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RESEARCH OF PATHOMECHANISM AND THERAPY OF COLITIS X

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ABSTRACT

During the conducted experiments the authors aimed at an explanation of pathogenesis of diarrheal disease of horses, called Colitis X. The effort of finding the most effective therapy and prevention of the disease was also undertaken.

The research was conducted in two stages and included twenty three (23) horses. During the first stage of the research, the experiments were conducted on 17 horses, 8 of which had permanent cecum fistula installed, and 9 horses constituted a clinical group with symptoms of diarrhea. In six (6) horses with fistula we caused diarrhea by oral and intravenous administration (with fodder and through nosogastric tube) of antibiotics. The horses

were subsequently infected with virulent cultures of Salmonella bacteria orally and through the fistula. During the second stage of the research 6 healthy horses had diagnostic laparotomy with evacuation of the cecum performed, and then we tried to induce diarrhea by administering antibiotics commonly recognized as causing diarrhea in horses.

The following basic tests were conducted: clinical, serologic, hematological and gasometric blood tests, microbiological and parasitologic stool tests, comparative fermentative analysis of the cecum and big colon contents of healthy horses and those with symptoms of diarrhea.

The authors proved that Colitis X is a polyetiologic entity and is difficult to induce by a single chosen causing factor. Basic therapy consisted of intravenous administration of compound electrolyte solution with acid sodium bicarbonate, short action glycocorticoids, NSAID group agents and blood plasma.

Key words: horses, diarrhea, Colitis X

INTRODUCTION

Acute diarrheal diseases in adult horses still constitute a diagnostic problem. In Hospitals for horses as well as in field work it is impossible to find the causing factor in many cases. The problem is extremely important since horse mortality in diarrheal diseases is still very high. The therapy of some cases is very costly and often gives no satisfying effects.

In the research of pathogenesis of diarrheal diseases in horses, commenced in our clinic in 1997, we concentrated on the explanation of etiology of one of the most dangerous diarrheal diseases, Colitis X.

It is an acute or sub-acute, polyetiologic, usually mortal disease (mortality of 75-95%) characterized by a suddenly occurring watery diarrhea and accompanying symptoms of hypovolemic shock. The term Colitis-X [40] is reserved for such cases of acute or sub-acute diarrhea, leading to the animal's death where precise determination of the disease cause is impossible even after complex clinical diagnostic procedures.

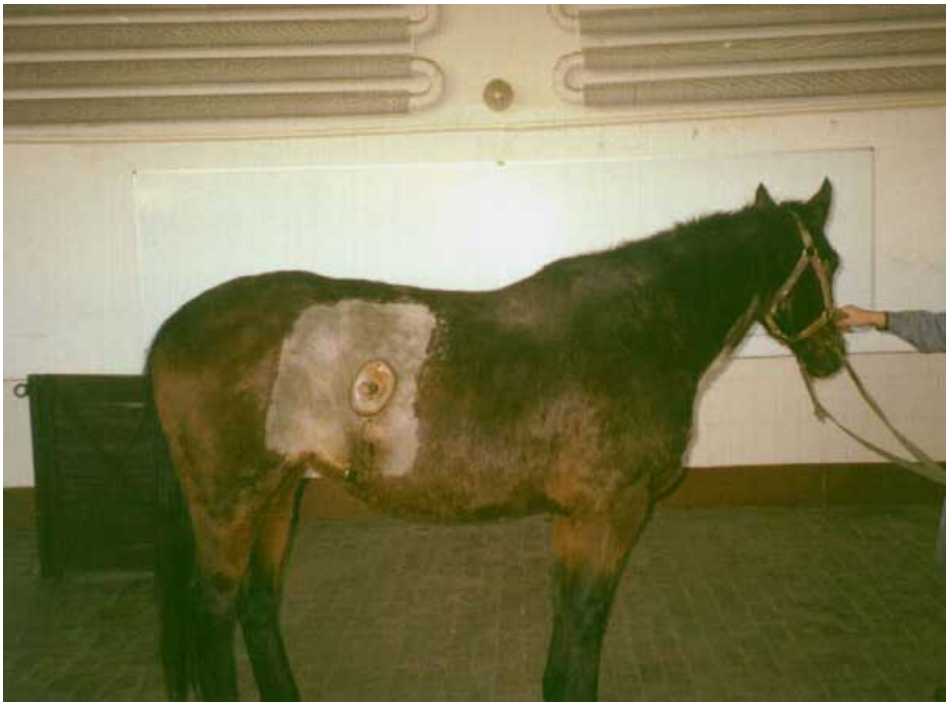
The disease occurs sporadically and is characterized by high mortality (90-100%). The mortality might be lowered to 75% after employing intensive therapy. The disease was first described in 1919 by Graham et al. [10], even though the authors called it a "transport disease". The official literature name (Colitis X), with incomplete symptom characteristics, was provided by Ronney and Bryans in 1963 [29]. In spite of several decades of research it was impossible to determine etiopathogenesis of the disease. The literature also describes it by several names: after-shock diarrhea, exhaustion shock, intestinal clostridiosis, typhlocolitis, hemorrhagic colon edema, acute idiopatic diarrhea, post-transport diarrhea or intestinal endotoxemia. Viruses, parasites, bacteria (*Clostridium difficile, Clostridium perfringens* type *A, Clostridium cadaveris, E.coli* and their toxins) as well as the use of certain antibiotics and sulfonamides [15a, 26a] are mentioned among pathogenic factors leading to the disease's occurrence. Stress in a broad meaning of the word is mentioned by the authors of all papers as a common causing factor.

The most prominent macro- and microscopic inflammatory lesions are observed within the walls of big colon and the cecum. It is assumed on this basis that typhlocolitis is a direct cause of diarrhea in this disease. Neutrophils, eosinophils, mast cells and monocytes are mentioned as components of inflammatory infiltration, whereas the inflammation mediators are leucotriens, prostaglandins, bradykinin, histamine and peroxides with free radicals. All the above mentioned cooperating elements cause damage of mucous membrane cells as well as its deeper layers. This in consequence leads to the unsettling of balance between water and mineral salts absorption, and their active and passive secretion, and causes the occurrence of hard to suppress diarrhea.

MATERIAL AND METHODS

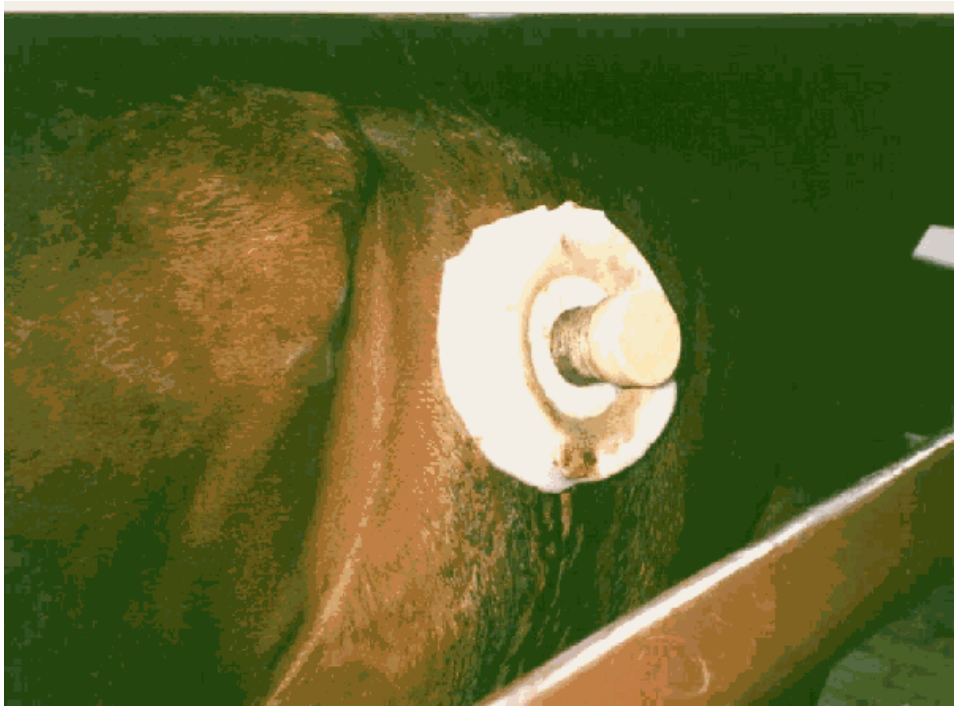
The realization of the first stage of research began from the elaboration of methods of placing permanent fistulas in the horses cecum. The way of fastening rubber and silicone fistula is shown in pictures 1, 2, 3, 4.

II.1. A horse with installed persisting, rubber cutaneo-intestinal fistula (general view).

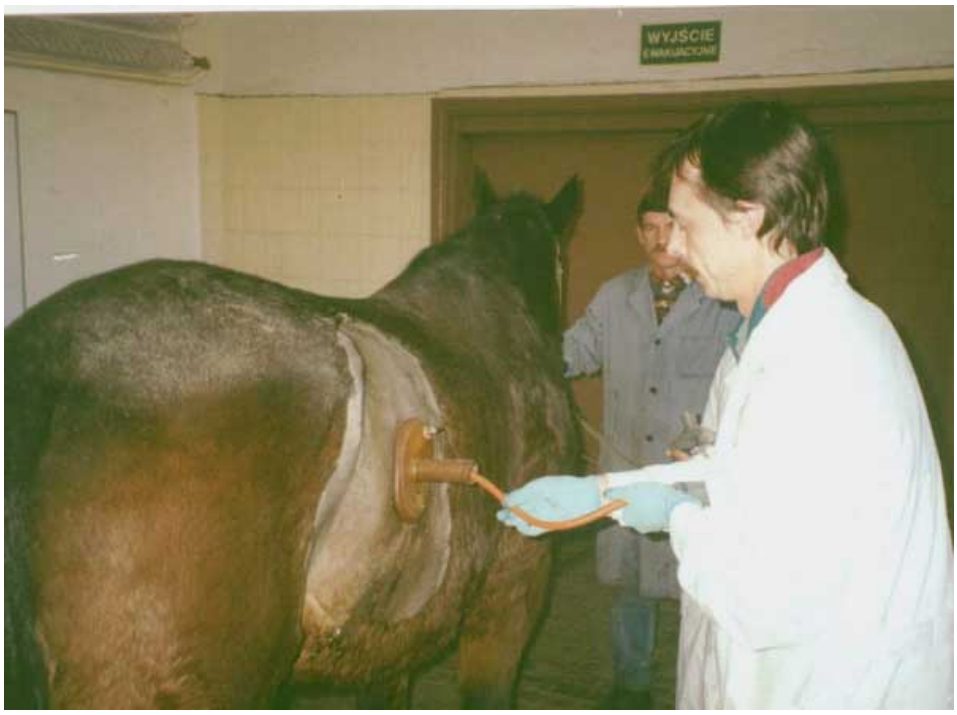


II.2. Persisting, rubber cutaneo-intestinal fistula.

II.3. Persisting, silicone cutaneo-intestinal fistula.



II.4. Taking contents from the rubber fistula.



