

CHRONIC FATIGUE SYNDROME IN HORSES: DIAGNOSIS AND TREATMENT OF 4 CASES

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Abstract

A report from England has suggested that Chronic Fatigue Syndrome exists in equines and constitutes an emerging veterinary problem. Preliminary epidemiological studies seem to confirm the zoonotic implications of CFS.

An arsenical drug, thiacetarsamide sodium, was administered to four horses with a diagnosis of Chronic Fatigue Syndrome (CFS), already treated unsuccessfully with different medications. The CFS-like lethargy, with accompanying symptoms and signs, of the four animals obtained a complete remission after intravenous treatment with this drug at low dosage (0.1

mg/Kg/day). No adverse side effects were ever noticed. This clinical response was associated with recovery from anaemia and decrease of muscular enzyme values in two of the four horses. In all patients, micrococci-like bacteria found before treatment adhering to the outer surface of many red blood cells, disappeared at post-treatment controls. Considerations are made on the possible action of an arsenical drug, used isolately, in the treatment of CFS.

Résumé

Une publication scientifique anglaise a souligné l'existence du Syndrome de Fatigue Chronique (CFS) chez les chevaux et récents études de dépistage semblent confirmer qu'il s'agit d'une zoonose. Un médicament arsenical, le thiacetarsamide sodium, a été évalué sur 4 sujets équidés dont le diagnostic était de CFS, traités auparavant sans succès avec les modernes thérapies disponibles.

L'inoculation intraveineuse du thiacetarsamide sodium en bas dosage (0,1 ml/Kg/jour) pour 2-3 jours, eut comme résultat la complète guérison du syndrome chez les 4 chevaux traités. Aucun effet collatéral négatif a pu être observé. L'efficacité clinique était associée à la résolution de l'anémie et à la diminution des enzymes musculaires à repos chez deux sujets. Certains globules rouges étaient parasités par des microorganismes micrococci-semblant avant la thérapie mais non plus après la guérison.

Key Words

Chronic Fatigue Syndrome, fatigue, CFS, muscular diseases, horses diseases, arsenic, thiacetarsamide sodium, zoonosis.

Mots clés

Syndrome de Fatigue Chronique, fatigue, CFS, maladies musculaires, maladies des chevaux, arsenic, thiacetarsamide sodium, zoonose.

Introduction

A human illness characterized by prolonged, debilitating fatigue and cognitive complaints, was called at first "Icelandic disease"(1948), "post-polio syndrome" or "myalgic encephalomyelitis", and has been anecdotically related to similar syndromes in animals. It is nowadays known as "Chronic Fatigue Syndrome"

(CFS) or "Chronic Fatigue and Immune Dysfunction Syndrome" (CFIDS), with many papers about it being published every year in journals of human medicine [7, 22, 23, 25, 38, 40].

Its chief symptom, fatigue, can be combined with many others, such as headache, fever, sore throats, lack of concentration, failing short-term memory, muscle and joint pains, insomnia, increased allergic reactions [4, 30] .

Recent magnetic resonance studies, showing specific damage of certain areas of the brain, have documented the really organic nature of the disease [21, 29, 36].

Immune abnormalities are also observed frequently in CFS patients [16, 30, 50], such as the reduction in the number and activity of the NK cells, a low CD4/CD8 ratio, and, in some cases, a fall in the absolute number of CD4 lymphocytes ("Idiopathic CD4 lymphocytopenia"). These abnormalities make the disease a true acquired immune deficiency syndrome.

Neurological disorders (episodic weakness, seizures and lethargy) are of common observation in veterinary medicine, but there are very few reports and epidemiological studies on CFS-*like* illnesses in animals. First in 1974, Kronevi & al. [20], in Sweden, reported a similar condition in a group of cats with muscular weakness, neurological symptoms ("staggering disease") and

leukopenia. Treatment with anti-microbial drugs and corticosteroids was unsuccessful and most cats deteriorated, died, or had to be put to sleep after several months. Researchers in Sweden and Germany have recently carried out intensive studies on this non-suppurative meningoencephalomyelitis, and the findings have been those of a pronounced inflammatory reaction of the central nervous system [24].

