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Hypoglycemia Caused by Septicemia in Pigs

Everlon Cid Rigobelo and Fernando Antonio de Ávila
Universidade Estadual Paulista, Campus Experimental de Dracena
Faculdade de Ciências Agrárias e Veterinárias de Jaboticabal
Brazil

1. Introduction

Swine production is continuously improving the quality of its products although of your living together with carcass fat content. The strategy of industry is offers natural products as special cuts semi prepared food. Others questions are the swine importance for Human medicine is related the products that are makes from swine used in Humans. The great variety of products originated of swine and used in Human medicine and mainly the use of organs as skin, cardiac valves for transplant shall to be interpreted as result of similarly that there is between the organisms: human and swine.

The pancreas swine is an organ that itself get insulin. This hormone is essentials for diabetics. It allows the entry of glucose in the cells and also decreases its fee in the blood avoiding that way that the glucose levels becomes fatal.

Other utility of pancreas of swine for Human is in the supply of pancreatic islets for implants into diabetic peoples that haven't. These implants will let the diabetics free of injections of insulin for many years. Actually the insulin is also made by genetic engineering through bacterial multiplication.

The pituitary gland of swine is used for get of ACTH. This hormone is used in human medicine for treatment of arthritis and inflammatory diseases that causes great suffering for many peoples in worldwide.

The thyroid of swine is used for get medicaments that will be used by peoples that have thyroid glands with lower actives.

The skin of swine may to be used temporally by Human in cases of burn that causes great discontinuity of your skin.

The gut mucosa of swine is used for obtaining of a substance called Heparin. This substance has function of blood clotting and is applied in Human medicine in hemorrhagic cases.

The heart of swine is used for get the cardiac valves that will may be transplanted in adults and also into children. The swine used for provide these valves weight of 16 to 25 Kg. Theses valves are withdraw of heart and conserved in the chemical preparation and they can be preserved for five years. The cardiac valves of Human can be replaced by mechanic valves made with artificial materials. The swine valves however have advantage on this mechanics on this account are less rejected by organism and have similar structure of valves human and also resist more against infections.

Modified genetically swine can produce Human hemoglobin (blood pigment that takes the oxygen for the all the body). In current researchers were injected three embryos of swine with copy of two genes responsible for producing of human hemoglobin. The technique

made with that 15% of hemoglobin found was of human type. The two hemoglobins may be after separate by difference of electric charge. This product can be stocked by months to the contrary of normal blood that itself conserve just for one week.

By similarity among swine and Human is being possible the realization of all events cited above. Also by similarity among both our study will has as focus the monitoring of some biochemical parameters into an experimental infection caused by *Leptospira interrogans wolffi* sorovar in eight swine. The biochemical parameters were tracked during 36 days. The main parameter analyzed was the glucose fee during all occurrence of septicemia. This chapter also will discuss the relation of occurrence of hypoglycemia caused by the septicemia in pigs that collaborates with critical condition of animal leading it the die.

2. Some drawbacks of swine

The swine when are produced without hygienic conditions can represent a high risk for several diseases. The medical science considers that swine can be host of many parasites and potential diseases. The meat of swine may content dangers toxins, vermin and latent diseases. Many theses infestations are found also in others animals, but some veterinary said that swine are more predisposed that the others animals, on this account are opportunist and highly omnivores with extensive feeding and including virtually any type of food comestible.

The swine meat contains amount of fat similar with others meat as birds and bovine and also it is responsible by nourish million of people in worldwide. Other advantage of consuming of swine meat is the great amount of protein for that the swine meat has both an economic and of public health. It is the meat further consumed in the worldwide allowed survival of many peoples.

However the swine meat also may forward many diseases as *Leptospira interrogans wolffi* sorovar.

The septicemia is an infection in the bloodstream. It appears when an infection is occurring in the people; this may be into the lungs, abdomen, and urinary routes or in the skin. The infections may also occur after a surgery in an infected area or in a body part that is colonized by many bacteria as for example the gut.