During the first stage of research, the experiments were conducted on 17 horses, 8 of which had permanent cecum fistula installed, and 9 clinical cases with symptoms of suddenly occurring diarrhea. Two of the horses with fistula died within 2 weeks from its suturing because of complications in the form of streptococcal enteritis and hemorrhaging disease *(morbus maculosus equorum)*. After healing up of postoperative wounds we tried to induce colitis "X" in 6 remaining horses with fistula by administering antibiotics (Oxytetracyclin) in the form of MEPATAR® p.o. and dose of 500 g of the preparation twice daily for 14

days/animal, and LINCO-SPECTIN® in the dose of 10 mg/kg b.w. once a day for 8 days i.v. and p.o. through nosogastric tube. The intestinal contents for fermentative tests, determination of gas composition and volatile fatty acids (VFA) concentration was taken intravitally through permanent fistulas from the cecum or directly after death during anatomico-pathologic examination. Fermentative tests were conducted under anaerobic conditions inside special washers constructed basing on the so-called artificial rumen model (Czerkawski's method modified by Zawadzki). The sample meant for incubation consisted of: cecum contents, "artificial saliva" and distilled water. The samples prepared in this way were incubated in shakers with water bath for 1, 2, 4, 6 and 12 hours in order to determine standard fermentation models and changes taking place in fermentation processes during diarrhea symptoms occurrence. We measured pH, percentage composition of gases produced by incubated cecum contents in blind horses, production of volatile fatty acids (VFA) and percentage of particular VFA in the general pool of the acids. After onset of diarrhea the cecum and small colon contents were taken for microbiological and parasitologic tests. Samples for culturing were taken sterilly directly onto the previously prepared medium - TH broth and tioglycolan medium with t. Oxoid ram blood and onto liquid medium of 15 mm column of water. Each of the supplied samples was additionally inoculated onto blood agar medium, MacConkay's medium, Sabouraud's medium, broth with glucose and SF medium (with acidic sodium selenate) as well as Toth Hevit's medium. In order to find pathogenic anaerobic bacteria, sample cultures meant for plates with tioglycolan agar and ram blood were incubated for 10 days in continuous culture at 37^{o}C under anaerobic conditions with addition of 10% CO_2 and use of chamber - GENBAG MicroAir manufactured by Biomerieux. Additionally, in order to isolate and identify *Clostridium sp*., and particularly *Cl.difficile*, the samples were inoculated onto selective medium CCFA (cycloserine + egg yolk + fructose agar) and also cultured for 48 hours under anaerobic conditions at 37^{o}C. Cultures from liquid media were repeated after 48 hours. After culturing, the isolation of micro-organisms and identification tests were conducted. Stool samples were also tested for *Salmonella sp*. infection. Parasitologic test was conducted by the use of standard methods of flotation and sedimentation in saturated NaCl solution. Additionally, in order to compare the changes occurring in the animals' organisms during Salmonella sp. infection with those occurring during Colitis X, 3 horses were infected with *Salmonella tymphimurium* (live, virulent broth culture of 10^5 bacteria in 1 ml density in the dose of 50 and then 80 ml/animal via fistula). Because of the lack of clinical symptoms the same horses were infected with *Salmonella eneritidis* (live, virulent broth culture of 10^5 and 10^8 bacteria in 1 ml in the dose of 50, 80, 100 ml/animal, twice via fistula). The were no disease symptoms in this case, either.

Then, the same 6 horses were given live, virulent (biologic test on mice) broth culture of Salmonella eneritidis of 10^{10} bacteria in 1 ml in the dose of 150 ml/animal, single dose p.o. with fodder (oat).

For the second stage of the research we used 6 healthy horses without fistulas conducting diagnostic laparotomy under inhalation anesthesia using halotan as the main anesthetic. For premedication we used Domosedan® and, as muscle relaxant, 5% solution of gwajamar intravenously. Directly after putting down the animal, and before intubation, Thiopental® was administered intravenously as an introduction to general anesthesia. Surgical procedures lasted about 90 minutes each. We emptied the cecum of the operated horses and additionally administered into its lumen a dose of 100 ml of LincoSpectin® antibiotic preparation. For 5 days after surgery the horses were given orally, with fodder or by catheter, a dose of 400 mg of Mepatar® preparation twice a day. In these cases also, in spite of many inter- and post-operative changes of the determined parameters, we did not find diarrhea symptoms.

Venous blood for tests was drawn from *vena jugularis externa dextra* and arterial blood from *arteria temporalis sinistra*. Histopathologic tests were made on sections of mucous membrane taken from the middle part of jejunum, body and apex of the cecum, pelvic flexure and the right upper layer of big colon as well as from the middle part of small colon. Some sections of intestinal mucous membrane were also worked up under electron microscope (transmission).

During hematological tests we determined the number of erythrocytes, leukocytes, hemoglobin concentration, hematocrit number and pattern of white blood cells.

Concentrations of Na^+, K^+, Mg^+, Ca^{++}, Pn., triglycerides, cholesterol, ammonia, glucose, urea, creatinine, total bilirubin with separation into unconjugated and conjugated bilirubin, total protein and albumin, alkaline phosphatase (AF), alanine (GPT, AIAT) and aspartate (GOT, AspAT) aminotransferase and cortisol in blood plasma were determined. We also determined blood plasma osmolality.

Gasometric analysis of arterial blood was also conducted, paying particular attention to blood pH, excess or deficiency of bases (BE) and HCO_3^- concentration.

Concentrations of Na^+, K^+, Cl^- and osmolality of the samples of the cecum and big colon contents were also determined.

Hematological blood tests were conducted according to traditional methods, biochemical plasma tests were performed using automatic biochemical analyzer EKTACHEM 60 DT II SYSTEM manufactured by Kodak. Serum osmolality, caecum and colon contents were determined by the use of Knauer osmometer.

Determination of Na^+, K^+, Cl^- concentrations in the intestinal contents were done using ionoselective analyzer 644 made by Kodak.

Gasometric blood tests were conducted with CORNING 860 apparatus.

Initial total cortisol concentration was determined after previous animal acclimatization to clinical conditions, i.e. after two weeks from bringing them to the Clinic. Blood samples for total cortisol determination were always drawn between 8.00-9.00 a.m.. Experimental horses with fistulas had reference values of total cortisol determined two weeks after surgery for 5 subsequent days. Total cortisol level in case of the horses that had laparotomy and cecocentesis was determined directly before surgical procedure, intra-operatively (in 20th and 40th minute of the operation), directly after surgery and after 24 hours from it. Horses with salmonellosis symptoms were monitored with regard to total cortisol level in blood, and the samples were drawn every day during the whole period of the disease at the above given times of the day. The total cortisol blood level of the horses with clinical form of colitis "X" was determined in a similar way.

Total cortisol blood level determination was conducted by radioimmunologic method with the use radioactive iodine (J^{125}) employing tests manufactured by "Immunotech" – The Czech Republic.

RESULTS

The effort of inducing diarrhea by administration of antibiotics such as oxytetracycline and lincomycine with spectinomycine did not bring any results. During the whole period of the experiment the horses showed no clinical symptoms. In microbiologic tests we found only a decrease of the total number of bacteria in stool cultures and in the bacterial pool Gramm "-" bacteria prevailed distinctly (*E.coli, Enterobacter cloacae, Enterobacter agglomerans*). That is why we also performed tests of 9 horses with symptoms of colitis X directed to our Clinic.

It was impossible to induce any symptoms of the disease by fistular infection of the horses infected with *Salmonella tymphimurium* and *Salmonella enteritidis*. However after oral infection distinct clinical symptoms occurred. Horses infected during this stage of the experiment died with symptoms of shock, colic pain and increased temperature within 72 hours from bacteria administration. Unfortunately, we did not obtain the expected effect in the form of diarrhea.

A. CLINICAL SYMPTOMS

1. Colitis X

a. Temperature 38,3±0,5^{o} C,
b. Retained appetite, decreased, lack of distinct colic symptoms, weakened peristalsis, scaphoid abdomen, strong rectal straining with frequent watery stool without blood (5-6 x/hour) and groaning, standing posture, mucous membranes congestion (intensively red color),
c. In rectal examination strong tonus of all sphincters, retraced spleen from abdomen wall, the cecum and ascending colon filled with liquid contents,
d. Liquid stool present in amulla recti and descending colon,
e. Oliguria to anuria,
f. Quickly deteriorating general condition,
g. Capillary vessel's filling time prolonged to 5-7 seconds.

2. Superacute Salmonellosis

a. Temperature 39,5±0,3^{o} C,
b. Apathy, lack of appetite and thirst, retention, strong colic pain, scaphoid abdomen, constipation, weakened peristalsis, lack of rectal straining,
c. No changes in rectal examination,
d. Cyanotic mucous membranes,
e. lack of diarhoea
f. Oliguria,
g. Quickly deteriorating general status,
h. Capillary vessel's filling time prolonged to 6-7 seconds.

Table 1. Results of hematological blood tests.

Hematological blood tests		
Parameter	**Colitis X** n=9, $\bar{X}$±SD, max. – min.	Superacute Salmonellosis n=6, $\bar{X}$±SD, max. – min.
L (G/l)	3,95±0,53 3,5 – 4,5	3,54±0,32 3,2 – 3,8
Bacteria (%)	5,11±2,62 2 – 10	18,89±3,82 15 - 25
Segments (%)	27,33±5,5 20 - 35	33,78±10,74 12 - 42
Eosinophils (%)	1,22±0,83 0 - 2	1,66±1,12 0 - 3
Lymphocytes (%)	58,89±5,97 50 - 68	61,44±3,57 56 - 65
Monocytes (%)	5,11±2,08 3 - 10	8,22±1,39 6 - 10

E (T/l)	9,03±0,47 8,45-9,96	7,65±0,73 6,88 – 8,98
Hb (g/dl)	20,13±1,82 18,4 – 23,1	13,89±2,01 11,8-14,4
Ht (l/l)	0,63±0,032 0,59-0,68	0,57±0,016 0,56 – 0,60

Table 2. Results of biochemical blood plasma tests

Results of biochemical blood plasma tests		
Parameter	**Colitis X** n=9, $\bar{X}$±SD, max. – min.	**Superacute Salmonellosis** n=6, $\bar{X}$±SD, max. – min.
Total protein (g/l)	78,45±4,28 60 – 84,5	72,58±5,12 68 - 75
Albumins (g/l)	35,49±4,02 28 - 39	37,16±3,18 35 - 39
AspAT (U/l)	192,45±6,15 188 - 201	279,43±39,32 223-325
AlAT (U/l)	27,14±6,54 14 - 32	23,65±3,7 18-29
FA (U/l)	230,4±8,71 219-240	261,5±17,88 230-286
Glucose (mmol/l)	6,99±0,16 6,8 –7,2	4,72±0,28 4,2-5,0
Bilirubin (µmol/l)	117,8±38,41 79,6-192	106,16±40,61 65,5 - 180
Urea (mmol/l)	6,96±1,73 4,2 –8,5	7,7±1,53 5,0-9,2
Creatinine (µmol/l)	194,14±7,2 182-202	208±15,95 190-235
NH_3 (µmol/l)	7,57±2,57 3 - 10	13,85±8,21 3 - 25

Table 3. Electrolyte levels and blood plasma osmolality.

Electrolyte levels and blood plasma osmolality		
Parameter	**Colitis X** n=9, $\bar{X}$±SD, max. – min.	**Superacute Salmonellosis** n=6, $\bar{X}$±SD, max. – min.
Na^+ (mmol/l)	123,5±3,63 118-128	124,5±2,33 120-127
K^+ (mmol/l)	3,19±0,17 2,99-3,47	2,97±0,15 2,8-3,2
Cl^-(mmol/l)	84,5±1,6 82 –87	90,38±3,93 86-95

Mg^{++}(mmol/l)	0,93±0,06 0,84 –1,0	1,13±0,19 0,9-1,3
Ca^{++}(mmol/l)	2,99±0,16 2,8-3,2	3,13±0,23 2,8-3,4
Pn (mmol/l)	1,11±0,16 0,9 – 1,3	1,11±0,09 1,0-1,2
Blood plasma osmolality (mOsm/l)	301,6±12,48 280 - 310	289,3±4,11 279 - 290

Table 4. Selected ABE (Acid Base Equilibrium) parameters of arterial blood

Selected ABE parameters of arterial blood		
Parameter	**Colitis X** n=9, $\bar{X}$±SD, max. – min.	**Superacute Salmonellosis** n=6, $\bar{X}$±SD, max. – min.
pH	7,28±0,04 7,24 – 7,36	7,31±0,03 7,28 -7,37
BE (mmol/l)	- 6,58±1,41 -8,5 - -4,7	- 3,8±0,65 -4,5 - -2,8
HCO_3^- (mmol/l)	19,9±0,61 19,1-20,8	20,74±0,26 20,4-21,1

The most prominent in hematological tests in cases of salmonellosis as well as colitis X is leucopenia. Total leukocyte number in the animals infected with *Salmonella enteritidis* and displaying acute symptoms of the disease decreased to 3,54±0,32 G/l. In case of the horses with acute symptoms of colitis X, the total leukocyte number was also low with the average 3,95±0,53 G/l. There was no statistically significant difference between the average leukocyte numbers in both groups of horses.

The most important changes in hematological and gasometric blood tests, and biochemical analysis of blood plasma in horses diagnosed with colitis "X" is shown below:

1. Leucopenia - 3,95±0,53 G/l with neutrophilia - 27,33±5,5% of neutrophils with segmented nucleus, 5,11±2,62% of neutrophils with rod nucleus, degenerative shift of Shilling's picture and relative lymphocytosis.
2. Polycythemia - 9,03±0,47 T/l, increase of hematocrit number to 0,63±0,032 l/l and hemoglobin concentration to 20,13±1,82 g/dl.
3. Increase of total protein to 78,45±4,28 g/l.
4. Increase of alanin transpherase activity (GPT, AlAT) to 27,14±9;6,54 U/l.
5. Decrease of Na^+ concentration to 123±3,63 mmol/l and Cl^- to 9;84,5±1,6 mmol/l.
6. Increase of glucose concentration to 6,99±0,16 mmol/l, total bilirubin to 117,8±38,41 µmol/l and creatinine to 194,14±7,2 µmol/l.
7. Metabolic acidosis with decrease of HCO_3^- to 19,9±0,61 mmol/l, base deficiency (BE) of 6,58±1,41 mmol/l and decrease of blood pH to 7,28±0,04.

