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The health articles are written to inform and educate. Please do not be alarmed by all the potential problems your Beardie may encounter. Most are rare, and you should not panic at the first sign of a loose stool or vomit, as most dogs do this from time to time and it is of little significance. Do watch your dog though, check his vital signs, and keep notes to share with your vet in case things do not resolve quickly with home care. You and your vet are partners in your Beardie's care, and fostering a great sharing and caring relationship with your vet is the best way to ensure a long and healthy life together for you and your friend.

Chronic small intestinal disease is a problem for many Beardies. In young dogs especially, chronic intermittent small bowel diarrhea often accompanied by weight loss or failure to gain weight may be the result of bacterial overgrowth. This isn't the only presentation, some dogs may not have diarrhea, others may vomit or have mild colitis, but in general they are young and not doing well. Bad bacteria can become established for a variety of reasons, but mostly these can be grouped as due to defective production of stomach acid, defective gut motility, defective local immunity, exocrine pancreatic insufficiency, defective mucus production, unabsorbed nutrients and malnutrition. Where possible the underlying cause of the problem should be treated. If this cannot be determined oral oxytetracycline or tylosin are usually effective treatments.

Dietary sensitivity (allergic reaction) and food intolerance can also cause chronic diarrhea. Usually the two conditions are difficult to distinguish, and are treated similarly. Exclusion diets using a protein and carbohydrate source the dog has not previously experienced. Owners should never feed any treats during this phase, just the prescribed diet. It can take 6 to 8 weeks for an improvement to be seen. At this point to confirm diagnosis the dog should be challenged with the original diet – which should cause problems to reappear (not surprisingly many owners are reluctant to complete this step). Foods should be reintroduced one item at a time.

Unfortunately, truly allergic dogs develop allergies to the new ingredients over time. Steroids may help reduce the allergic response. Raw and home cooked diets may also prove successful for these dogs, and evidence of allergy to the grain mites in kibble has recently been reported.

Infiltration of the lamina propria of the small intestine wall is characteristic of inflammatory bowel disease (IBD). In the most common form the invading cells are lymphocytes and plasma cells; less commonly the invading cells are eosinophils. This condition may also co-occur with dietary sensitivity, bacterial overgrowth, giardia, campylobacter and histoplasmosis and other fungal infections as well as lymphosarcoma. Co-existing problems should be addressed. Grossly the intestinal wall may appear normal or thickened, and definitive diagnosis is made from biopsy samples taken during endoscopic examination. Treatment is similar to that for dietary sensitivity. Reducing carbohydrate and/or replacing other sources with rice can be very helpful, as can replacing long chain fatty acids with medium chain ones.

Intestinal lymphangiectasia is a protein losing condition in which flow of lymph from the intestines is blocked, the lymph ducts can rupture and release plasma proteins into the intestines. It may be congenital or acquired, most often subsequent to congestive heart failure. A diet high in good quality protein and low in fat, supplemented with fat soluble vitamins is helpful. Steroids may help relieve clinical signs. Where possible the underlying cause should be treated.

Adenocarcinoma is the most common intestinal tumor, although lymphosarcoma, leiomyoma, leiomyosarcoma, fibrosarcoma and intestinal polyps can occur. Signs of these are vague and progress slowly. Anorexia and weight loss are usually the first signs. Adenocarcinoma usually occurs in the duodenum or large intestine, and may spread locally and sometimes to more distant sites. Mean survival after surgery is about 7 months. Lymphosarcoma usually spreads to the lymph nodes and response to chemotherapy in dogs is poor. Leiomyoma and leiomyosarcoma are tumors of the muscle wall, and if you can resect the tumor this is usually curative as they rarely metastasize.

The large intestine is between 28 and 90 cms in dogs, and runs from the end of the ileum to the anus. There are three sections. The cecum is a 8 to 30 cm long pouch off the colon shortly after it leaves the ileum. The colon has two distinct bends as it passes through the abdomen to the rectum. The cell layers of the wall are similar to those of the small intestine; however, there are no villi and fewer microvilli, but more mucous secreting cells. Cell turnover here is slower (4 to 7 days). The large intestine's primary function is to extract water and electrolytes from the effluent from the ileum, and to store feces prior to defecation. A small amount of fermentation of organic material occurs in the first part of the colon, but this is of little significance, unlike the same process in herbivores.