Cheney published, on *The CFIDS Chronicle* of Spring 1991, the first informal study on the correlation of CFS in humans and their pets, reporting a 50% of unusually severe illness, even with sudden deaths, among pets owned by subjects suffering from CFS . None of the controls (animals in contact with people not affected by CFS) showed any of the neurological disorders (seizures, weakness of limbs and unsteadiness) exhibited by the diseased animals. Following Cheney's studies, Breitschwerdt & al. [6] reported canine cases of episodic weakness associated with lactic acidosis from exertion and myopathy, and pointed out the number of similarities between this condition and human mitochondrial myopathies. The size and shape of mitochondria have been found to be abnormal in up to 75% of patients [3]; these features , however, are shared with other syndromes.

Human herpesviruses (HHVs) have been considered as a possible cause of CFS since the early '80's. Similarly, in the '90's, equine herpesviruses (EHV-1, EHV-4) have been thought to be the cause of myopathies in horses. It is known nowadays that HHV-6, HHV-7, Epstein-Barr virus and Cytomegalovirus are not implicated in the etiology of CFS in human subjects [49]; and, that elevated levels of antibodies against several viral agents indirectly reflect the degree of

immune system suppression in some CFS patients, without showing a direct causal relationship [4].

In 1992, circulating enterovirus antigens and leukopenia were respectively found in 79% and 88% of 32 horses with persistent, marked lethargy, stationed in Newmarket, UK. The condition was called "Equine Fatigue Syndrome" by Ricketts & al. [32]. These authors found similarities between the conditions affecting the two species, and pointed out that a certain number of human patients with CFS suffer from persistent enterovirus infection. Long-term rest was adopted, with controversial results, as treatment for these cases.

Similar equine cases were observed, in the same year, in this writer's veterinary practice. It was remembered that, until recently, some arsenical preparations had been used in CFS-like veterinary conditions, including 'asthenia in horses' and 'general debility'[48]: for instance, arsonoacetic acid as 'general stimulant in nervous diseases', sodium arsenate in rheumatism; arsenic acid solution in blood diseases and arsonoacetic acid (*Tonarsan*) as 'injectable tonic for horses'. With the advent of modern antibiotics and chemotherapy, arsenical drugs fell into disuse in both human and veterinary medicine (respectively, in the '50's and in the '70's).

The purpose of this paper is to report the author's personal experience, that arsenical drugs can still be useful - at least in veterinary practice - in inducing complete remission of a CFS-like equine disease. The four cases described here were resistant to conventional chemotherapy and shared common hematological abnormalities, including the unexpected presence of micrococci-like bacteria scattered on the outer surface of red blood cells.

Material And Methods

A diagnosis of CFS was made on four horses, all personal observations, that had suffered a relapse of symptoms after standard therapies with antibiotics, anti-helminthics and steroids. They were treated with an arsenical drug, sodium thiacetarsamide, administered intravenously at a dosage of 0.1 ml/Kg/day, for 2-3 days. Before treatment was started, fresh blood smears dyed with the May-Grunwald-Giemsa stain were examined under light microscopy (x100) and checked for bacteria and hemoparasites.

Similar controls were performed 7 months later in horses #1 and #2 and 2 months later in horses #3 and #4, which were also anaemics and required a CBC count and the evaluation of the serum activity of muscular enzymes at rest before the onset of therapy.

Clinical Cases

Horse #1 and #2

These two animals were examined at a riding school in Aosta (Northwestern Italy) in late October 1992. They had taken ill at the beginning of August, and no clinic improvement had followed previous treatments.

Symptoms consisted of chronic weakness and easy fatigability after moderate physical effort, with difficulty in carrying out their work. The animals did not feed well, had lost weight and suffered from constipation and dryness of feces. Generalised muscle tremors were observed; the rectal temperature was 39°C. Both animals appeared to lack vitality and to be depressed, keeping their heads low and extended, with drooping lips. Their owners reported that interruptions of the meals had been noticed frequently, with a mouthful of hay hanging from the side of the mouth, "as though smoking a pipe". Their coat of hair was shedding and dull. There were times when the animals were abnormally drowsy and apathetic, with closed eyes, and apparently indifferent to the environment.

The condition was more serious in horse #1, that also had pyoderma and generalized acne, spreading from the knees to the distal end of the legs, and a unilateral chronic kerato-conjunctivitis.

The diagnosis of CFS was based upon these symptoms and the findings on fresh-blood smears from either horse, of a great number of micrococci (0.3-0.5 mm in diameter) attached to the outer surface of many RBCs (Figs 1, 2, 3). Such a finding, not in common with the blood smears obtained from healthy horses, was the only differentiating feature between the blood of healthy and CFS-affected horses.