The most distinct deviations from reference values in cases of experimentally induced salmonellosis are shown below:

1. Leucopenia - 3,54±0,32 G/l, with neutrophilia - 33,78±10,74% of neutrophilia with karyolobism, 18,89±3,82% of neutrophilia with rod nucleus and relative lymphocytosis.
2. Decrease of Na^+ concentration to 124,5±2,33 mmol/l and Cl^- to 90,38±3,93 mmol/l.
3. Increase of total bilirubin concentration to 106,16±40,61 µmol/l and creatinine to 208±15,95 µmol/l.
4. Metabolic acidosis with decrease of HCO_3^- concentration to 20,74±0,26 mmol/l, base deficiency (BE) of the order of 3,8±0,65 mmol/l and decrease of blood pH to 7,31±0,03.

In cases of diagnosed colitis "X", the total cortisol concentration at 8.00-9.00 a.m. in a twice-conducted test within the first 48 hours of disease averaged 298,45±6.8 nmol/l with minimal value of 281,62 nmol/l.

In experimentally induced salmonellosis, the total blood plasma cortisol concentration at 8.00-9.00 a.m. averaged 254,72±9,3 nmol/l with maximal value in a twice-conducted test (until the horse's death) of 271,15 nmol/l.

Reference concentration of total cortisol in blood plasma was determined in experimental horses before the administration of antibiotics, and it averaged 128,56±7,9 nmol/l. The range of reference values for the tested parameter before the beginning of the experiment was within 125,38 - 134,42 nmol/l. Blood samples for total cortisol determination were also drawn between 8.00 - 9.00 a.m.

B. EXAMINATION OF THE CECUM AND BIG COLON CONTENTS

Changes in percentage of fermentative gases produced in the cecum and big colon of the horses during colitis "X" symptoms occurrence are presented in comparison with determined physiological values in pictures 15-18.

Significantly lower production of CO_2 was found during the xamination of fermentative gases composition in the cecum contents as well as in big colon contents of the horses with colitis "X" symptoms. The capacity of the produced CO_2 in the contents of both of these segments of large intestine in sick horses decreased of about 5-7% in relation to the initial values. At the same time we observed the increase of hydrogen level of about 5% in relation to initial values, and decrease of CH_4, which fell almost to zero in the cecum and was distinctly lowered in big colon.

Together with percentage changes of the fermentative gases composition in horses with colitis "X" symptoms, pH value of the examined cecum and big colon contents increased. In relation to reference values (n=25) oscillating between 6,9 - 7,5 it increased to 7,8 - 8,3.

There were also changes in total quantity of the VFA produced in the cecum and big colon (picture 19-22). Both the global quantity of VFA in the intestine contents, and percentage content of particular VFA in the global pool of the intestine contents VFA decreased. In the samples taken from the cecum contents, the global content of VFA in the sick horses oscillated between 7,5-12,9 µmol/ml, and in big colon content it was between 6,09-10,47 µmol/ml. Reference values determined for total VFA were for the cecum and big colon respectively: 8,8-15,1 µmol/ml and 7,1-12.3 µmol/ml.

We did not find lactic acid presence in the examined large intestine contents. The content of acetic acid in total pool of VFA in the cecum and big colon content increased. We also noted an increase in the percentage content of propionic acid in the general VFA pool in both parts

of large intestine. A decrease of butyric and isobutyric acids was noted in the general VFA pool of large intestine contents.

Concentration of basic electrolytes in the cecum contents of healthy horses was respectively: Na^+ - 122±2,87 mmol/l, K^+ - 13,22±3,67 mmol/l, Cl^- - 28,56±6,39 mmol/l with osmolality of 280,56±15,16 mOsm/l.

Concentrations of electrolytes in big colon contents of the healthy horses were respectively: Na^+ - 82,44±11,39 mmol/l, K^+ - 53,88±8,1 mmol/l, Cl^- - 27,18±5,18 mmol/l with osmolality of 295±11,56 mOsm/l.

In case of horses with colitis "X" symptoms, the concentration of all the determined electrolytes in the cecum and big colon contents increased. For the cecum contents the values were respectively: Na^+ -131±4,56 mmol/l, K^+ - 18,39±3,17 mmol/l, Cl^- - 32,14±6,18 mmol/l. The osmolality increased to 299.59±11,45 m Osm/l.

In the big colon contents, the electrolyte concentrations were: Na^+ - 87,28±8,04 mmol/l, K^+ - 59,14±4,25 mmol/l, Cl^- - 34,21±8,25 mmol/l. Osmolality increased only a little to 297,12±15,31 mOsm/l.

Additionally we conducted electrolyte analysis of stool samples in order to determine whether diarrhea had an osmotic character. Electrolyte concentration in diarrheal stool was: Na^+ - 86,69±6,9 mmol/l, K^+ - 62,34±4,12 mmol/l, Cl^- - 38,57±7,12 mmol/l. Osmolality of diarrheal stool averaged 298±11,4 mOsm/l. The ionic gap calculated from the difference between total stool osmolality and doubled sum of Na^+ and K^+ concentrations averaged 4,62±1,3.

C. MICROBIOLOGIC EXAMINATION OF CECUM CONTENTS AND STOOL

Total bacteria quantity in the cecum contents of healthy horses was determined as $10^{10} – 10^{12}$ bacteria/content gram. This included *Lactobacillus sp.* – $10^3 – 10^5$ bacteria/content gram, *Enterococcus sp.* - 10^2 - 10^3 bacteria/content gram, *Enterobacteriaceae* including *E.coli* - 10^3 - 10^4 bacteria/stool gram. There was no observation conducted of anaerobic bacteria except *Lactobacillus sp.*

After the administration of antibiotics (Mepatar® and Linco-Spectin®) only the general number of bacteria decreased to 10^8 - 10^9 bacteria/stool gram. Within this number the quantity of bacteria from *Enterobacteriaceae (E.coli)* family increased to 10^4 - 10^5 bacteria/content gram, and the quantity of bacteria from *Enterococcus sp.* family decreased to 10^2 and *Lactobacillus sp.* to 10^3 bacteria/content gram.

Similar examinations were done for the healthy horses stool and during the administration of the mentioned antibiotics. We found analogical general number of bacteria as in case of the cecum contents. The number of *Lactobacillus sp.* was slightly smaller and fluctuated between 10^3 - 10^4 bacteria/stool gram. The number of bacteria belonging to the remaining families was: *Enterococcus sp.* 10^3 - 10^4 bacteria/stool gram, *Enterobacteriaceae*, including *E.coli* - 10^4 - 10^5 bacteria/stool gram.

After the use of the above mentioned antibiotics we observed a decrease of the general number of fecal bacteria as in the cecum. Also in stool there was an increase of bacteria from *Enterobacteriaceae (E.coli)* family in stool increased to 10^6 bacteria/stool gram, and a decrease of *Enterococcus sp. bacteria* number to 10^2 bacteria/stool gram and *Lactobacillus sp.* to 10^2 bacteria/stool gram.

The biggest group of bacteria isolated from the cecum cultures consisted of: *Streptococcus viridans, Streptococcus faecium, Enterobacter clocae, Enterobacter agglomerans, E.coli, Staphylococcus intermedius, Staphylococcus epidermis and Klebsiella pneumoniae.* We isolated *Streptococcus zooepidemicus* and *Staphylococcus aureus* from the cecum contents and stool of only two horses.

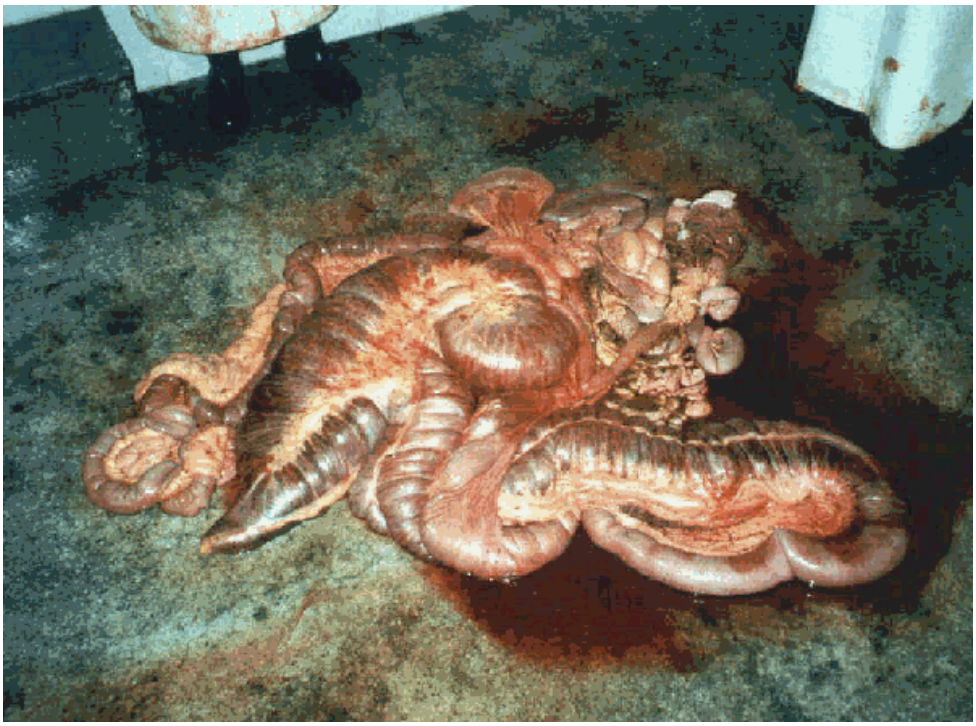
Colitis X - the most frequently isolated from the cecum contents and stool were non-hemolytic *E.coli, Streptococcus faecalis*, and after multiplication *Pseudomonas aeruginosa* and *Candida albicans*. In any of the 9 cases of colitis "X" we did not find anaerobic bacteria of *Clostridium sp.* kind.

Superacute salmonellosis - we found abundant growth of *Salmonella enteritidis* in cultures from stomach, small intestine, the cecum, big colon and stool as well as from mesenteric lymph nodes, liver and spleen.

D. AUTOPSY AND HISTOPATHOLOGIC PICTURE

Colitis X - macroscopic change of the cecum and large intestine color to purplish (il.5). Similar color changes are observed in the above mentioned intestine's mucous membrane. Edemas and infiltrations of the cecum walls and big colon. In some cases also of small colon. Lack of macroscopic changes in stomach and small intestine (il.6). Small, numerous supraepicardial and postendocardiac extravasations in the vicinity of heart auricles and in the course of coronary vessels, the size varying from pinhead to lentil bean (il.13 and 14). Pinhead size extravasations were observed also in myocardium (il.14). Similar extravasations with tendency of smaller ones to merge into bigger were found in lungs (il.7). Degeneration of intestinal vilii epithelium cells and those lining leading out intestinal glands, secretory segments showed little damage. We observed numerous dilated capillary vessels in the proper layer of mucous membrane as well as cellular infiltration: lymphocytes, neutrophils, mast cells.

Il.5. General view of the digestive tract of the horse with colitis "X".