Most muscle contractions are actually away from the rectum, slowing down the passage of the contents while they are mixed, stored and dehydrated. Towards the anus, spontaneous giant contractions propel the contents into the rectum. The large bowel has a limited capacity for removing water. Normally it removes 90% of the remaining water, but if excess water comes from the small intestine, it may be overwhelmed, and the result is diarrhea. Sodium is also absorbed, and potassium and bicarbonate secreted. The latter neutralizes acids produced by fermentation. Bacterial content in the gut is highest in the large intestine, with 10^{11} organisms in each gram of feces – nearly 50% of its dry weight. The bacteria resist bacterial overgrowth with unfriendly bacteria, while metabolizing any remaining carbohydrates, proteins and lipids.

Diarrhea is the most common sign of large bowel disease. It is characterized by a lot of mucous, and often accompanied by straining. Blood will be red rather than the black, tarry melena seen with small intestinal bleeding. Frequency of defecation is increased, but the amount is diminished. Dogs usually remain bright and normal; weight loss is uncommon. Strictures or tumors may result in the production of abnormally shaped feces. Vomiting and weight loss indicate small intestinal disease is present too. Diarrhea can be the result of dietary indiscretion or changing diet too quickly for the enzymes to adapt; whipworm infection; IBD or neoplasia. Tumors can be benign – adenoma, leiomyoma or malignant – adenocarcinoma, lymphosarcoma or leiomyosarcoma – although the latter can usually be

surgically removed completely. Irritable bowel syndrome, also called nervous or spastic colon, is a vague term for large bowel diarrhea that is often fiber responsive (psyllium is curative) or caused by toxins produced by clostridial bacteria. Other causes of large bowel diarrhea are fungal, bacterial or parasitic.

Constipation may result from too efficient removal of fluid from the bowel or insufficient mucous production. Megacolon – enlargement of the colon leading to poor motility – is rare in dogs, and is usually acquired secondary to prolonged mechanical or functional obstruction of defecation.

Function of the rectum and anus depends on the coordination of conscious and unconscious muscular movements. The rectum begins as the colon enters the pelvis. The region is rich in mucous secreting cells. If these cells become inflamed then mucous secretion increases, as does straining and blood appears in the feces. Three kinds of gland empty into the anal region. Anal glands are modified sweat glands that secrete lipid into the lumen of the anus. The glands of the paired anal sacs that lie at positions 4 and 8 just below the skin around the anus secrete a mixture of dead cells, protein, sebaceous fluid and bacteria into the sacs. The circumanal glands surround the anus and are non-secretory. The anus has two sphincters, the internal one is not under conscious control. The external sphincter surrounds the internal one, and is under conscious control. The two sphincters are normally perfectly coordinated, but damage to the pudendal nerve can result in fecal incontinence.

While the anus is not involved in digestion, problems can frequently result in owners deciding to euthanatize the dog. Problems in the area can include: perineal hernia – rectum, urinary bladder or prostate gland can herniate into the anal region; rectal polyps and other tumors; rectal prolapse; proctitis – inflammation often secondary to colitis; rectal stricture – usually the result of trauma or surgery; rectal foreign bodies – these may lodge in the rectum having passed through the rest of the intestinal tract. Foreign bodies can cause secondary fistulas and abscesses. Perianal fistulas are extremely painful and consist of one or multiple tracts running from the lumen of the anus through the skin in the region around the anus. Dogs with broad tail

bases that clamp their tails are at increased risk. Low thyroid and poor immune function may also be inciting factors. Surgery and/or topical tacrolimus is usually curative.

Anal sac impaction, inflammation and/or abscessation is common, and owners notice their dog licking or biting at the area, scooting their butts, having trouble sitting (or showing reluctance to do so), pain and straining on defecation. One or both sacs may be involved, and they can readily be palpated through the skin. Normal secretions are clear to pale yellowish brown. Granular material, pus, blood and turbidity are all abnormal. Normally impacted sacs can be expressed easily, but sometimes the secretions form a cement-like block which has to be cleared before you can express them. Abscesses are extremely painful, and can cause fever. They can also lead to fistulas forming. In dogs with a chronic problem, removal of the sacs is recommended. Feeding a high fiber diet may help express the sacs. Adenocarcinomas may affect the anal sacs, and usually metastasize to the nearby lymph nodes.