During the septicemia occurrence are found three distinct processes hence interconnected that occurs together as infectious focus hemodynamic changes and inflammatory answers local and generalized. The treatment of sick with septicemia is made with antibiotic and drugs that interfere in cardiac changes without intervene in inflammatory answers can be this reason of right mortality of patients with septic shock. Moreover still not has been established contribution of each inflammatory mediator in lethally resultant of septic shock.

3. Sepsis pathophysiology

The sepsis is defined as systemic inflammatory answers syndrome caused mainly by bacterial infections although also may be caused by fungus helminthes and virus. The infections caused by gram negatives bacteria are the further frequent, despite of last decade have been an increased of cases of sepsis due gram positive bacteria. The definition of sepsis included sepsis and also similar diseases from of causes noninfectious as trauma ischemia, burning, pancreatitis and hemorrhage.

The inflammatory response represents an important component of sepsis because elements of the response drive the physiological changes that become manifest as the systemic

inflammatory response syndrome. The inflammatory response eliminates the invading microorganism without to cause damage to tissues, organs or other systems.

Abnormalities in the coagulation system resulting from systemic diseases which cause local disturbances in homeostasis and the thrombotic potential of cancer patients have been described since the time of Virchow.

Virchow's classic triad consists of changes in coagulability endothelial cell injury and abnormal blood flow to vital organs. In septic patients, all three classic changes are present and culminate in reduced blood flow to vital organs.

Septic patients frequently have poor tissue perfusion and addition to inappropriate use of oxygen with resulting cytopathic hypoxia. The coagulation abnormalities in septic patients are profound and have led to a successful; Food and Drug Administration approved therapeutic intervention activated protein C.

The sepsis occurs when patients present hyperthermia or hypothermia, tachycardia, total white cell blood number upper of $12.000/\text{mm}^3$ or below of $4.000/\text{mm}^3$ or with further of 10% of immature forms. A lesion of sepsis that may arise is due the dysfunction of syndrome of multiple organs that affects approximately 30% of patients with sepsis while almost all develop dysfunction of an organ. The septic shock is characterized by high hemodynamic changes.

The clinical manifestations of sepsis are fever hypercoagulation and periferic hypotension caused by release of inflammatory mediators by immune and endothelial cells. The triggering factors cellular activation and of cascade of events of plasma are components of cell wall of this organisms lipoteichoic acid and peptidoglycan derivatives of gram positive bacterial or the lipopolysaccharide of gram negative bacterial. The lipopolysaccharide (LPS) is a molecule composed by hydrophilic polysaccharide chain divided in O antigen and core lipid A portion. The lipid A is a conserved region of toxin being responsible by your toxicity. The LPS importance in the triggering of sepsis was demonstrated after your administration in healthy Humans propagation of hemodynamic changes in patients with sepsis in experimental models.

3.1 Hyperinflammatory response

The sepsis is directly related with the high production of pro-inflammatory molecules. This problem have as result a rather simple when the inflammation is excessive. Usually this occurs in three cases. First, in septic patients with increased levels of specific mediators such as tumor necrosis factor (TNF) are at increased risk for death. Second, injection of TNF molecules at experimental animals results in widespread inflammatory changes. Third, experimental animals injected with a lethal doses of endotoxin elevated levels of the same mediators. The inhibition of these specific mediators improves survival in endotoxin shock models.

Whereas under normal conditions the endothelium exhibits antithrombotic properties by expressing tissue factor pathway inhibitors thrombomodulin surface releasing tissue factor during pathogenesis sepsis. Endothelial cells respond to LPS through toll like receptor followed by the release of pro-inflammatory cytokines such as interleukin - 6 (IL-6) and monocyte chemoattractant protein-1 and increased expression of adhesion molecules including intracellular adhesion molecule and vascular cell adhesion molecule.

The expression levels of cytokines and cell adhesion molecules are regulated by factor in inflammation.