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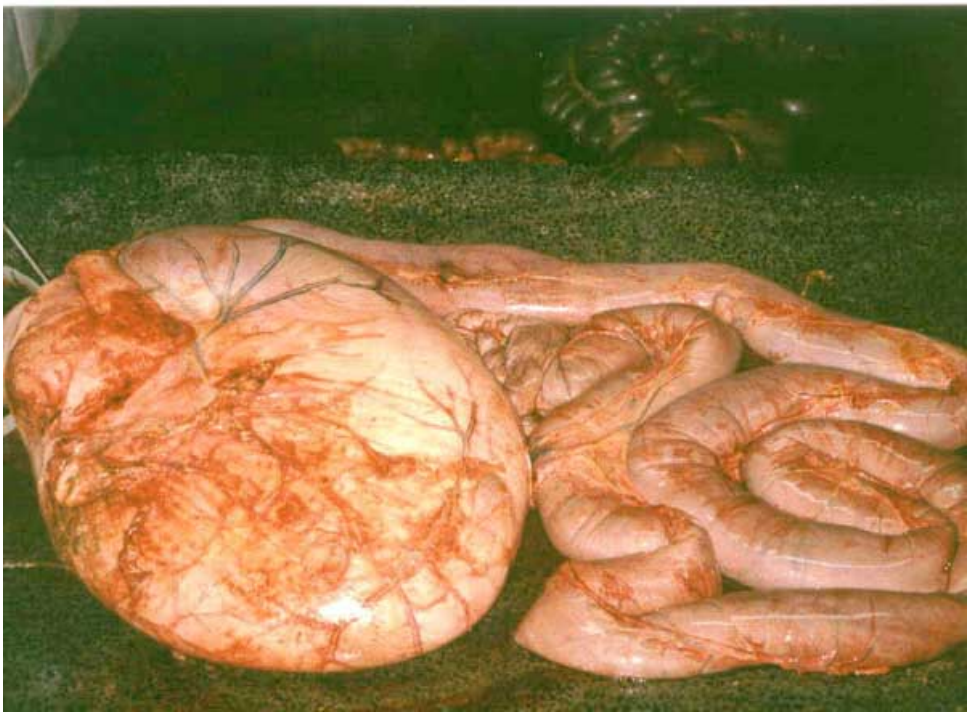
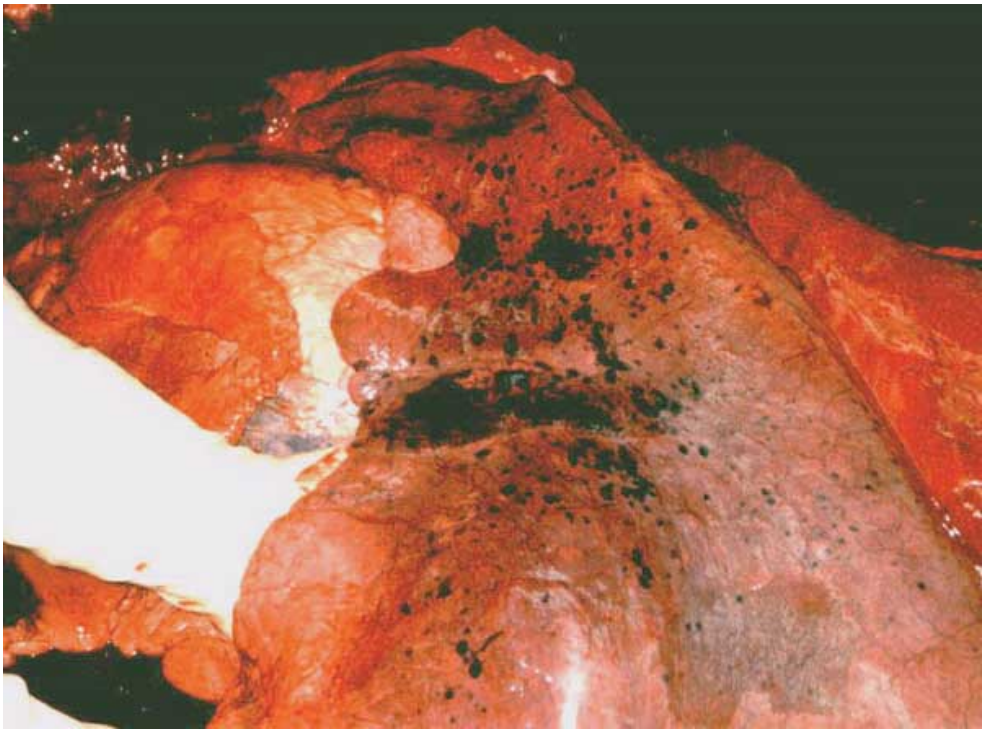
II.6. General view of the stomach and small intestine loops of the horse with colitis "X" symptoms.



II.7. Extravasations in the lungs of the horse with colitis "X".

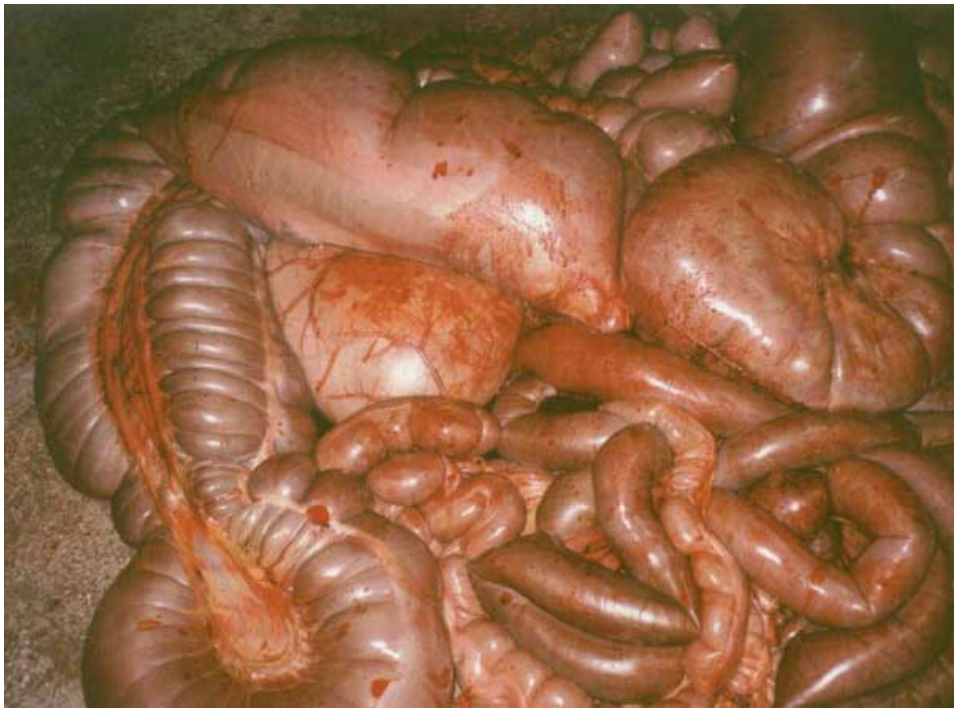


In the cecum and in big colon to a greater degree, there was vacuolization and degeneration of epithelium of almost whole intestinal crypt zone. A massive cellular infiltration consisting of lymphocytes, neutrophils, single eosinophils and mast cells was present around dilated capillary vessels of submucous membrane and proper layer of mucous membrane.

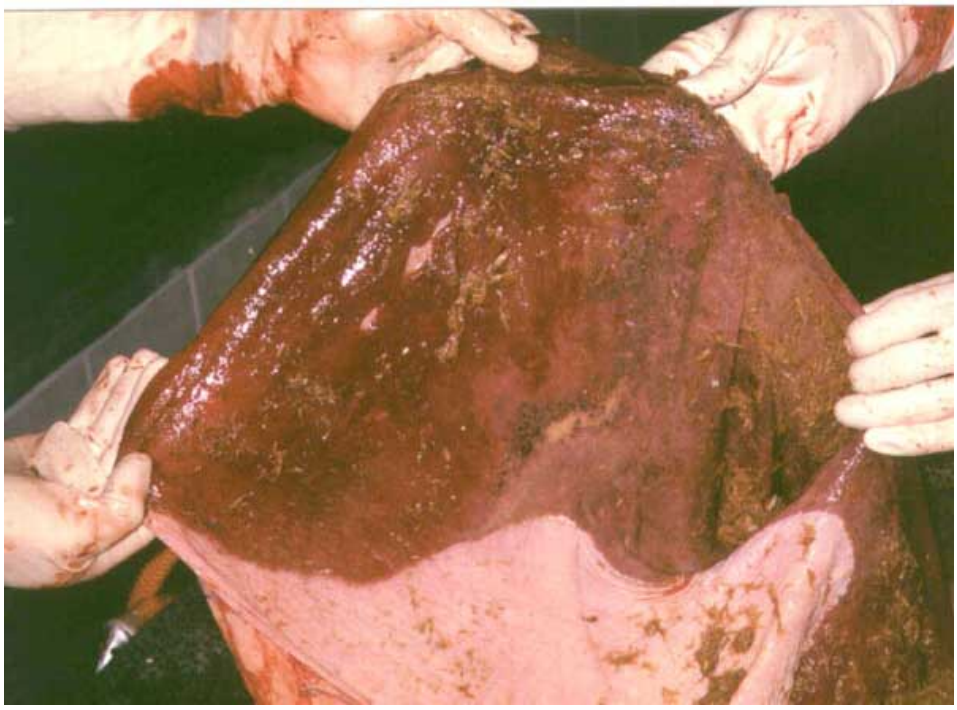
Histopathologic examinations of two cases of the disease showed that the most important changes occurred in the cecum. They concerned mainly vascular channel of the proper layer of mucous membrane. Distinct density reduction of capillary and precapillary vessels endothelium texture was observed. We also observed distinct dilation of venous vessels with contraction and decrease of arteries diameter. Mucous membrane epithelium showed signs of degradation characteristic in disorders of absorption processes. There was a decrease of enterocytes number and their degradation and tearing off from basement membrane of intestinal epithelium. Similar signs were observed with regard to mucogenic cells (goblet cells), however, in a slightly smaller degree. Vascular channel of the remaining layers of the cecum wall presented a basically normal picture. Histopathologic picture of big and small colon mucous membrane was similar but the changes were distinctly smaller. Histopathologic picture of the cecum and stomach showed no changes.

Superacute Salmonellosis - there was a macroscopic color change of the outer surface of the whole alimentary tract to dark violet with the most intensive coloration of stomach and small intestine, gradually disappearing in the direction of the cecum and big colon (il.8). Mucous membrane of stomach and small intestine was necrotically changed and covered with a peeling layer of epithelium and fibrin (il.9 and 10). We found ulcerations of the glandular stomach part (il.10). Slight changes which disappeared within the right upper layer of colon were also present in the cecum and big colon (il.11). Spleen was enlarged and swollen. Cardiac muscle and liver were also degenerated and fragile. We found only small and few subepicardial extravasations (il.12) and massive hemostasis in coronary vessels (il.12).

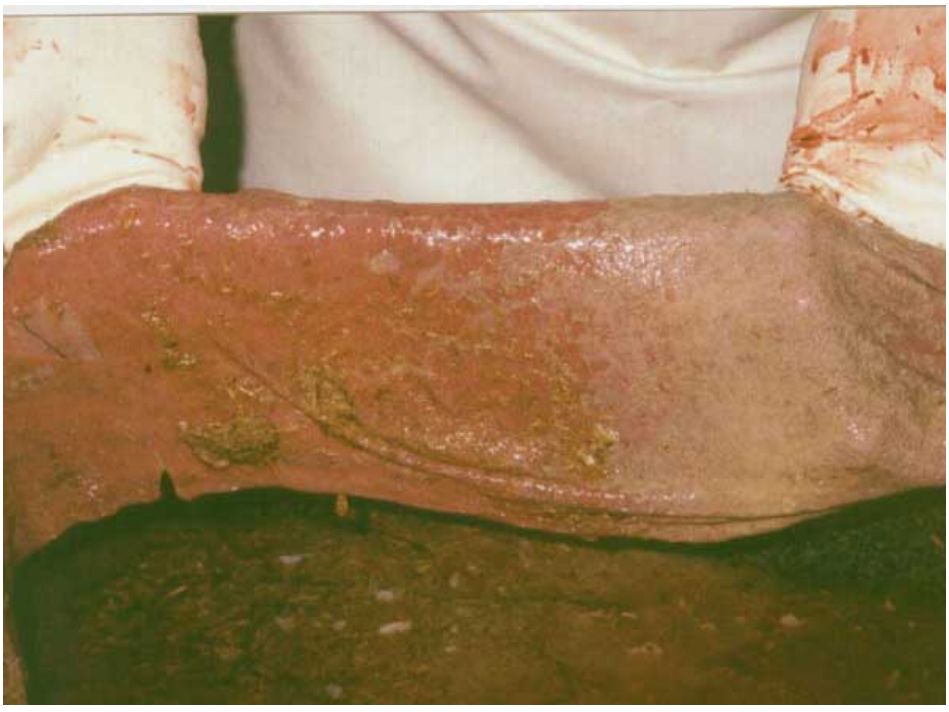
Il.8. General view of the digestive tract of the horse with superacute salmonellosis.