The Liver carries out at least 1500 biochemical functions essential to a dog's survival. It is involved in the metabolism of carbohydrates, lipids, protein, vitamins and endocrine hormones; immune function; storage; making blood clotting factors, iron regulation and even making blood in utero and in extreme situations; making, storing and regulating the secretion of bile; and the detoxifying and excreting of drugs, hormones and several other substances. Its storage capacity, functional reserve and regenerative capabilities are the stuff of legend, but this doesn't make it easy to recognize when something is amiss; and often disease is severe and advanced before a problem is detected.

The liver is composed of six lobes. About 80% of the volume consists of hepatocytes. Another important cell type is the Kupffer cell, these line the blood vessels passing through the liver. These are fixed macrophages – cells that ingest and detoxify substances. They are also needed for the metabolism of iron, lipid, cholesterol and certain hormones. In addition, they have several important functions in the immune system. Its cells are rich in retinoids and store lipids; they also produce most of the collagen that results

in fibrosis of the liver. The capillaries passing through the liver have fenestrae or gaps allowing the passage of much larger molecules than most blood vessels. When blood pressure increases in the liver though, these close and become less permeable. Blood sinusoids serve to dissipate the pressure of blood entering the liver and store blood; the system is usually maintained at low pressure. Certain bile salts can increase blood flow and pressure within the liver.

Hepatocytes are arranged in cords with one side abutting a blood vessel and the other a bile canaliculus. On both sides surface area is magnified by the presence of microvilli, greatly increasing the surface for nutrient, metabolite, drug, toxin and bile exchange. These cords are supported on a framework of collagen and reticulin fibers.

Bile is formed in the hepatocytes and passes into the canaliculi, then to ductules, ducts and ultimately the gallbladder. Electrolyte and fluid content is modified during this passage. In the gall-bladder it is concentrated and stored until it is expelled into the duodenum to aid in digestion.

Nutrient rich blood from the stomach, intestines, spleen, pancreas, colon and gall-bladder flows into the portal circulation and passes through the liver before entering the rest of the circulation. Nutrients are removed and further processed while undesirable substances absorbed from the gut are removed and/or detoxified. At any one time 10-25% of the blood is in the liver. Much of it is being stored. The liver can actually double its blood storage which alone can lead to liver congestion. During hemorrhage, it can compensate for the loss of 25% of the total blood volume. At rest about 25% of cardiac output is passing through the liver, this changes with exercise, posture and at meal times. While two-thirds of the blood in the liver comes from the portal vein, one third comes through the hepatic artery, which supplies the oxygen needed for liver function. Even brief interruption of blood flow through the hepatic artery can lead to lethal, septic necrosis.

In newborn puppies most of the abdominal cavity is occupied by the liver, in the young dog the ratio of liver to body weight is about 4 to 5: 100, but in older dogs this drops to 2:100. Small livers may be the result of reduced blood perfusion, chronic fibrosis, atrophy of the hepatocytes, or loss of their

cellular content. Enlarged liver can result from passive congestion, infiltrative or inflammatory conditions, blockage of the bile ducts and cystic liver disease. Drug exposure – barbiturates etc.; infection or inflammation of the hepatocytes can result in increased liver mass secondary to enlargement of the organelles within the cells. If 70% of the liver is removed, in 6 weeks the remaining liver can have regrown to pretty much normal size and functional capacity. During that time, the body must have adequate glucose and coagulation factors provided, however.

Bile acids are formed from cholesterol and bound to an amino acid, usually taurine but sometimes glycine. Bile is secreted in volume into the intestines when food is consumed, and helps digestion and absorption of fat. Bile is released in smaller quantities, sometimes by-passing the gallbladder, at other times. Some dogs will vomit up bile if they have not been fed – particularly before the morning feed. Giving a bed-time cookie is usually enough to prevent this happening.