4. Experimental models

4.1 Intravenous administration of live bacteria or bacterial components

Intravenous administration of LPS (endotoxemia) or of bacterial as *E. coli* widely used for sepsis study, as for example, the hemodynamic changes and cardiac, decrease of urine output, reduction of tissue perfusion, hyporesponsiveness vasoconstrictor agents, disseminated coagulation and production of large amount of cytokines in the circulation. Moreover is a practice model and reproducible in many species as mouse, rabbit, dogs, primate and including Humans. However the incidence of sepsis and septic shock in the clinic is due the entry of large amounts of LPS or of bacteria in the circulation same when amounts this bacterium is small. This puts in doubt effectiveness of this model.

4.2 Intraperitoneal administration of live bacteria or microbial components

This model also is very used for study of sepsis for reproduce of signs observed in diseases presented reproducibility as observed in endotoxemia model. Furthermore the administration of LPS or bacterial in the peritoneal cavity itself close of sepsis situation observed in the clinic because the process itself start from infectious focus or of dissemination of LPS administrated in the peritoneal cavity and not in the circulation. Even so, the start of process occurs rapidly and not gradually as happens in the majorly of clinic cases.

4.3 Gut injury model with consecutive release of microbial flora

The injury model with release microbial flora is the further similar to the sepsis situation in Humans, arising of traumas with perforations of gut, colitis or postoperative peritonitis. In this model after perforation of intestinal wall occurs the gradual liberation of contents causing peritonitis that may to evolve for a sepsis and septic shock.

Although this model is near the clinical and for that to be model further interesting for a study of sepsis the majority of studies in experimental sepsis is based into models where the bacterial or the LPS are administrated by IV or IP. The literature data shown that the pathogenesis of sepsis caused by LPS or bacterial IV differs those induced by an infectious focus as happens into peritonitis. The difference of results these models is due the amount of stimulus to the local and also administration form inducing the distinct kinetic of liberation of inflammatory mediators.

The biological activities of endotoxin and exotoxin are due of active of serum systems of endothelial cells and also leucocytes. Consequently the this infectious process occurs the syntheses or release of endogen mediators as cytokines, radioactive oxygen of nitrogen and lipid mediators being the activation of inflammatory cells the predominant factor for the development of sepsis.

The introduction of an object as an intravenous catheter, a urinary catheter or drainage-tube also may cause septicemia. The probability of septicemia increases with the time during the period that the object remains placed. This situation usually occurs between the people drugs dependents.

4.4 Relationship among hypoglycemia and septicemia

In septicemia the homeostasis finds itself threatened by invaders microorganisms. The body reacts to the challenge establishing a complex response: first prioritizing the supply of energy for vital organs, second, stimulating immune system and after stimulating the return of homeostasis.

When an infection occurs the cells need of glucose to synthesize defense molecules and also increases your metabolism in result of all changes physiological and morphological caused by the diseases. This result in a hypoglycemia by increase of consume of glucose by tissues. In majority of domestic animals during a septicemia occurs a hypoglycemia. This hypoglycemia caused by septicemia increases much the severity of diseases and also is the great responsible by high mortality in these situations.

Changes of hepatic gluconeogenesis and a depletion in glycogen content at liver is responsible by changes of glucose homeostasis this occurs by metabolic hallmarks in shock and sepsis. The shock and sepsis-induced glucose dyshomeostasis is characterized by an initial hyperglycemia followed by a progressive hypoglycemia.

The depletion in hepatic glycogen content following endotoxin administration is associated with an increase in glycogen phosphorylase coupled with a decrease in glycogen synthase activities.

The endotoxin-induced changes in glucose metabolism are augmented by the in vivo treatment of animals with protein kinase C (PKC) activator, PMA, while they are antagonized by PKC inhibitors, H7 and polymyxin B. The PKC plays a pivotal role in the pathogenesis of altered hepatic glucose homeostasis in shock and sepsis. Since the available information regarding the involvement of PKC in glucoregulatory disturbances in shock and sepsis derived mainly from the use of activators or inhibitors of PKC.

Previous studies demonstrated that cytosolic PKC activity was inactivated during late phase of sepsis in rat liver. During the sepsis, the CLP-induced septic rat model used exhibited two metabolically distinct phases: an initial hyperglycemic and a subsequent hypoglycemic phase.