Previous aggressive treatment with antibiotics and steroids had proven unsuccessful in both horses. Indications for the use of arsenical compounds as a possible therapy were inferred from the Merck Index [48]. Sodium thiacetarsamide (*Caparsolate*, Abbott Laboratories), as the only arsenical drug available on the market, was injected intravenously at the same low dosage (0.1 ml/Kg/day, for two days) proposed in literature [41] for Haemobartonellosis in cats .

Both animals obtained a striking and rapid improvement in a few days; after one week, they could be considered as cured. The pyoderma and acne of horse #1 disappeared without any topical treatment, and its chronic kerato-conjunctivitis healed with the administration of a topical anti-fungal remedy.

Seven months later (May 1993), both horses were visited again : the fatigue and related symptoms and signs had never recurred, and the control fresh blood smears were negative for micrococci.

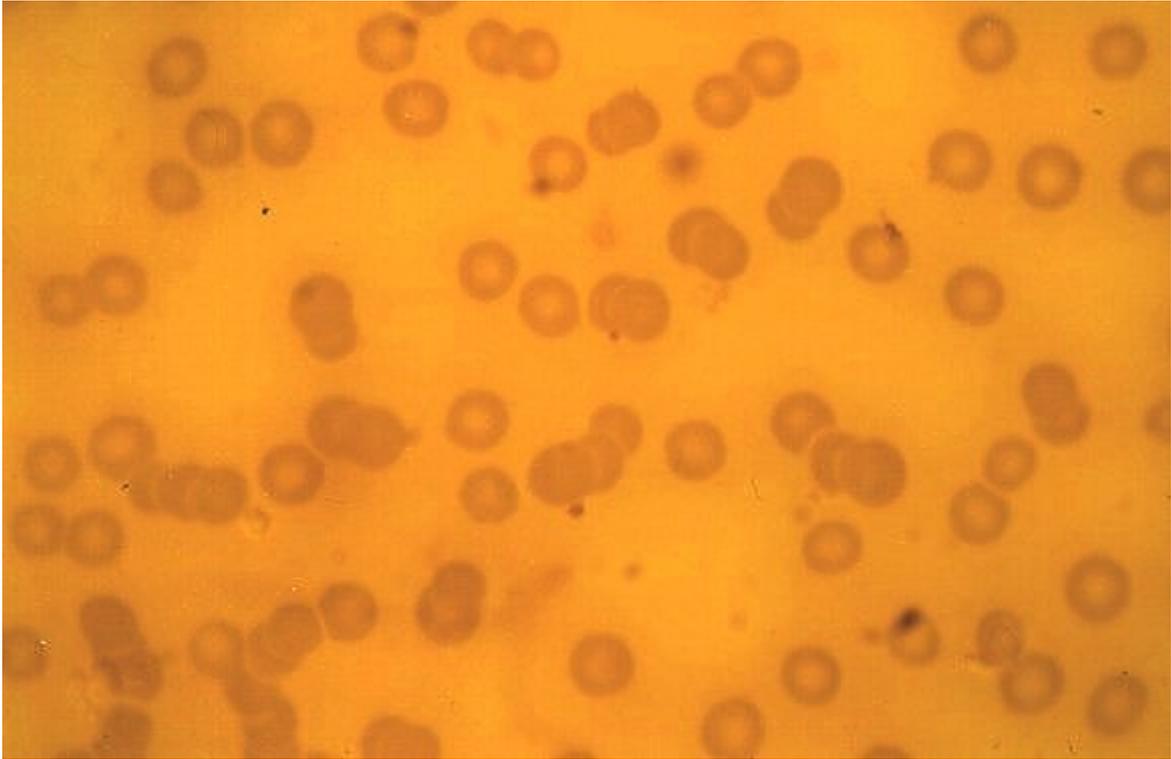


Figure 1

Horse #3

This 2-year-old male horse was visited in Castiglione del Lago (Central Italy) in May 1994. The animal had already been treated for intestinal worms twice (one and two months before), with the purpose of eliminating the symptoms of asthenia it had developed since shortly after birth (owner's statement). The appetite was normal, but the animal was grossly underweight. Head and neck were constantly kept low, with drooping lips and profuse sialorrhea. Tiredness and reluctance to perform normal activities, also present for the same length of time, were confirmed at the visit. The internal temperature was normal (37°5 C). The coat of hair was dull, shedding plenty of hair and with abundant scurf.