Early signs of hepatobiliary disease are usually vague – anorexia, vomiting, diarrhea/constipation, weight loss, intermittent fever. A more specific sign would be jaundice – yellowing of the mucous membranes and non-pigmented skin and eye whites – this can appear rapidly with major occlusion of the bile duct or very slowly. Gastrointestinal ulceration and hemorrhage may occur as disease progresses. Bleeding tendencies, due to Vitamin K deficiency, usually take a couple of weeks to appear. Feces may become dark green or dark-green/orange due to increased blood break down or pale gray or tan and fatty if bile flow is obstructed. Significant bleeding into the bowel produces black tarry feces. Increased drinking and urination and the appearance of urobilinogen in urine indicate liver disease, although some animals have problems urinating. Change in liver size can often be palpated. Neurobehavioral changes – ataxia, lethargy, stupor, head-pressing, obsessive circling, sudden unexplained blindness, seizures or coma can indicate severe acquired liver insufficiency or congenital portosystemic shunt – where some or all blood from the digestive tract by-passes the liver and goes directly into the main circulation. Ascites, the accumulation of fluid in the abdomen, is often the result of increased blood pressure in the portal vein usually indicating obstruction.

Diagnosis of liver disease begins with basic blood testing a complete blood count and biochemistry profile, in fact in many cases liver disease can be discovered before any physical signs become apparent. However, liver enzymes can be elevated by a number of unrelated conditions – bone disorders or growth; endocrine disease; gastrointestinal and splenic disease; hypoxia; drugs; low blood pressure; neoplasia; systemic infection; trauma; fever; wasp stings or after general anesthesia! If none of these are apparent follow up with ultrasound and biopsy are probably the most helpful procedures for characterizing the cause of the liver disease. X-rays and nuclear scintigraphy may also be helpful.

Acute hepatic failure occurs when a sudden severe insult to the liver results in compromise of at least 70 to 80% of functional liver mass, exceeding the liver's functional reserve and resulting in physical signs. Diffuse necrosis of liver tissue is the most obvious and consistent pathological sign. Causes can include hepatotoxic drugs and anesthetic agents; chemical and biologic substances (aflatoxin; amanita mushrooms; blue green algae; pennyroyal oil; heavy metals; herbicides; fungicides; rodenticides; household cleaners; industrial chemicals, etc.); infectious or parasitic agents (viral hepatitis, acute bacterial cholangiohepatitis; leptospirosis; liver abscess; extrahepatic infections and sepsis; systemic fungal infection – esp histoplasmosis; toxoplasmosis; postcaval heartworm infection); systemic or metabolic disease (acute pancreatitis; acute hemolytic anemia); trauma; diaphragmatic hernia with liver entrapment; heat stroke; surgery where blood pressure and oxygen perfusion is compromised; liver lobe torsion. Treatment depends on the underlying cause of the liver failure. Given the liver's role it is especially vulnerable to a vast array of substances, and this is something we should consider before introducing any substance into our dog's or our family's environment. Apart from acetaminophen antidotes exist for most acute hepatotoxins.

Cholestatic hepatobiliary disease is the result of impaired flow or excretion of normal volumes of bile. Substances normally secreted in the bile build up in circulating blood serum – bile acids, bilirubin, cholesterol – and there is increased activity of enzymes associated with the cells of the biliary tract – alkaline phosphatase (ALP) and gamma-glutamyltransferase (GGT). Jaundice

is the hallmark of this condition. Cholestasis can result from blockage or rupture of the bile ducts. This often requires surgical correction. Common causes are pancreatic disease (edema, abscesses, cysts or cancer), or gallstones. Retention of bile in the liver can cause secondary injury to hepatocytes.

Chronic liver disease – hepatic fibrosis and cirrhosis – can also result from a great many causes. Repeated exposure to drugs or toxins; infection; cholestasis; immune injury (chronic idiopathic hepatitis) and hypoxia often secondary to cardiac failure are all potential problems. A single episode of massive hepatic necrosis could cause end stage liver disease. However, the cause is never determined in most cases. One study showed that cirrhosis was responsible for 15% of the cases of liver disease as determined by biopsy.

In cirrhosis fibrous tissue replaces much of the normal liver and the remaining cells become disorganized further limiting function. It is irreversible, and while removing the underlying cause may slow progression of the disease it cannot restore the liver. Blood flow to the liver is compromised, and blood pressure increased, so remaining cells are less able to function.