The finding some authors showed that cytosolic PKC activity was inactivated during late stage of sepsis may have a pathophysiological significance in contributing to the development of hypoglycemia during late phase of sepsis.

The kinetic analysis of the data showed by some authors indicated that the V_{max} for PM Ca^{2+} pump was decreased by 42% while the K_m value for Ca^{2+} remained unaffected.

The similarity in the patterns of change in the kinetics between the PKC-mediated phosphorylation of PM Ca^{2+} -ATPase and the sepsis-induced impairment of PM Ca^{2+} transport strongly suggests that the impairment in Ca^{2+} transport by rat liver PM during late sepsis is a result of inactivation of PKC. Thus, a decrease in cytosolic PKC activity, as reported in this study, would impair PM Ca^{2+} transport, impede Ca^{2+} efflux, and hence elevating intracellular Ca^{2+} in hepatocytes during late phase of sepsis.

5. Hypoglycemia

The hypoglycemia is a disorder where the glucose serum concentration finds itself usually low.

Usually the organism keeps the serum glucose concentration in a range of 70 to 110 mL/deciliter of blood. In hypoglycemia the glucose concentration remains low. This results in a malfunction of brain that is sensitive the low glucose serum concentration because the glucose is the main energetic source of brain. It reacts through of nervous system and stimulates the adrenal glands to release epinephrine. This hormone stimulates the liver to release glucose for adjust the glucose concentration into the blood. When the concentration becomes very low the brain function may be damaged.

The hypoglycemia has several different causes between them the excessive secretion of insulin by pancreas an excessive dose of drugs for reduce the glucose serum concentration, an abnormality in the pituitary or of adrenal or an alteration of carbohydrate storage or into

the production of glucose by liver. Generally the hypoglycemia may be classified as related with drugs or no related. The majority of hypoglycemia cases related into diabetic people are related with drugs.

The hypoglycemia that is not related with drugs may be subdivided into fasting and reactive. In this case a reaction occurs to the carbohydrate ingested. Further frequently the hypoglycemia is caused by insulin or others drugs as sulfonylurea that are administered to the diabetic peoples for reduce the glucose serum concentration. When the dose is very high for the food ingested, the drug may cause an excessive reduction of glucose serum concentration.

The people with severe diabetics are particularly prone for the severe hypoglycemia. This occurs because the pancreatic islet cells not produce normally glucagon and the adrenal not produce normally epinephrines that are main mechanisms for combat the low glucose serum concentration. Some drugs that are not used for treatment of diabetics especially the pentamidine used for treat a type of pneumonic related with the SIDA may cause hypoglycemia.

Sometimes the hypoglycemia is observed into people with psychological disorders by administer insulin in themselves or oral hypoglycemic. The people that may present these types of behavior are those that have access to the drugs as health professional or diabetic's family.

The alcohol consumption into people that drink heavily without consuming food by long period may cause a severe hypoglycemia by stupor.

A long fasting only leads a hypoglycemia when the people are carriers of other diseases especially pituitary diseases or of adrenal or when this people consumes a large amount of alcohol. The neonates that present problems often of hypoglycemia need be investigated as to the metabolism functioning of carbohydrates or amino acids mainly when that occurs in the diseases absence diagnosed as septicemia and endotoxin. When the neonates present hypoglycemia periodically is necessary suspect of glycogen storage diseases when this clinical is accompanied of hepatomegaly, acidosis and ketosis

When the animal present hypoglycemia by result of a hydrolytic complication your probability to die increases in up to eight times in septicemia situations. The metabolic homeostasis need be maintained in neonates because the hypoglycemia may cause neurological damage when it isn't identified

The carbohydrates reserves of liver may decrease into very low level that people cannot keep a glucose serum concentration appropriate. Some people with liver dysfunction into only some hours of fasting may cause hypoglycemia. The infants and children with an alteration of either of liver enzymatic systems that metabolize the glucose may present hypoglycemia between the meals. Others people that were submitted the certain types of gastric surgery present hypoglycemia between the meals, the alimentary hypoglycemia, a reactive hypoglycemia type. The hypoglycemia occurs because the glucose is quickly absorbed stimulating the excessive insulin production. The high insulin concentration causes a rapid drop of glucose serum concentration. Rarely the alimentary hypoglycemia occurs in people not submitted for gastric surgery.