The fresh blood smears demonstrated, also in this horse, that 5-8 % of RBCs were carrying micrococci-like organisms 0.3-0.5 mm in diameter, hanging on their outer surface (Figs 1,2,3). The horse had normocytic normochromic anaemia (PCV = 25%, haemoglobin = 9,8 gr/dl, RBCs = 6.160.000/mm³, MCV = 40,6 fl., MCH = 15,9 pg.) .

There was a slight serum magnesium deficiency (Mg = 1.4 mEq/L). At rest, serum activity of creatin-kinase (CK = 125,9 IU/L), lactate dehydrogenase (LDH = 365,9 IU/L) and AST (GOT = 273 IU/L) were between the ranges. Total proteins were 6.35 g/dl, with the g-globulin fraction at 1.11 g/dl.

After diagnosing CFS, treatment with intravenous thiacetarsamide sodium was started. In a few days, the condition of the horse improved considerably.

At the 2-month interval control (August 1994), the anaemia had disappeared (PCV = 31 %, haemoglobin = 11,8 gr/dl, RBCs = 7.520.000/mm³) and the serum level of magnesium was in the high range of normality (Mg = 2.4 mEq/L). At rest, the LDH activity in the serum was reduced to 254.7 IU/L; and that of CK was at 106.4 IU/L. Total proteins were slightly increased to 6.54 g/dl, especially in the g-globulin fraction (1.34 g/dl). Repeated fresh blood smears were negative for micrococci. The horse did not show tiredness anymore, was thriving with its muscle mass grown to normal, and its coat of hair had regained luster.

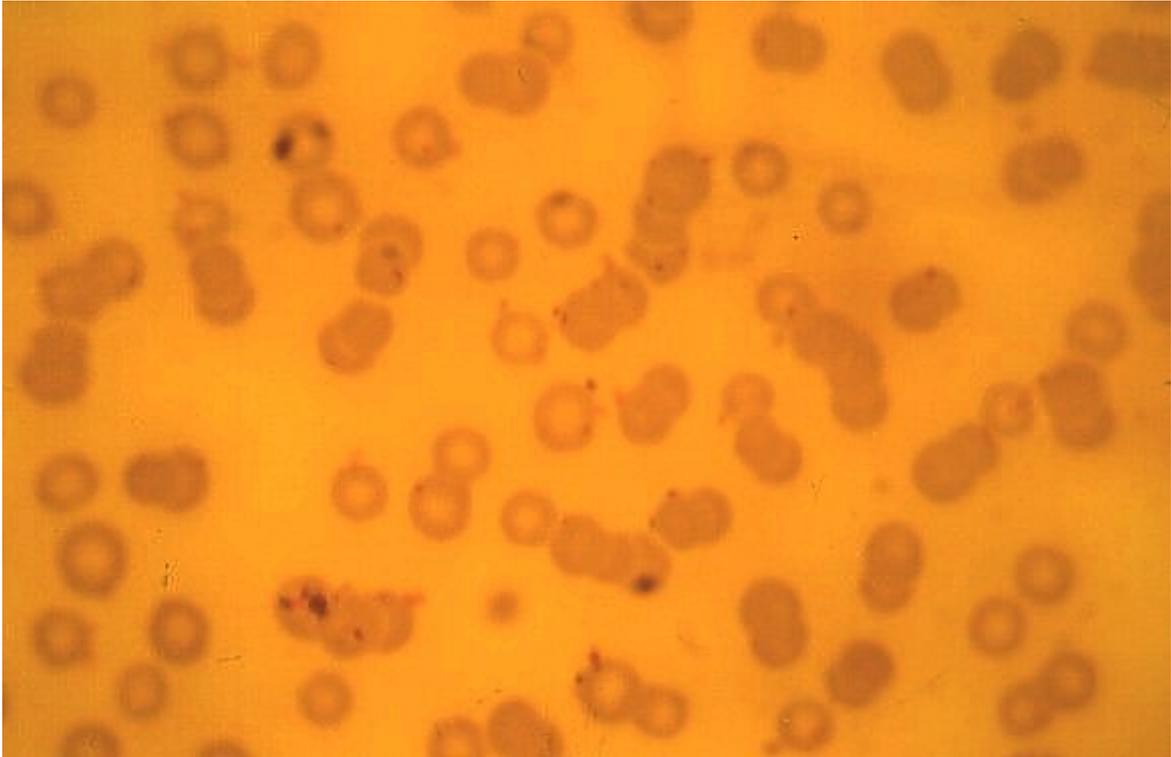


Figure 2

Horse #4

This 4-year-old male horse was visited in nearby Panicarola (also in Central Italy) in June 1994. The prominent aspect of the disease was a chronic infection of the upper airways, with cough and bilateral nasal mucous-purulent discharge, marked weakness and reluctance to being ridden. One month before, it had been treated for a week with kanamycin and desametasone. The owner had observed that symptoms might subside during treatment, but would flare up again after its completion.