Nodular hyperplasia is a common post-mortem finding in dogs over the age of 8. These nodules are not precursors to cancerous lesions, and they are not associated with clinical signs. Unfortunately, they cannot be distinguished from primary or secondary neoplasia on ultrasound, only by biopsy.

Liver cancer may be primary or metastatic and virtually all types of cancer have been reported. Metastatic cancer from pancreas, lymph nodes, spleen, mammary glands, adrenal glands, bone, bone marrow, lungs, thyroid glands and gastrointestinal tract is more common, and lymphosarcoma and pancreatic carcinoma are the most common types. Primary tumors are rare, and they are not associated with viral infection, exposure to chemical carcinogens, toxins, drugs or prior liver disease as they are in humans. These tumors can be benign or malignant.

I am not aware of any cases of congenital portosystemic shunts being reported in Beardies. Multiple acquired portosystemic shunts can result as a compensatory response to prolonged elevated portal blood pressure. Likewise hepatic arteriovenous fistulas can form as a result of elevated blood pressure in the hepatic artery diverting blood into the portal system. Neither condition is common. Both are more common in younger dogs, and in certain breeds, but not in beardies.

Hepatic lipidosis is an excessive accumulation of fat (triglycerides) in the liver. It is caused by an imbalance between rate of deposition and dispersal of fat, and can be nutritional, metabolic, hormonal, toxic or hypoxic in origin. The clinical significance depends on the severity and underlying cause. Excess fat does not impair liver function, but results in a large, pale yellow liver – such as that of the foie gras goose. Diabetes mellitus is one of the most common causes. Treating the underlying cause is desirable.

Hypertriglyceridemia – elevated triglyceride (TG) levels in serum - is the most prevalent lipid disorder in dogs. It may result in vomiting, diarrhea and non-localized abdominal pain. Signs frequently resolve with fasting. Seizures may also be a presenting sign. Reducing dietary fat is often curative, but feeding gastrointestinal diets (such as Hill's i/d) may make the condition worse. Blood triglycerides must be measured after fasting the dog to distinguish the condition from normal post feeding elevation of TG. Other rule-outs include diabetes mellitus, which can result in marked increase in TG and mild elevation of cholesterol (CH); protein losing nephropathy due to kidney disease which increases both TG and CH. The primary cause of elevated CH is hypothyroidism, although 30% of dogs with Cushing's Disease (hyperadrenocorticism) have elevated CH, too.

The major function of the **exocrine pancreas** is to secrete digestive enzymes and coenzymes. It also secretes bicarbonate to help neutralize stomach acid, and factors that assist in absorption of Vitamin B_{12}, zinc and probably other nutrients. Pancreatic fluid inhibits bacterial overgrowth in the duodenum and jejunum, helps with normal degradation of old brush border cells, and promotes growth of the mucosa together with biliary secretions. The pancreas protects itself from digestion by several mechanisms, including

producing an enzyme inhibitor (pancreatic secretory trypsin inhibitor), which it secretes together with the digestive enzymes.

The pancreas has left and right lobes and a small central body where they join together. Embryonically it grows out from the duodenum to which it stays connected by two secretory ducts –pancreatic duct and accessory pancreatic duct. The right lobe lies alongside the duodenum and the left lobe along the pyloric region of the stomach.

The acinar cells of the pancreas secrete enzymes to degrade proteins, lipids and polysaccharides. Proteolytic and phospholipolytic enzymes are stored as inactive zymogens, which are normally activated in the intestines by cleaving a small peptide from the zymogen, so trypsinogens become trypsins etc. This is achieved by an enzyme – enteropeptidase – formed in the enterocytes. The trypsins, chymotrypsins and elastases cleave polypeptides at specific sites, while carboxypeptidases lop off terminal carboxyl residues.

At rest the pancreas secretes about 2% of the bicarbonate and 10% of the enzymes it does when the animal eats a meal. There are cyclic increases though in the amounts secreted. After a meal secretion occurs in two phases, the first, which peaks an hour or two after eating, is rich in enzymes. The second phase occurs about 8 to 11 hours after the meal, is more voluminous and rich in bicarbonate. Low levels of amylase, lipase and zymogens leak into the blood stream.