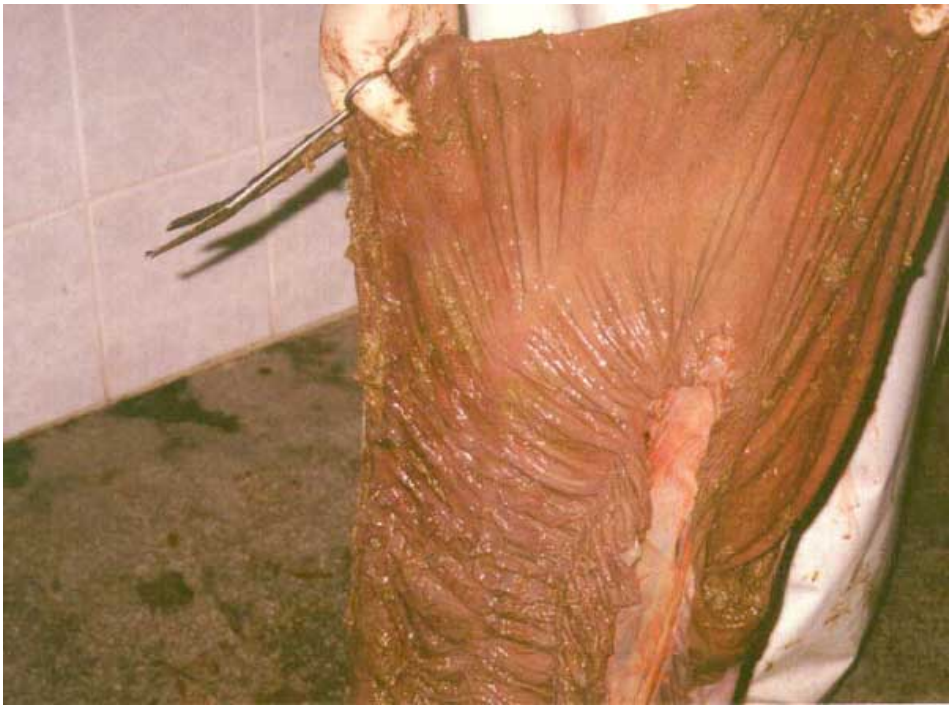
Il.9. Cyanotically-red, soft stomach mucous membrane with ulcerations of the horse with superacute salmonellosis symptoms.



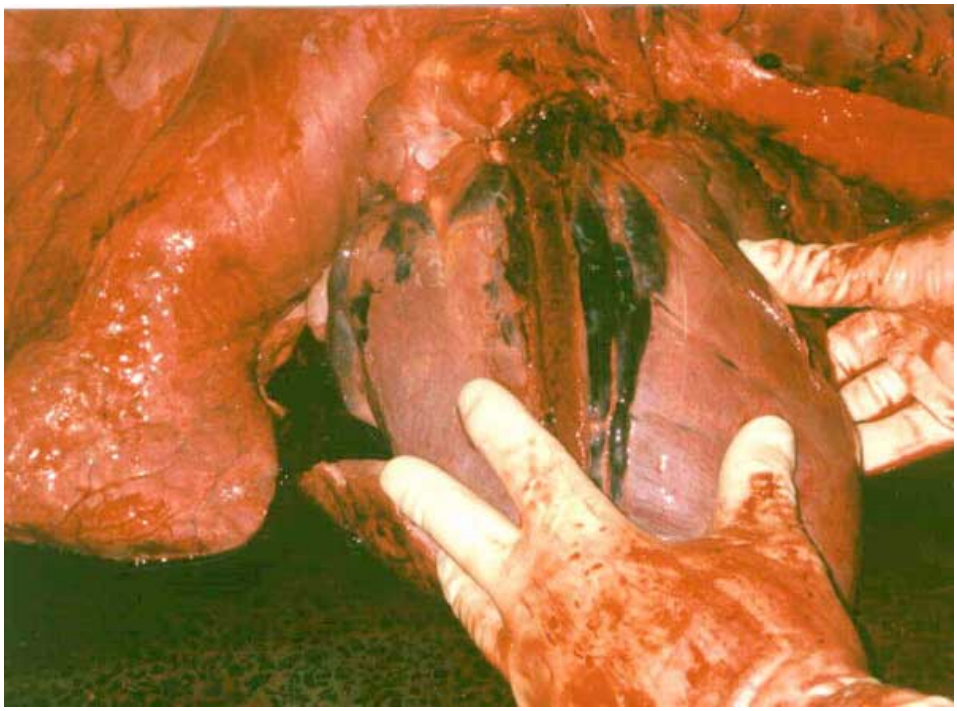
Il.10. Strongly congested, soft, locally necrotically changed and covered with fibrin coat mucous membrane of the jejunum of the horse with superacute salmonellosis symptoms.



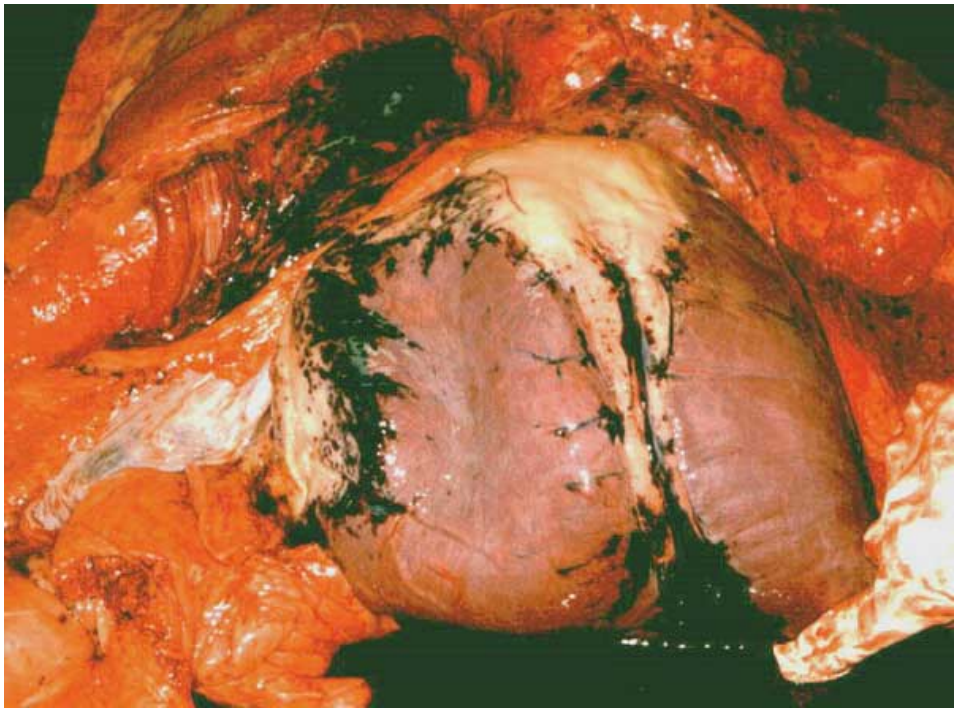
Il.11. Strongly congested, soft and without signs of necrosis mucous membrane of the upper and lower layer of big colon of the horse with superacute salmonellosis symptoms.



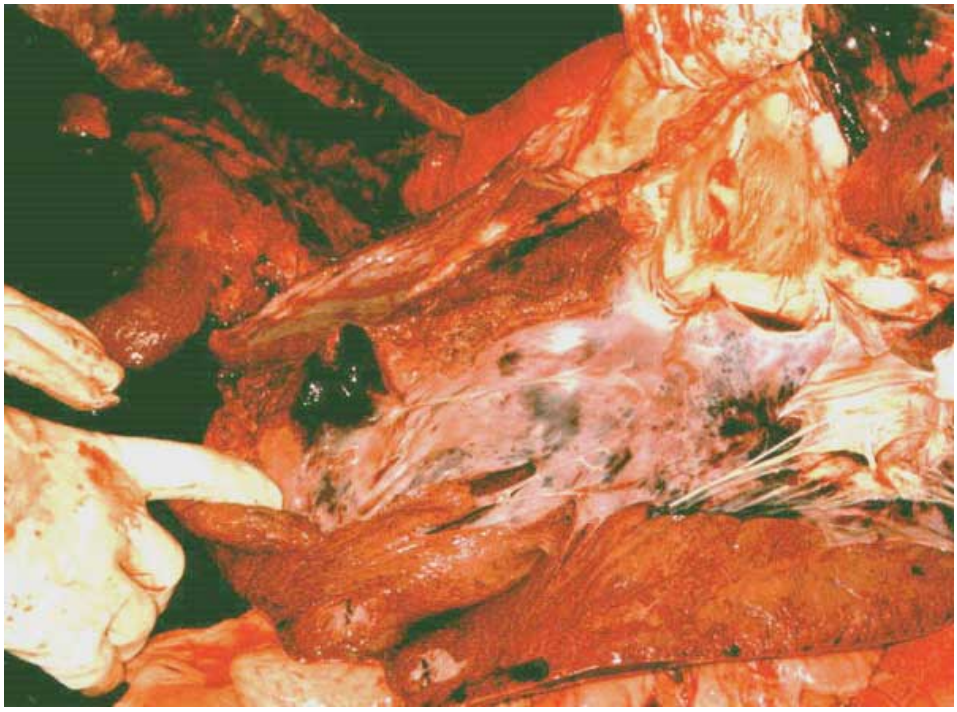
Il.12. Hemostasis in the main coronary vessels of the horse with superacute salmonellosis symptoms. Several, pinhead size subepicardial extravasations in the vicinity of the main coronary vessels.



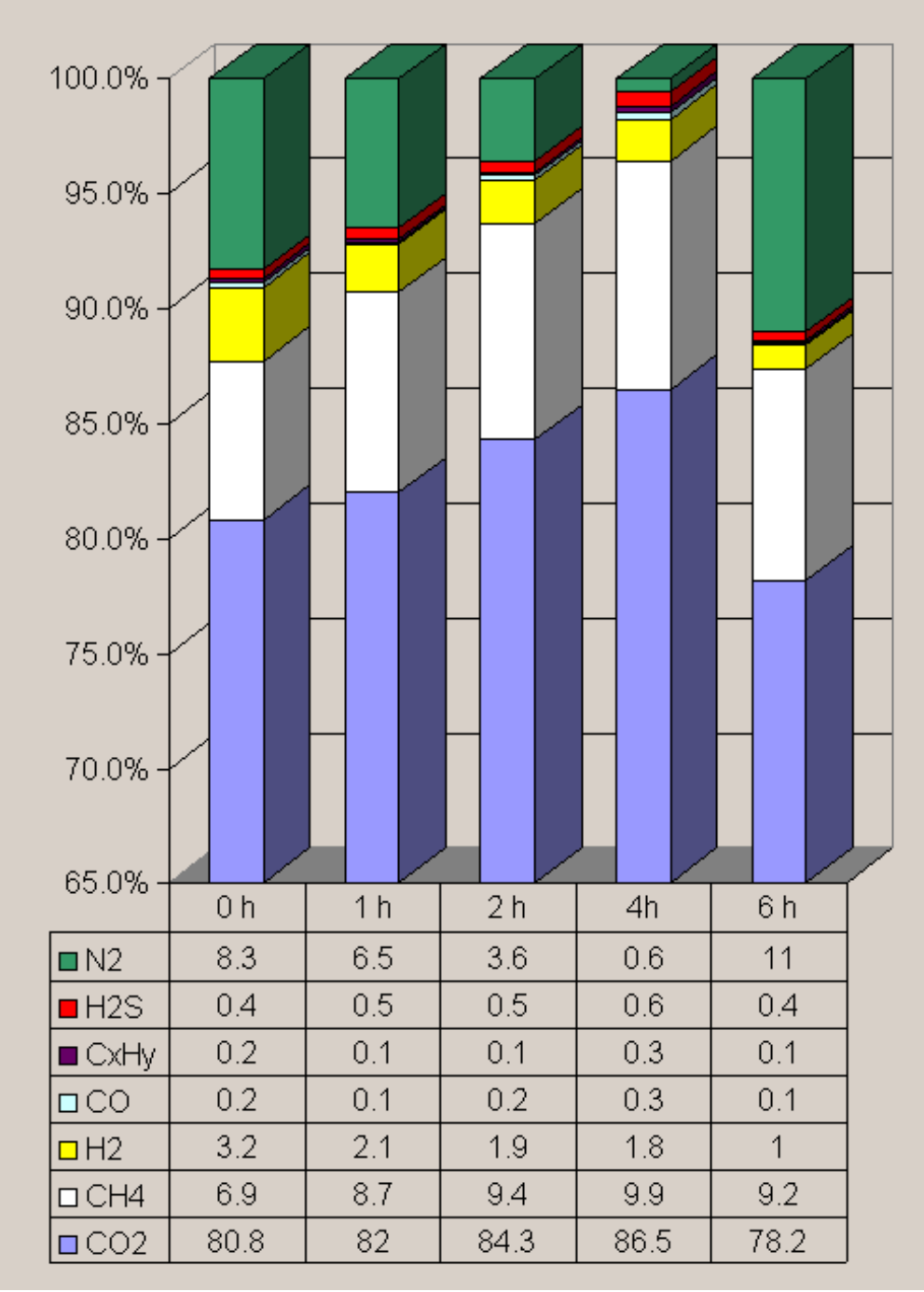
Il.13. Numerous, subepicardial extravasations in the heart of the horse with colitis "X" symptoms.