Rectal temperature was normal (38°C). There was a normocytic normochromic anaemia (PCV = 27,8 %, haemoglobin = 10,3 mg/dl, RBCs = 6.840.000 mm³, MCV = 40,6 fl., MCH = 15 pg.), meanwhile WBC and platelet count was normal (respectively at 7.400/mm³ and 220.000/mm³).

In this horse, too, fresh blood smears showed 5-6% of RBCs with micrococci on their surface. All other laboratory examinations gave results within normal limits, with the exception of an increased LDH activity (1.394 IU/L) at rest.

Culture from a swab of the nasal discharge on a specific agar plate gave growth to a *Staphylococcus* species.

A diagnosis of CFS was made, based upon the fatigue-related symptoms, the ineffectiveness of the previous treatment, the presence of unusual bacteria in the blood and, by now, the previous personal experience. In this case, treatment with *Caparsolate* was given, by the same route and at the same dosage, for 3 days instead of two, with the aim of eliminating first the underlying chronic immune dysfunction before attacking the upper respiratory infection. No other drug was used. The mucous-purulent discharge decreased and stopped altogether in a matter of a few days, while the weakness made a progressive disappearance in 3-5 days.

At a control 2 months later (August 1994), the horse looked healthy and had no evidence of upper respiratory infection. Blood examinations showed remission of the anaemia (PCV = 34,5%, haemoglobin = 13,5 gr/dl, RBCs = 8.960.000/mm³) and total disappearance of the micrococci. At rest, LDH levels were restored to within normal limits (371 IU/L).

Discussion

Throughout the recorded history of CFS, animals have frequently been implicated by their owners, with anecdotal reports of strange diseases or disfunctions.

A recent report from England [32] has suggested that CFS also affects equines and is becoming a problem in veterinary practice. Preliminary studies seem to confirm the zoonotic implications of CFS. A recent study [14] showed that there is in humans a definite association (97%) between CFS and ownership of animals (usually indoor pets), and/or frequent contact with them; and, that most (75%) of these animals suffer from unusual diseases that certainly have points of similarity with CFS. Publications on CFS-like illnesses in animals, apart from the afore mentioned study on Equine Fatigue Syndrome [32], can hardly be found. Muscular weakness [6,18], neurological disorders [12, 20, 24] and immune dysfunction [20] are frequently studied in veterinary medicine, but apparently never in relation with the human illness known as CFS or CFIDS.

The present study seems to confirm the existence of an equine form of CFS, which can then be well called "Equine Fatigue Syndrome"; and, also, it introduces the interesting feature of the striking effectiveness of an arsenical compound, thiacetarsamide sodium, in its therapy.

The unexpected finding of micrococci-like bacteria in the blood led to the suspicion of a chronic infection, resistant or scarcely responsive to previously

given, standard therapeutic agents. This abnormal microbial presence, no longer found after treatment with the arsenical preparation, was the only remarkable difference in the fresh blood smears taken from, respectively, "chronically fatigued" and healthy horses. According to these observations and to advances in research reported in recent literature [4, 27, 49], which rule out the HHV's as causative agents of CFS, a search for EHV's was never attempted.

Symptoms and signs, in horse #1 and #2, were compatible with those of the initial stage of Borna's equine encephalomyelitis, caused by an RNA virus [24]. However, the second stage of this sickness is characterized by a rapid, acute worsening of the neurological disorders, and death. In these horses, instead, the illness had had its onset three months before, followed by some worsening of the symptoms but in a chronic course.

The real nature of the bacteria found in our cases is difficult to assess, in the absence of culture studies that could not be performed because of the rural conditions of work .