The hypoglycemia may be due a kidney or heart failure, a cancer, malnutrition, pituitary or adrenal dysfunction or shock an infection serious.

6. Hypoglycemia in animals

Some studies realized in rats in 4 day old monitoring the glucose levels during seizures the authors reported that the metabolic cerebral balance during sustained seizures suggests that

energy balance may be maintained in hyperglycemic animals and its decline occurs slowly in normoglycemia, but this not occurs while the animal have more old. The results suggest that the hypoglycemia in old animals can become critical when associated with other types or metabolic stress. The differences are reflecting in cerebral energy metabolism. In adult animals the ATP keeps whether invariable. This decline is rapid when the animals are convulsing and slower when the systemic effects of anoxia and convulsions are prevented by paralysis and oxygenation.

The hypoglycemia is characterized by low levels of blood glucose. Against the hypoglycemia in the individual is involved the release of glucagon, norepinephrine, cortisol, epinephrine and growth hormone. These elements are related with limit glucose utilization. The main stimulus for increase of glucose production is the glucagon and it is also a response to insulin induced hypoglycemia in the normal individual. When individual has diabetes its cells are more prone to low blood sugar due the abnormalities in the cell response in relation to hypoglycemia. Some studies verified using a conscious catheterized dog model that the hypoglycemia increased glucagon's ability overcame the inhibitory effect of insulin on hepatic glucose production.

The glucagon is main defense against a low blood glucose level. The insulin exerts a great effect on glucagon's action. The some studies have showed that the glucagon can have such a prominent role in counterregulation.

7. Leptospire interrogans wolffi sorovar

Adolf Weil in 1882 described the diseases that He observed in two situations involved four patients in 1870. The clinical signs were similar and much private at patients. The disease was characterized by sudden appearance, high fever, splenomegaly and icterus.

In 1881 in Praga city, Weiss described the disease called "*icterus catarrhalis*" that probably will be the disease of Weil. Globig in 1890 described the "Badeepidemie" the disease that showed a great differ when compared to disease of Weil. In 1891, F. Muller described the *Schlammfieber* epidemic in chleisen the disease with symptoms much similar. Rimpau et al., described *Feldfieber* in which was the name that descrived the Leptospire not icterus. The Lepiospirose was recognized with different names including bilious typhus by Weil others authors called it of Weil disease, icterus infectious.

The agent was isolated by first time, in Japan, in 1915 by Inada & Ito. The researchers isolated Leptospira of minas workers called *Spirochaeta icterohaemorrhagiae*.

In 1915, Uhlenhut & Fromme, showed the existence of etiologic agent, inoculating the army blood suspect of have Weil disease in guineas pigs. The animals inoculated died and Leptospira were identified microscopically, being called of *Spirochaeta icterohaemorrhagiae*. Miyajima, Ido, Hoki, Ito & Wani (1917) demonstrated that mice were carriers of leptospira showed that 40% them were renal carriers.

8. General characteristics

The cells are flexible helical with 0.1 μm of diameter and 6-20 μm of length. They are faintly stained by aniline dyes. The cells not cored are visible by contrast microscopy or by darkfield microscopy. The helical conformation is to right side (clock spring) existing in one or both extreme typical hook. Two periplasmatic flagella (fibril axial and endoflagello) occurs in each cell where is inserted in each extreme and rarely whether overrides in central

region. When it is liquid medium has characteristics movements with alternated rotation to the long of axis and translation in direction from extreme without hook. In viscose medium are observed snak movements. They are aerobic its colonies are diffuse and formed surface below of medium with 1% of agar and turbid colonies at agar 2%. Optimal temperature is of 28-30°C. The genus is chemical organotrophs using fatty acids or fatty alcohol having 15 carbonic atoms with energy source. Not use carbohydrates with energy source being necessary serum and albumin to your growth.