Il.14. Numerous, subendocardial and intramiocardial extravasations in the heart of the horse with colitis "X" symptoms.

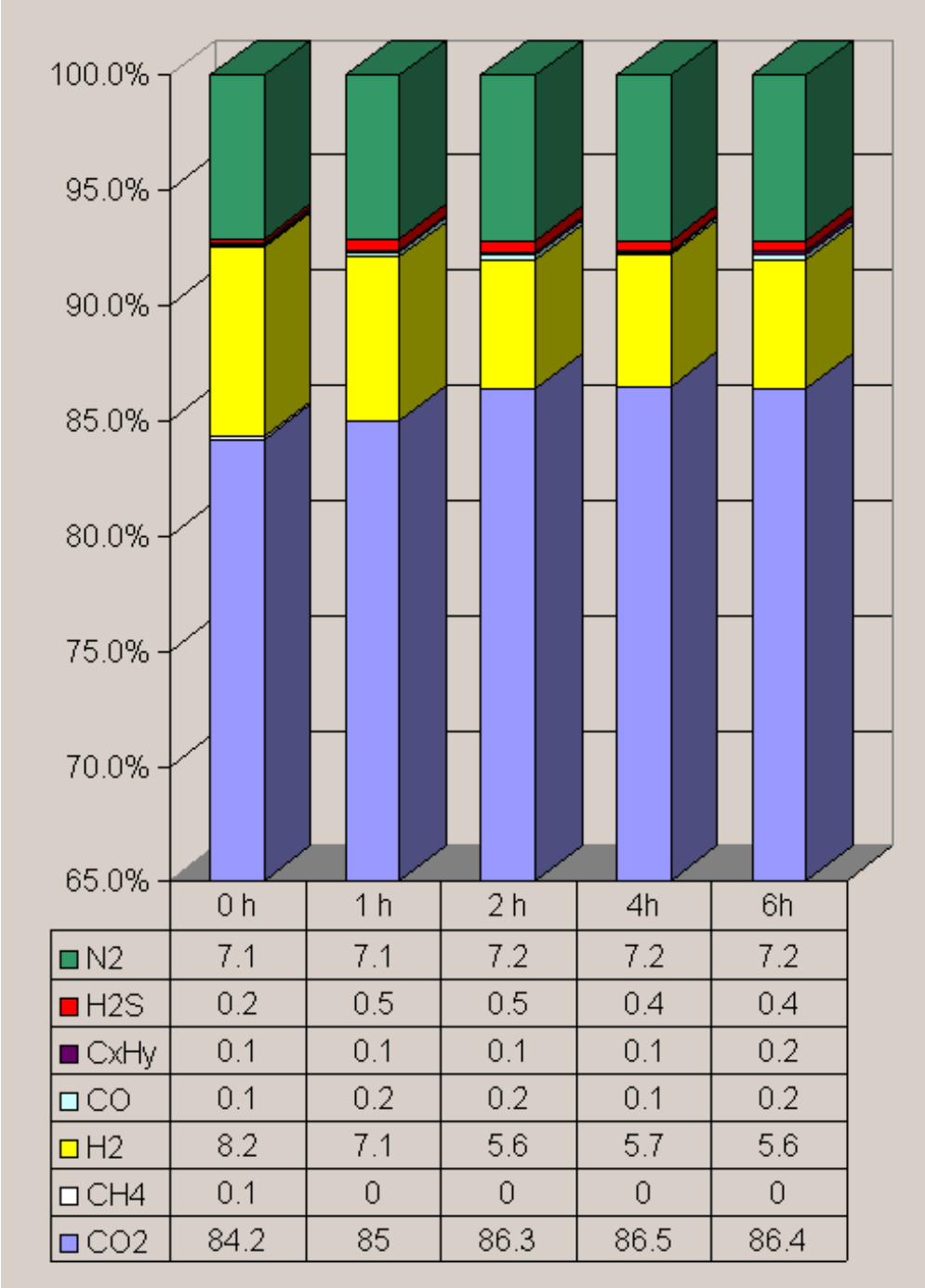


Il.15. Percentage composition of the gases produced in the cecum of healthy horses (%, n=25)



	0 h	1 h	2 h	4h	6 h
N2	8.3	6.5	3.6	0.6	11
H2S	0.4	0.5	0.5	0.6	0.4
CxHy	0.2	0.1	0.1	0.3	0.1
CO	0.2	0.1	0.2	0.3	0.1
H2	3.2	2.1	1.9	1.8	1
CH4	6.9	8.7	9.4	9.9	9.2
CO2	80.8	82	84.3	86.5	78.2

II.16. Percentage composition of the gases produced in the cecum of the horses with colitis "X" (%, n=9)



	0 h	1 h	2 h	4h	6h
N2	7.1	7.1	7.2	7.2	7.2
H2S	0.2	0.5	0.5	0.4	0.4
CxHy	0.1	0.1	0.1	0.1	0.2
CO	0.1	0.2	0.2	0.1	0.2
H2	8.2	7.1	5.6	5.7	5.6
CH4	0.1	0	0	0	0
CO2	84.2	85	86.3	86.5	86.4

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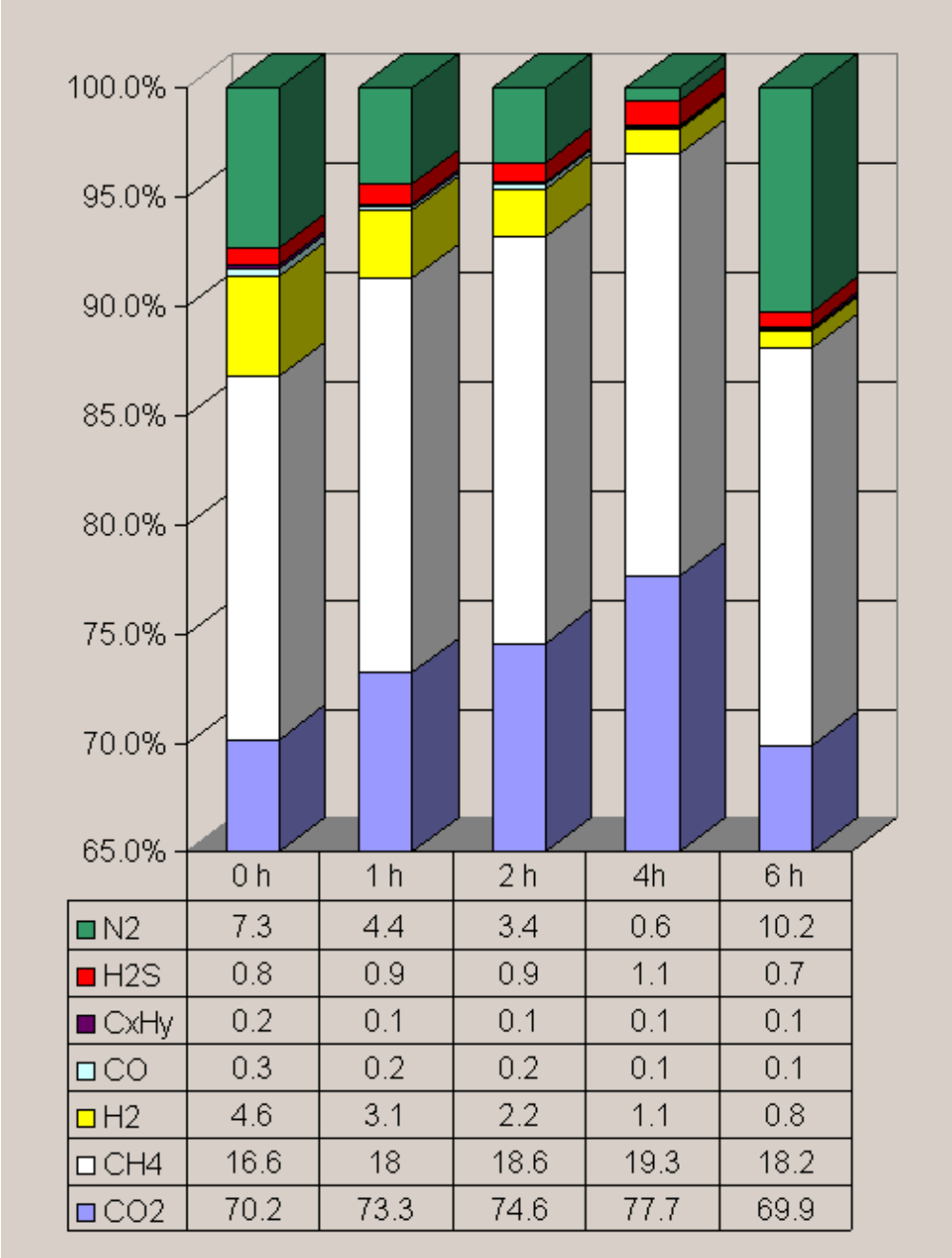
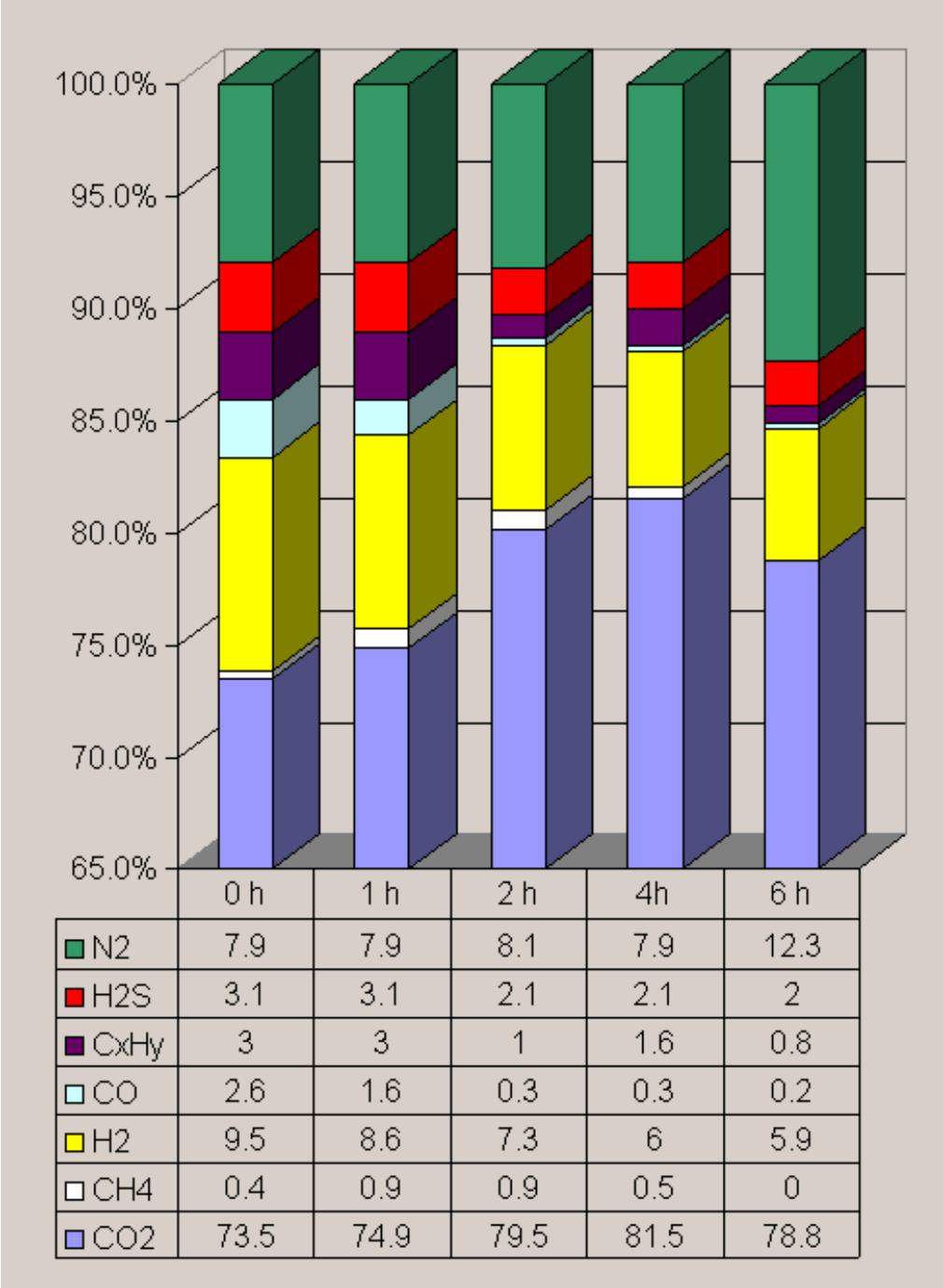
II.17. Percentage composition of the gases produced in the big colon of healthy horses (%, n=25)