However in 1993, 15 similar cases of CFS in cats and dogs came under this writer's personal observations (unpublished material). These animals also were the carriers of a high number of micrococci-like germs adhering to the outer surface of their RBC's. Bacteriological studies with blood cultures were then possible and allowed a better identification. The necessary sterile conditions were obtained with a laminar-flux hood (*Mini Securitas*, PBI); blood cultures were rapidly carried out (1-2 minutes for sampling, insemination on 5% ram blood in Columbia plates and placement under incubation at 37°C in a CO₂-enriched atmosphere). Cultures from five cats and four dogs proved positive for the growth of *Staphylococcus spp.* (Gram + and catalase-positive cocci)[19], whereas no growth was obtained in the other plates. In 2 cats and 2 dogs of the nine animals thus affected (*Staph*-positive cases), a biochemical method (*Api-Staph*, bioMerieux) of identification of the bacteria was carried out, leading to one good identification (98,6%) of *Staphylococcus intermedius* and 3 very good identifications (99,8%) of *Staphylococcus xilosus* , all mannitol-fermenting.

Material taken from an interdigital pustule of a dog suffering from CFS and pyoderma gave a 99.8% identification of a catalase-positive, vancomycin-resistant *Staphylococcus xilosus* strain.

All these house-pets obtained a total recovery after low-dosage arsenical treatment. The therapeutic efficacy of arsenic on pyoderma and various respiratory tract illnesses is acknowledged in both human [34, 45] and veterinary [15] medicine . Personal experience suggests a frequent relation of these ailments with chronic fatigue and micrococci in the blood. Such was the case, in this study, of horse #1, that presented pyoderma which, in veterinary practice [19], is notoriously caused by *S. intermedius*, and of horse #4, suffering from an upper respiratory infection sustained by *Staph.* species.

All four horses of the present study presented the clinical picture of CFS as seen in humans, had proven resistant to a variety of previous treatments, and

had various hematological and biochemical abnormalities in common. They were submitted to a course of treatment with thiacetarsamide sodium at least one month after previous therapy: the beneficial effect of the arsenical compound by itself, even against pyoderma (horse #1) and upper respiratory disease (horse #4), was soon evident. Complete recovery was obtained in a matter of days (2-10) and maintained in the time.

It appears to be conjectural, if this effect could be due to some peculiar anti-microbial action of arsenic.

The treatment of infectious diseases with synthetic chemicals (chemotherapy) began in 1907, with Ehrlich-Hata's "magic bullet" (or "preparation 606": arsphenamine, *Salvarsan*) against protozoan (trypanosomiasis) and bacterial (syphilis) infections [17]. The discovery paved the way for the preparation of hundreds of drugs based on arsenic.

Arsenic (As) is commonly known for its toxicity, but has also been shown to have beneficial effects when fed in minimal amounts to laboratory animals [2]. Several studies on rats, hamsters, minipigs, goats and chicks have provided circumstantial evidence suggesting that As is essential as an oligodynamic element; its physiological role, however, has not been clearly defined (there is some evidence [47] that it could have to do with the metabolism of methionine). The Merck Index [48] lists several arsenical preparations as 'tonic for horses' useful against 'asthenia in horses' and 'general debility'. However, no relationship has ever been established with underlying chronic bacterial infections or with the presence of micrococci in the blood.

Recent research [35] seems to confirm such 'obsolete' indications, since myopathy with atrophy of both types of muscular fibers and mitochondrial abnormalities have been observed in goats artificially raised in conditions of dietetic arsenic deficiency. Similar damage was noticed in the muscles of dogs suffering from episodic weakness associated with exertional lactic acidosis and myopathy [6] and humans with Postviral Fatigue Syndrome [3]. Another recent study on humans [47] correlates low arsenic in the serum with disorders of the CNS and with certain forms of cancer. In the past, arsenic receives much "bad press" as a 'carcinogen', but it is all based on some statistical results in poor epidemiological studies.

Separate studies in China, U.S.A. and Europe are showing that inorganic arsenic trioxide (As_2O_3) exhibits an ample anti-leukemic activity in both newly diagnosed and relapsed patients with acute promyelocytic leukemia (APL) [31,42]. An As-containing organic compound, *melarsoprol*, has been found effective in APL, inducing programmed death of leukemic blood cells both *in vitro* and *in vivo* [43]. The anti-cancer action of arsenic trioxide and *melarsoprol* is due to the induction of apoptosis. The effectiveness of As_2O_3 has recently been demonstrated *in vitro* against cancer cell lines of gastric [52], head and neck [37], oesophageal [39], epithelial [53] and neural [1] origin, and against the plasma cells of myeloma [33].

Apoptosis and cell-growth inhibition in malignant lymphocytes, after treatment with arsenic trioxide may prove it useful even against malignant lymphoproliferative disorders [54].