Leptospirose is a disease caused by bacteria of Leptospiracea family genus Leptospire that might to be found in worldwide. The infections by leptospire have been reported in human being, cattle, pigs, horses, sheep, dogs, rodents and also severe wilds animal's species in the Brazil and also worldwide. Leptospirose is disease of acute manifestation of third to tenth four day after infection. Leptospire enters the host through mucosa and broken skin, resulting in bacteremia. The spirochetes multiply in organs, most commonly the central nervous system, kidneys, and liver. They are cleared by the immune response from the blood and most tissues but persist and multiply for some time in the kidney tubules. Infective bacteria are shed in the urine. The mechanism of tissue damage is not known.

This disease might itself make chronic after this period and, in the last thirty years the pigs have been appointed as main domestic animals carriers of Leptospire being accountable by epidemics occurrences in the Human and others domestic species. Leptospire could to be considered main agent of problems related with reproductive failure in pigs.

The symptoms of chronic infection are known to induce reproductive failure in farm animals, the acute lethal form of leptospirosis is generally observed in animals. There is various serogroups of Leptospire and in farm animals; bacterins need to contain five serogroups because of variation in local epidemiological condition.

Pathogenic leptospires infect a variety of animals as has been said, but the naturally acquired clinical disease has been documented only in a limited range of mammals. Leptospirosis has been reported mainly in sheep and goats are among the domestic species which are less susceptible to the pathogenic action of leptospires. In most cases of leptospire infection are asymptomatic, severe outbreaks do occur with a significant loss of sheep, goats and pigs.

The animals considered of high risk to leptospire infection are gravid and young animals be infected by any pathogenic serovar depending upon the specific epidemiologic situation.

The Leptospiroses are divided in further of 200 sorovar grouped in 23 serogroups. In pigs the Leptospirose is characterized by occurrence of abortions in the final third of gestation, heat repetition, fetal mummification, birth of weak piglets, and low number of piglets, vulvae discharge and embryonic death.

The pigs are might to be definitive hosts especially, *pomona*, *bratislava* and *tarassoli* sorovars and still accidental hosts as in cases of infection by *icterohaemorrhagie*, *canicola* sorovars. In first case there is a hosts parasite adaptation where the Leptospire are kept in urinary tract for long period being eliminated by urine in conditions for infect others animals. The signs are moderate being detected the infection just in pregnant female. In accidental infection when are infected by an adapted sorovar the other specie the signs of diseases are further evident but the permanence in urinary tract occurs by low time occurring the elimination of lower number of Leptospire in urine.

Although actually be available a large number of techniques for laboratorial diagnostic of routine for Leptospira this techniques still not satisfy some requirement as sensibility, specificity and practice. The antibody presence anti-Leptospire in serologic samples

collected in animals of slaughterhouse no represents adequate sampling for a study with Leptospire in pigs in a region determined. This samples also no reflect the situation grange inside. Nevertheless it allows that itself has a general basis of its occurrence and may to suggest what are the Leptospire sorovars that has large importance in region of animal origin. Other method of detection of Leptospira is the agglutination serum, in which it is employed in suspensions of strains.

The results of serologic test applied to the diagnostic of Leptospira depends of technique employed, of antigen collections used and also variations related the farms localization year of period into that samples were performed moving of animals. The interference of these factors becomes necessary the existence of epidemiologic sanitary systems permanent that enables the monitoring of spatial distribution of sorovars of Leptospira present in different regions so to rationalize the control using the immunoprophylaxis.

In pigs the biochemical dosage in blood involved bilirubin, glucose fatty acid and plasma proteins in responses the experimental infections by leptospira are scarce in literature. The blood dosage may to assist in diagnostic, prognostic and in the treatment of animals. The bilirubin determination represent a parameter for detect acute hemolysis.

The disease caused by Leptospira is characterized by clinical stages with remissions and exacerbations.

Leptospira organisms are very thin, tightly coiled, obligate aerobic spirochetes and also are characterized by a unique flexuous type of motility.

The genus is divided into two species: the free-living leptopire *L biflexa* and the pathogenic leptospiras *L interrogans*. This leptospira is of serotypes causes of zoonotic disease.