	0 h	1 h	2 h	4h	6 h
N2	7.3	4.4	3.4	0.6	10.2
H2S	0.8	0.9	0.9	1.1	0.7
CxHy	0.2	0.1	0.1	0.1	0.1
CO	0.3	0.2	0.2	0.1	0.1
H2	4.6	3.1	2.2	1.1	0.8
CH4	16.6	18	18.6	19.3	18.2
CO2	70.2	73.3	74.6	77.7	69.9

II.18. Percentage composition of the gases produced in the big colon of the horses with colitis "X" (%, n=9)



	0 h	1 h	2 h	4h	6 h
N2	7.9	7.9	8.1	7.9	12.3
H2S	3.1	3.1	2.1	2.1	2
CxHy	3	3	1	1.6	0.8
CO	2.6	1.6	0.3	0.3	0.2
H2	9.5	8.6	7.3	6	5.9
CH4	0.4	0.9	0.9	0.5	0
CO2	73.5	74.9	79.5	81.5	78.8

There was a distinct necrosis and degeneration of mucous membrane epithelium cells in the cecum. We observed a massive infiltration consisting of lymphocytes, mast cells and neutrophils inside the proper layer of mucous membrane and in submucous membrane.

We also found vacuolization and degeneration of intestinal crypt cells of the cecum and colon. This concerned mainly upper zone of intestinal crypts while their bottom showed smaller degree of damage. The observed massive infiltration consisted of lymphocytes, neutrophils, single eosinophils and mast cells. We also observed numerous dilated capillary vessels of proper layer of mucous membrane and submucous membrane.

E. TREATMENT AND PREVENTION

The following procedures were routinely employed for prevention and early diagnosis of colitis "X":

- Daily blood test in all patients with colic diseases (leucopenia!),
- Postoperative fasting shortened to 12-14 hours,
- After positive diagnosis of colic disease feeding with small amounts of hay or mixture (excluding cases of small intestine resection),
- After occurrence or diagnosis of colitis "X" isolation in separate boxes (quarantine),
- Special care as to hygienic and disinfection principles employment in quarantine boxes where horses with colitis "X" were kept,
- Prophylactic examinations,
- Use of chemotherapeutic agents - for prevention of infection,
- Use of probiotics,
- Postoperative care as to the use of analgesics and sedatives (Diazepam (Relanium®) - 40-50 mg/animal i.v. every 12 hours)

Therapeutic procedures should include:

- Supplementation of liquids and electrolytes,
- Controlling metabolic acidosis by administration of acidic sodium carbonate,
- Plasma transfusion,
- Normalization of peristalsis (Neostygminum) or operative evacuation of bowels,
- Use of analgesics and anti-inflammatory drugs, mainly cyclooxigenase inhibitors (Flunixin-Meglumin-Flunimeg®),
- Probiotics,
- Antibiotics?,
- Procedures preventing thrombophlebitis during intensive intravenous infusions.

Hypovolemia must be controlled by permanent and massive intravenous infusion of compound electrolyte solution - up to 80 litres per day while conducting observations of hematocrit number fluctuations. In single cases, intravenous infusions had to have greater capacity, up to 100-120 litres/animal per 24 hours. In case of plasma albumins concentration decrease to 40 g/l we administered intravenously 2 to 10 l of blood plasma obtained from healthy animals. The quantity of blood plasma necessary to compensate hypoalbuminemia was calculated according to the following formula:

$$\frac{MC \times V_{Po} \times (Alb_1 - Alb_0)}{Alb_2}$$

MC - body mass (kg)
V_{Po} - plasma volume (ml/kg b.w.)
Alb_1 - desired albumin concentration (g%)
Alb_0 - patient's albumin concentration (g%)
Alb_2 - donor's albumin concentration (g%)

Normal plasma volume:
newborns: 95 ml/kg b.w.
foals 4 weeks old: 62 ml/kg b.w.

foals 12 weeks old: 53 ml/kg b.w.
beginning from 4, 6 month of life: 48 ml/kg b.w.

In case of metabolic acidosis we initially administered 50% of the calculated dose of Natrium bicarbonatum i.v. or in the form of intravenous infusion of 5% $NaHCO_3$ solution with compound electrolyte solutions. It is also possible to administer sodium bicarbonate orally.

$NaHCO_3$ dose was calculated according to the following formula:

BE (mmol/l x 0,3 b.w. (kg) = ml 8,4% solution $NaHCO_3$

8,4% solution of $NaHCO_3$ was diluted to 5% before intravenous administration.

In the diagnosed cases of colitis "X" we frequently observed great degree atonia of the cecum and colon. Rectal examination in such cases shows overfilling of the cecum and weak tonus of its wall. This necessitates immediate cecum evacuation by administering Neostygmin, Polstygmin or, in some cases, by laparotomy with cecostomy.

As shock controlling agent we used Flunixin-Meglumin i.v. acting pretty good in this species.

Administration of antibiotics was carried out by p.o. use of preparations containing acidophilic bacteria cultures. In our research we used preparation intended for various animal species - Enteroferment® which contains freeze-dried Lactobacillus acidophilus, in standard dose - 3 times a day full table spoon/animal. Administration of antibiotics is still a matter of discussion. They are used only sporadically as metaphilactic agents – enrofloxacin and metronidazol. We found out that metaphilactic use of enrofloxacin did not bring the expected effect of inhibition of colitis "X" occurrence, however, postoperative and intrasymptomatic use of metronidazol brings a significant decrease of the disease incidence and increases survival rate. Metronidazol was used in the dose of 10-15 mg/kg b.w. 4 times a day p.o. This allows for maintaining of the proper therapeutic concentration. However, metronidazol preparations are bitter in taste and the horses do not tolerate them well which causes problems with their administration.

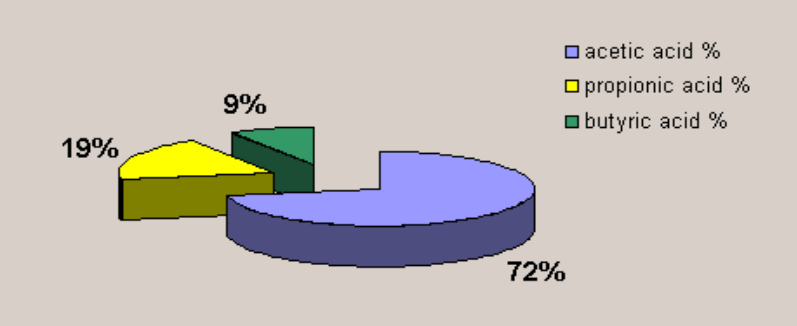
During colitis "X" therapy it is necessary to obtain a permanent venous access by catheterization of big venous vessels. Massive and permanent infusions may damage endothelium of the catheterized vessels leading to complications in the form of thrombophlebitis. For this reason, in some cases not only the jugular vein but also *vena epigastrica cranialis superficialis* was catheterized. Venous catheter was sutured into this vessel with Seldinger's method. After each infusion the catheter was filled with heparinized solution and closed.

Heparin was used in antithrombotic prevention according to the following formula:

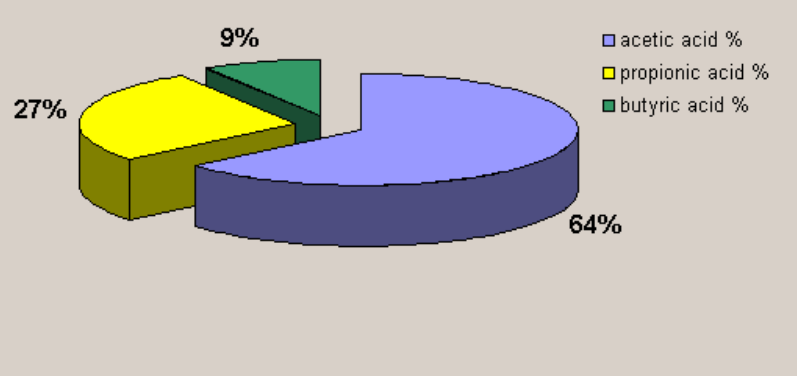
- initially 150 IE/kg b.w.
- 2-3 day - 2 times a day 120 IE/kg b.w.
- 3-7 day - 2 times a day 80 IE/kg b.w.
- beginning from day 8 - 2 times a day 40 IE/kg b.w.

Concluding, we can state that in cases of diagnosed colitis "X", the prognosis, in spite of therapy, is poor. It can't be expected that prevention and metaphilactic will significantly decrease number of clinical cases of the disease. However, the earlier the therapy is employed, the better therapeutic results are obtained.

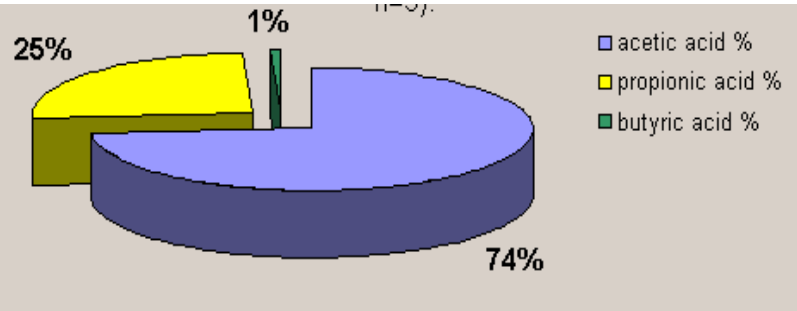
II.19. Particular VFA contribution in the general VFA pool in the cecum contents of healthy horses (%, n=15).



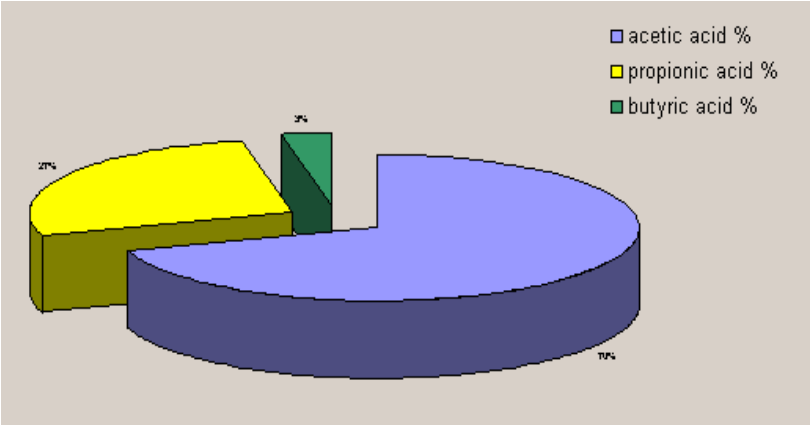
II.20. Particular VFA contribution in the general VFA pool in the big colon contents of healthy horses (%, n=15).



II.21. Particular VFA contribution in the general VFA pool in the cecum contents of the horses with colitis "X" (%, n=9).



II.21. Particular VFA contribution in the general VFA pool in the big colon contents of the horses with colitis "X" (%, n=9).