A working hypothesis for research is that a similar mechanism of action could be involved even in the therapeutic results apparently obtainable in CFS-like illnesses of animals associated with the presence of micrococci in the blood. As *melarsoprol*, thiacetarsamide sodium is a trivalent organic arsenical, and these compounds are known to be effective binders of –SH univalent radicals (sulphydrils). Apparently, such is the mechanism of arsenical deactivation of enzymes, especially those containing two contiguous –SH groups.

Evidences is available [5] that solutions in certain concentrations of iron and arsenic inhibit the groth of thermophylic bacteria in mixed cultures, with As(III) being more active than As(V) in reducing the rate of bacterial oxidation .

Until the '70's, CFS-resembling conditions in horses were frequently treated with arsenical drugs. These medicaments were later abandoned with the advent of more modern chemo-therapeutics and antibiotics. A comparison of thiacetarsamide sodium with other therapies would not be allowable without randomized studies. However, it is intriguing how all CFS-diagnosed horses reported here could obtain such a rapid improvement and complete, lasting remission from a chronic state of exhaustion with a drug that is considered as obsolete and useless, apart from treatment of heartworm disease in dogs. These results seem notable, considering also that arsenicals have been widely used for thousands of years, in particular against syphilis, tuberculosis, malaria and, even nowadays, the African sleeping sickness due to *Trypanosoma brucei*, in both human and animals [42].

The preliminarily consideration, borne out of the evidence gained from these four horses, and other animals with CFS where bacteriological studies (blood cultures) were possible, is that bacteria of the *Micrococcaceae* family and of the *Staphylococcus* genus are to be found in the blood of such cases (Figs 1,2,3). There is no direct evidence that they cause the disease, but surely, they could no longer be found with the control fresh blood smears of the horses at the post-treatment controls.

It can therefore be suggested that their presence could be used as a coadjutor tool in the diagnosis of this particular kind of arsenic-responsive 'general debility' of horses.

For at least 15 years the CFS-related symptoms were thought to be caused by a virus , possibly a retrovirus [29, 38, 51]. Claims of improvements following anti-viral treatment have been advanced, but no consistently effective, single viral agent has yet been found [44, 46]. However, an increased prevalence of reactivation of multiple viruses has been reported [29, 51] in CFS patients: it may be the result of increased protein turnover [27] and therefore, of secondary nature.

Recent advances in human medicine strongly indicate a bacterial etiology . Australian researchers [8,10] claim evidence that the symptoms and signs of debilitation in CFS are the product of infection from otherwise harmless commensal bacteria and consequent changes of the intestinal bacterial flora. An increase of the prevalence of the toxic *Staphylococcus* species was found in patients complaining of chronic pain and/or fatigue [26] or diagnosed with CFS by compliance with a clinical definition [13]. The coagulase-negative staphylococci found in these patients produced a significant association of membrane-damaging toxins (d- and/or 'horse' –haemolysins), whereas those isolates from an ideal musculo-skeletal symptom-free control group did not [9].

In chronic muscle pain patients, who usually complain of fatigue and muscular weakness, an increased toxicity of the two *Staph* hemolysins was associated with increased fibrillar and non-fibrillar proteolysis corresponding to increase of pain, cardiac palpitations, chest pain, irritable bowel, muscle fatigue and nocturnal sweat and/or fever [26]. The control subjects who did not complain of musculo-skeletal symptoms or fatigue, were free of these *Staphylococcus spp.* Thus, the carriage of toxin-producing commensal staphylococci does initiate an increase in proteolysis, and may act to trigger off reactivation of viruses of the herpes family. It has been suggested [27] that CFS outbreaks such as those that occurred in Incline Village, may result from the acquisition of low-grade toxic *Staphylococcus* which in turn may facilitate the reactivation of HHV-6 and other herpesviruses [27]

Furthermore, Dr. Luther Lindner, pathologist on the faculty of Texas A&M University, is reportedly studying a newly recognised bacterium, usually present in high numbers in the blood of patients with CFS or multiple sclerosis. He has no evidence that the bacterium can be completely eliminated using the standard FDA-approved antibiotics and he affirms that, under certain circumstances, antibiotics can actually stimulate bacterial growth and make the patient worse.

The resistance to antibiotics of bacteria that cause diseases in the community and in hospitals is leading to an increase in illness, deaths, and social costs. The extent of the problem has not yet been fully assessed, but such a resistance has become a major public health problem in Europe and in the U.S.A today [28].