The Humans may be accidental hosts. However the primary hosts are domestic animals and also wild. In Humans this disease may have severity from fatal to subclinical. The first case of leptospirosis, in Humans was described in 1886 as a severe icteric illness and was referred to as Weil's disease; however, most human cases of leptospirosis are nonicteric and are not life-threatening.

In contrast to the pathogenic leptospiras, serotypes of *L biflexa* exist in water and soil as free-living organisms.

Although *L biflexa* has been isolated from mammalian hosts on occasion, no pathology has been found.

The explanation of why the leptopire not occurrence of infections at animals of laboratory yet not is knowledge. The widespread distribution of *L biflexa* in fresh water and the leptospiras has the capacity to pass through 0.45 to 0.22- μ m-pore-size sterilizing filters, they have been found as contaminants of filter-sterilized media.

9. Prophylaxis

In current days the immunization by vaccination is a practice more important in cattle hygienic with results direct and an economic return of activity and warrant of excellent sanitary standard of flocks and the opening and maintain of makers. The vaccination represents the minor costs of inside of productive process and may be decisive for obtaining of good results at animal production.

10. Experimental infection

In Brazil occurs a high incidence of *Leptospira interrogans wolffi* sorovar. This data was reported after a serologic survey in pigs with historic of reproductive failure. This same

study showed a possible relation between biochemical results of blood with infection induced by this sorovar. That way, the present study was realized with aims of verify itself is possible to relate biochemical parameters of blood including glucose fee with occurrence of septicemia caused by *Leptospira interrogans wolfii* sorovar. In our experiment eight, 90 days old pigs of the Wessex lineage all castrated male were used experiment divided into two groups of four animals. Biochemical alterations in the serum of the animals were analyzed in both groups during 36 days. Control (Group I) received 0.5mL of a 0.9% sterile sodium chloride inoculated by intracranial vein injection; Group II animals were inoculated by the same way with 5.0mL of Brazilian “armadillo”. Three days after inoculation blood was collected without anticoagulant; the same process was repeated at 72 hours intervals during eighteen days in both, control and experiments groups. Quantitative biochemical parameters were direct, indirect and total bilirubin all were observed after six days. Glucose fatty acid decreased after the third day inoculation. The increased bilirubin levels could be due to acute hemolysis, hypoglycemia, hypolipidemia that could be related to hepatic lesions and septicemia.

In the Group II has been observed an increased of direct bilirubin levels in the third day after inoculation which came back the initial values from the sixth day when compared to Group I. This increase of direct bilirubin in the third day observed in the pigs of Group II may be due the hemolysis which indicates that liver no presented any lesions and suggest efficiency in the hepatic conjugation of bilirubin with glucuronic acid. When there is hepatic lesions this cause damage in parenchymal hepatic cells difficult the conjugation.

In values of indirect bilirubin might itself to observe that between start of experiment and third day there was a decrease followed of a increase of levels in the sixth day in the inoculated animals with *wolfii* sorovar and that from ninth day has been verified a fall in levels that itself kept stables to fifteenth day similar behavior has been observed in control. However this bilirubin increased has been discrete when compared to animals inoculated. This decreased of levels of bilirubin to third day after the inoculation with serum *wolfii* sorovar has been verified by others authors. After hemolysis the indirect bilirubin is not apparent in the first hours. The marked increase of bilirubin seems to indicate a hemolysis excessive. Some endotoxins cause changes in carbohydrate metabolism of erythrocytes with a consequent decrease of ATP. That would be a possible explanation for loss of motility of contractile system of erythrocytes membrane.

That loss of motility causes changes in the morphology of erythrocytes, passing from biconcave disk to spherical shape (spherocytosis). That abnormality would result in the detection and removal of spherocytic cells by reticulum macrophage system, spleen, liver and bone marrow where would be destroyed with release of hemoglobin that would be transformed in bilirubin.

In the inoculated pigs has been observed a fall of levels of fatty acids while in control Group there was the fall then an increase, being the major value detected to twelfth day. The decrease of fatty acids in the pigs inoculated with *wolfii* sorovar caused a secondary hypoglycemia and a hypolipidemia.