Pancreatitis is inflammation of the exocrine pancreas. Acute pancreatitis has a sudden onset, may occur repeatedly, but causes little or no permanent pathologic change. Chronic pancreatitis is a continuing inflammatory condition resulting in permanent impairment of function. Pancreatitis seems to result when the proteolytic enzymes are activated while still in the pancreas causing autodigestion. This is probably because of a failure of the normal secretory process. In most cases the inciting cause is unknown. Some potential causes are: nutrition/hyperlipoproteinemia – low protein, high fat diets, and especially prevalent in obese animals; drugs, toxins, hypercalcemia; duct obstruction – gall stones, tumors, parasites, trauma, edema, sphincter spasm; duodenal reflux, pancreatic trauma, loss of

circulation/reperfusion injury; viral, fungal or parasitic infection. The Spec cPL® Test is a new, fast and accurate test for canine pancreatitis.

Signs usually include depression, anorexia, vomiting, sometimes diarrhea and pain – splinting the stomach (praying). In severe cases the dog may have collapsed and be in shock. They are usually mildly to moderately dehydrated and have a fever. In some dogs a mass at the front of the abdomen can be felt. CT scans are the most useful for diagnosing pancreatitis, but ultrasound may be helpful. Fluids and careful electrolyte balance together with nothing given by mouth is the basis for treatment. In uncomplicated cases, prognosis is good for complete recovery, although it is recommended that high fat foods be avoided in future.

Exocrine pancreatic insufficiency (EPI) is quite common in Beardies. Pancreatic acinar cells are progressively lost and replaced by fibrous tissue so that the body ultimately fails to produce sufficient digestive enzymes and food is not absorbed but passes through to the feces largely unchanged. Signs do not appear until most of the tissue is lost, for example fat in the feces is usually not observed until 85-90% of the secretory capacity has been lost. Even without pancreatic enzymes, alternate pathways do exist, and up to 63% of ingested protein and 84% ingested fat will be absorbed without pancreatic enzymes.

In the majority of dogs pancreatic acinar atrophy is the primary reason for the EPI. The cause is unknown, although nutritional deficiencies – amino acid imbalance, copper deficiency, protein-calorie malnutrition – have been postulated. Malnourishment secondary to small intestinal mucosal abnormality has also been suggested as dogs often show g/i disturbance long before there is significant weight loss. In humans, and apparently in quite a lot of Beardies, chronic pancreatitis is the cause of EPI. In some cases diabetes mellitus may co-exist with EPI. In some dogs congenital EPI has been reported, as well as EPI secondary to surgical resection of the duodenum.

In many dogs with EPI, enzymes malfunction, there are changes in the mucosa of the small intestine resulting in abnormalities of transport mechanisms and changes in bacterial presence. Dogs have often suffered

from malabsorption a long time before diagnosis is made or help sought however, and this may result in some of the associated changes that have been reported.

The best test for EPI is a blood test – serum trypsin-like immunoreactivity (TLI). This test rules out small intestinal disease (IBD) as the cause of the malnourishment. Dogs are managed by supplementing each meal with pancreatic enzymes and most do quite well. The enzymes – especially lipase – are largely digested themselves though before they reach the small intestine. Attempts to maximize enzyme efficacy - such as predigesting food with enzymes prior to feeding - have not proven to have any advantage. Highly digestible diets should be fed, and in most cases dogs require slightly more food than their healthy counterparts to maintain their ideal weight. Like all exocrine pancreatic diseases, EPI can be very painful and dogs may become more aggressive as a result of the pain as well as hunger. Vitamins B_{12} and E may need to be supplemented in dogs with EPI.

Adenocarcinoma of the acinar or pancreatic duct cells is relatively uncommon in dogs. When it does occur, the dogs are older. These tumors are highly malignant and have usually metastasized to the duodenal wall, liver and lymph nodes prior to diagnosis. Signs are usually non-specific - anorexia, depression, vomiting. If the bile ducts are involved the dog may develop jaundice, if the pancreatic duct is blocked there will be signs of EPI, and if the beta cells are affected signs will be of diabetes mellitus. An abdominal mass may be palpated, or a tumor visualized via ultrasound, but diagnosis is usually made via exploratory surgery. Prognosis is extremely poor.