DISCUSSION

According to many authors who, clinically or experimentally, obtained sub-acute form of colitis "X", the processes taking place in the organism are of shock-like character, and the primary changes within intestines are of shock and not inflammatory origin [8,27,30,41]. They are assumed to be responsible for leading to suppression of intestinal barrier for toxins cumulated within the digestive tract lumen and to generalization of the intoxication process [22]. This fact seems to be confirmed by limitation of arterial capillary vessels patency in early stage of the disease development and, subsequently, to paralysis of muscular coat of all capillary vessels (arterial and venous) in submucous membrane and proper layer of mucous membrane. We obtained such histopathologic picture of the intestinal wall only in 2 cases of the disease. This might have been caused by relatively short time of the disease duration. Death occurred after 6 hours from the first clinical symptoms. The remaining clinical cases were autopsied after longer disease period, that is as late as during a developed shock characterized by paralysis of the muscular coat of all blood vessels of the large intestine wall. This leads to serious disorders in blood flow of the intestine wall and to Starling's balance shift in the direction of increased liquid filtration into the intestine lumen. The hydrostatic blood pressure increased in this way in the vascular bed of mucous membrane leads to subsequent impairment of water and electrolyte absorption and hypoxia and undernourish-ment of the intestinal wall as well as of mucous membrane cells. The shock process itself may have generalized character - and in this case large intestine and lungs are the shock effector - or local character (shock process starts from circulatory disorders in the large intestine). In the latter case circulatory disorders in the large intestine were a direct cause of massive liquid excretion into the intestine lumen which causes the occurrence of the generalized hypovolemic shock. This is confirmed by morphologic and histopathologic changes, limited only to the cecum and big colon in most clinical cases. The changes localized in the small intestine are so slight in comparison to the histo- and anatomopathologic picture of the large intestine that it might indicate their secondary character. They may be the result of the primary disorders developing in the large intestine.

Alimentary and non-alimentary factors leading to intestinal disbacterioses are considered as factors causing inflammatory states of the intestinal mucous membrane in most scientific papers. Most frequently they cause multiplication of the potentially toxin creating Gram "-" or anaerobic bacterial flora [7,8,13,20,26,27,28,30,32,36,37,45].

Toxins produced by some anaerobic bacteria of *Clostridium sp.* kind [43,45] have especially damaging effects on the mucous membrane (enterotoxin A s. D-1, cytotoxin B s. D-2) and G "-" bacteria (*Enterobacteriaceae*). They may lead to ulcerations of the large intestine wall mucous membrane and, after infiltration into blood circulation system, cause the occurrence of the general symptoms, intoxication and shock.

The most frequent feeding reason for the digestive tract disbacterioses are: feeding with digestible nutritive fodder (green fodder) and sudden qualitative changes of feeding. This results in the decrease of the pH value of large intestine contents, damage of the intestinal epithelium cells and, in consequence, to absorption of ecto- and/or endotoxins contributing to the development of colitis "X" syndrome [14,15,19,31,44]. During our experiment the horses were fed according to a permanent model. Alimentary dose consisted of a good quality hay given in abundance and 3-4 kg of crushed oat/24 hours/animal. Before and after surgical procedures on the abdomen and during experiments consisting only of antibiotic administration, we tried not to change alimentary dose and pre - and postoperative fasting was

limited to 5-6 hours. It was probably this rigorously observed quantitative and qualitative stability of the daily alimentary dose during the experiment that made it difficult or even impossible to induce typical colitis "X".

Greiß [11] and Versphol [43] suggest in their elaborations still different pathomechanism of colitis "X" development. Basing on microbiologic, histopathologic examinations and intra-operative observations of the horses displaying symptoms of this syndrome they prove that even insignificant initial damage of the large intestine mucous membrane turn into distinct ulceration within 14-20 hours. In their opinion these observations confirm the influence of the special necrotoxin kind produced by anaerobic bacteria on the development of full symptoms of colitis "X". In our experiment we were unable to obtain symptoms of colitis "X" even after laparotomy with cecotomy. The cecum incision was made along greater curvature at the boundary line of the cecum body and apex and was about 25 centimeters long (postoperative injury). Additionally we conducted manipulations always leading to the occurrence of micro-injuries of the mucous membrane of the operated horse's intestine. We did not isolate pathogenic anaerobic flora from the intestine contents of the horses with colitis X symptoms, and did not find any development of the especially dangerous bacteria of *Clostridium sp.* kind. This seems to indicate at the possibility of the occurrence of colitis "X" without active role of the anaerobic bacteria population in the pathomechanism of the disease. In our opinion, finding anaerobic, toxin producing bacteria of Clostridium sp. kind or their toxins in the microbiologic examination of intestine contents and stool should qualify the disease as intestinal clostridiosis and not as colitis "X".

Many authors [6,15,17,19,39] mention the relation of colitis "X" occurrence with the previous disorders of intestinal contents passage. Slowing down or stasis of the intestinal contents is observed in many cases of colic diseases, which include true as well as false bowel obstructions. All these diseases may lead to the increase of endotoxins' concentration in the intestinal contents and damage of mucous membrane barrier of the intestine. This leads to the development of endotoxemia, initially of the local character (large intestine wall), and after absorption of the suitably big endotoxin dose into circulation, to generalized symptoms of endotoxemia, including shock reaction. Gram "-" endotoxins constitute an integral part of their cellular wall. They are glycolipidic compounds and form lipopolisaccharide chains (LPS). They are also potentially responsible for induction of local and general inflammatory processes and for complex immunologic response of the organism resulting, among others, in systemic shock. It should be mentioned that a certain number of endotoxins is always present in the horse's the cecum and in the healthy ones their number is about 80 µg/ml of intestinal contents [23]. Damage of the big surface of mucous membrane, constituting protective barrier for the organism against endotoxin action, may lead to their absorption into intestinal circulation, and from there they are distributed in the whole organism. Another interpretation of colitis "X: pathogenesis assumes that endotoxins acting within the intestinal wall initiate release of inflammatory state mediators, which, leading to unsealing of intraepithelial junctions, cause the absorption of endotoxins and infiltration of liquid from blood vessels into mucous membrane and lumen of the intestine. In case of longer lasting obstructions of large intestine and after surgical procedures performed with incision of the intestinal wall, various authors [6,15,17,19,39] found anatomopathologic changes similar to those of colitis "X". They also observed increased concentration of endotoxins in blood and intestine contents.

Biological effects of endotoxins are very similar to the symptoms observed in colitis "X" [2,3,4,26,29]. After intravenous administration of endotoxins no changes in the mucous membrane of the intestine are found. The administration of 32-200 µg/kg b.w. caused the

occurrence of many characteristic changes in the general condition without intestinal mucous membrane damage [3]. However, Schmall et al. [33] obtained large intestine mucous membrane erosions by administering E.coli endotoxin in the dose of 40µg/kg b.w. to ponies. Bryans [2] and Ronney et al. [29] obtained changes of the intestinal mucous membrane similar to those observed in spontaneous colitis "X" after the administration of E.coli endotoxins. The increase of temperature belongs to distinct differences between the symptoms of colitis "X" and endotoxemia. In our experiment, the mean temperature of the horses with colitis "X" symptoms averaged 38.3±0,5^{o}C. In cases of endotoxemia macrophages stimulated by endotoxins produce cytokines: **IL_1**, **TNF** [18,24]. They cause the increase of PGE synthesis which, acting on hypothalamus, gives body temperature increase [12,25]. The minimal pirogenic dose of endotoxin for horses is 1 ng/kg b.w. [21]. Rectal temperatures measure after intravenous administration of endotoxins in the dose of 0,03-0,12 mg/kg b.w. were within 39,3-40,2^{o}C [21]. Rectal temperatures of the horses with colitis "X" recorded in our experiment were below this range.

In experimental research of fermentative disorders of the horses digestive tract we found a distinct overproduction of lactic acid and other VFA in the cecum leading to intestinal mucous membrane damage, after feeding with great amounts of oats [23,34,35]. This also caused the development of endotoxemia symptoms. Such fermentative disorders with decrease of intestinal contents pH was regarded as pathogenic factor of colitis "X" syndrome [27]. However, in the current information one more frequently finds references concerning relatively high pH of the large intestine contents of the horses with colitis "X" [6,11,22]. It may be between 7,0-9,0 in this disease entity. We obtained similar results in our research, with pH values of the cecum and large intestine contents oscillating between 7,8-8,3. pH increase causes might be very different. It is assumed that VFA concentration, caused by fasting or decrease of fermentative bacteria population, dilution of the intestine contents due to infiltration of diarrheal liquid into the intestine lumen, increase of bicarbonates excretion into the large intestine lumen neutralizing VFA with CO_2, whose percentage in the general fermentative gases pool may then increase, may be the cause. The increase of pH level may also have some relation to the decrease of hydrogen production in the course of intestinal fermentative processes. In our observations we recorded an increase in the general fermentative gas pool of CO_2 quantity and a decrease of the produced H_2, which seems to confirm this theory.

In some research papers a special attention ispaid to, widely understood, stress occurrence during the period preceding clinical symptoms of colitis "X" [1,30,42]. We used total cortisol concentration as stress indicator. Total blood cortisol concentration in the course of colitis "X" was distinctly increased in relation to physiological state and averaged 298,45±6.8 nmol/l. It must be stressed that concentration of the measured parameter in the course of this disease entity did not fall below 281 nmol/l in 9 of the observed horses. The value of total cortisol concentration did not exceed 263,5 nmol/l during the attempts of inducing colitis "X". One might suppose that the increased cortisol concentration above 280 nmol/l may have diagnostic as well as pathogenic significance in the development of disorders leading to colitis "X". We also observed an increase of blood glucose level which may be related to the persisting hypercisolemia. There are similar observations in Vaughan's paper [42]. The elimination of somatic and psychical stress shall also be considered in prevention of this disease.

We found an increase of Na^+, K^+ and Cl^- concentration in the diarrheal stool in relation of these electrolytes concentration in the stool of healthy horses. Simultaneously, the existence

of ionic gap between total stool osmolality and the doubled sum of Na^+ and K^+ concentrations in stool of about 4,62±1,3 confirmed the non osmotic character of the diarrhea in cases of colitis "X".

The employed therapy (9 clinical cases) proved successful in only 2 horses, 2 of them died on the 3rd day from the onset of diarrhea, and 3 following ones - between 5th and 14th day from getting ill. The last 2 horses with recurrent diarrhea symptoms were subject to euthanasia after 6 and 10 months from the beginning of therapy in spite of its intensity.

For the therapy of all horses we used:

1. Great volumes of compound electrolyte solutions i.v. - PWE, Sol.Ringeri, NaCl 0,9% (80-100 litres/24 hours)
2. Dextran 70.000 1-3 litres/24 hours
3. Hydrocortisonum haemisuccinatum - 5-10 g/animal
4. vitamins: C, B complex, B_{12}, A+E
5. Cocarboxylasum 200-500 mg/animal every 6 hours i.v.
6. Flunimeg - 0,25 mg/kg b.w. i.v. once a day
7. $NaHCO_3$ - 5% solution in the dose calculated according to the following formula:

   BE (mmol/l) x 0,3 body mass (kg) = ml 8,4% of $NaHCO_3$ solution

   Gasometric test of arterial blood was conducted 2 times in 24 hours.

8. Probiotic preparation Enteroferment® containing *Lactobacillus acidophilus* culture 3 times a day 1 table spoon
9. Antibiotics were administered periodically in order to limit Gram "-" bacteria number and to inhibit the development of anaerobic flora (Metronidazol® 3 times a day 10 mg/kg b.w. p.o., Enroxil® - 4,0 mg/kg b.w. 1-2 times a day i.v.)

In four of the horses we additionally used heparinized blood plasma in the amount of 1-5 litres/animal i.v.

It must be stressed that better results (higher survival rate) was obtained in case of the horses where blood plasma was additionally administered.

CONCLUSIONS

1. Colitis "X" is a polyetiologic entity and is difficult to induce by introducing only one causing factor.
2. The lack of diarrhea symptoms in horses after the administration of antibiotics with wide activity spectrum for several days in the doses exceeding a daily dose and the lack of digestive tract sterilization may be explained by constantly growing immunity of bacteria to antibiotics.
3. In the course of this disease entity, there occurs a decrease of VFA production in the cecum and large colon.
4. Diarrhea in colitis "X" is of non-osmotic character.
5. There are no cellular receptors in the horses' cecum or there are no suitable conditions for the development of Salmonella enteritidis bacilli, and therefore adult horses may become infected with this bacteria orally. The introduction of Salmonella enteritidis

bacteria directly into the cecum of a healthy horse does not cause the occurrence of disease symptoms.

6. Early treatment beginning is very important.
7. The basis of the therapy of colitis "X" is intravenous administration of compound electrolyte solutions with the addition of sodium bicarbonate, short action glycocorticoids in big doses during the first 2 days, agents of NSAID group and blood plasma. Oral administration of probiotics during the whole disease period is also recommended.
8. The use of vitamins of B, A, D and C group is recommended.

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