The glucose levels presented a decrease to third day after inoculation then of constant increase thus to overcome the initials values in the fifteenth. In the control Group also has been verified a fall of glucose fee then an increased from third day reaching to the maximum value in the ninth day and decreased the lower values than initials between the twelfth and fifteenth day. The hypoglycemia observed occurs by increase of consumption of glucose by tissues in septicemia case. The plasma protein levels have been unchanged despite to has

increased in third day in pigs of Group II after the inoculation with *wolfii* sorovar. This hypoproteinemia in inoculated animals could to be related with a hepatic lesion discrete that may have been caused by leptospire infection. In some cases of septicemia may have an increase of capillary permeability that allow the leakage of albumin for extracellular compartments which possibly could prove the septicemia have started just in the third day of experiment. The leptospire induction model with intravenous inoculation of *wolfii* sorovar showed effective. The blood biochemical variations of pigs inoculated were hypoglycemia, suggesting a hepatic lesion and the occurrence of a bacterial septicemia and also hyperbilirubinemia, indicating with this that a main cause of toxicity of *wolfii* sorovar showed in this study is grave anemia hemolytic. The lost of piglet ranging of 4 to 10% in childbirth, others 20% may die before weaning. The causes of die of piglet are many. The hypoglycemia may to be caused by septicemia or to be a result of all a complex evolving needs specific temperature interfering in glycogens feeding frequency and amount of colostrums that subsequently the milk ingestion.

11. Conclusion

Concluding the model of induction of leptospire caused by intravenous inoculation of *wolfii* sorovar showed itself effective. The biochemical variations in the blood of inoculated pigs with *wolfii* sorovar were: hypoglycemia, hypolipidemia and hypoproteinemia suggesting a hepatic lesion and bacterial septicemia. The hyperbilirubinemia might to indicate that main cause of toxicity of *wolfii* sorovar is a severe hemolytic anemia. However the low glucose fee has aggravating role in the septicemia in pigs.

Fig. 1. Comparative of glucose level in pigs inoculated and uninoculated (control)

The figure shows the comparison of two Groups of four pigs. The Group I (pig control) the pigs received 5.0mL of a 0.9% sterile sodium chloride solution by intracranial vein injection;

Group II (pig inoculated) animals were inoculated by the same way with 5.0mL of a cell culture containing 1.0×10^8 cells mL⁻¹ of *Leptospira interrogans* sorovar *wolffi*, wild strain L-10, isolated from a wild species of Brazilian.

The biochemical changes were analyzed in the serum of the animals in broth Groups during 36 days. All parameters returned to normal levels after fifteen days, in all animals tested.

Fig. 2. Fatty acids levels in pigs inoculated and uninoculated (control).

Fig. 3. Plasma protein levels of pig inoculated and pig uninoculated (control).

12. Acknowledgments

The authors thanks to Prof. Dr. José Carlos Rende by realization of these experiments.

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Hypoglycemia - Causes and Occurrences

Edited by Prof. Everlon Rigobelo

ISBN 978-953-307-657-7

Hard cover, 238 pages

Publisher InTech

Published online 10, October, 2011

Published in print edition October, 2011

Glucose is an essential metabolic substrate of all mammalian cells being the major carbohydrate presented to the cell for energy production and also many other anabolic requirements. Hypoglycemia is a disorder where the glucose serum concentration is usually low. The organism usually keeps the glucose serum concentration in a range of 70 to 110 mL/dL of blood. In hypoglycemia the glucose concentration normally remains lower than 50 mL/dL of blood. This book provides an abundance of information for all who need them in order to help many people worldwide.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Everlon Cid Rigobelo and Fernando Antonio de Ávila (2011). Hypoglycemia Caused by Septicemia in Pigs, Hypoglycemia - Causes and Occurrences, Prof. Everlon Rigobelo (Ed.), ISBN: 978-953-307-657-7, InTech, Available from: <http://www.intechopen.com/books/hypoglycemia-causes-and-occurrences/hypoglycemia-caused-by-septicemia-in-pigs>

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中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

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