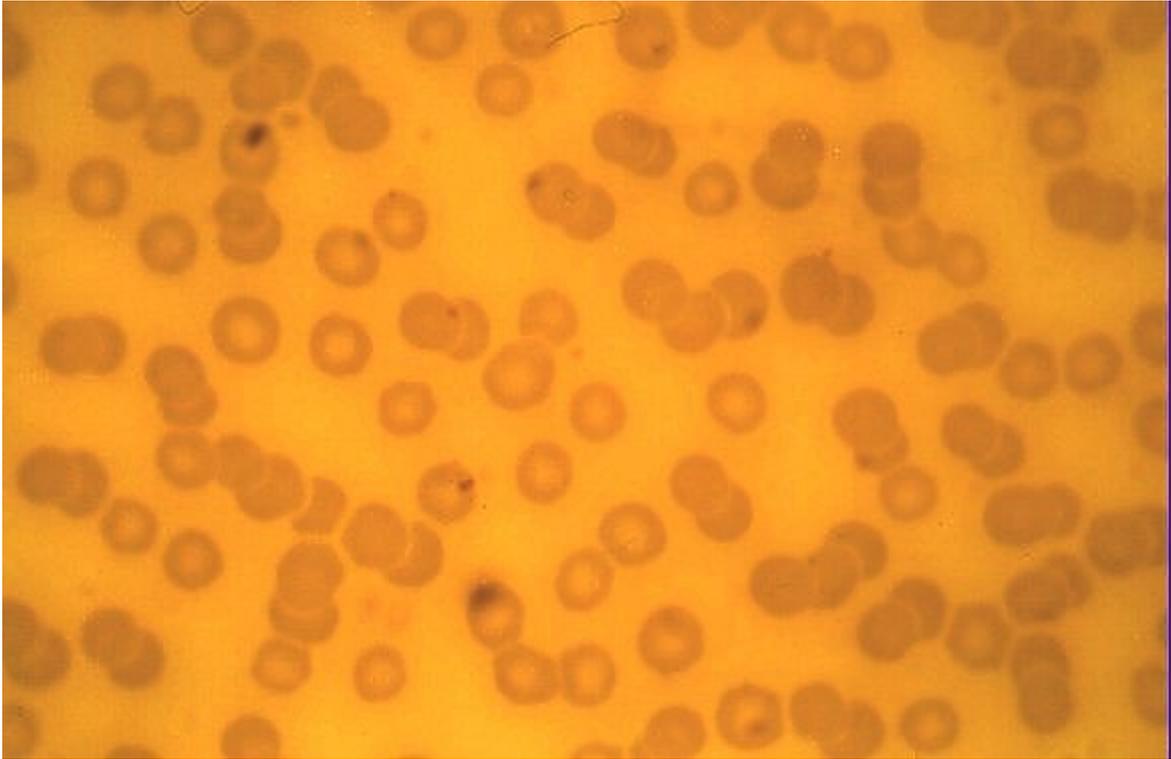


Figure 3

Conclusions

The uncertainty about the diagnosis of CFS and the increasing public demand for an effective therapy and proper support, has produced a certain degree of confusion and emotion in human medicine. Many medicaments have been tried and some partial success has been obtained. Treatment has mostly been focused on vitamins, aminoacids and health foods, in the belief that the fatigue is due to some metabolic impairment. These lines of treatment cannot be successful, as the disease is caused by factors that cannot be influenced by vitamins [11]. Until now, few therapies designed for CFS have enough clinical trial data to support their validity, and a curative and resolving effect cannot be attributed to any of them [11, 46].

It was thus deemed worthy reporting these four horses with Chronic ("Equine") Fatigue Syndrome, on which intravenous thiacetarsamide sodium in low dosages was successful in obtaining complete and lasting remission, whereas recurrences had occurred after extensive prior therapy following current criteria. The use of this single drug was able to cause a fast recuperation from lethargy and, in some cases, a cure of some associated condition such as anaemia, pyoderma and upper respiratory infection, concomitant with the primary chronic illness. These observations are not in contrast with the indications of The Merck Index for the use of similar arsenical drugs against some chronic equine conditions.

An added element of interest of this report is the finding of micrococci-like bacteria in the blood of the described horses before treatment, with constant and stable disappearance after treatment and clinical recovery. This element seems to suggest a possible connection of CFS with an underlying chronic bacterial infection resistant to other treatments.

It has been personal experience that the same treatment also appears to be useful in cats and dogs similarly affected by a CFS-like illness, where identical findings were obtained in fresh blood smears and culture studies produced bacteria of the *Staphylococcus* species (*-intermedius* and *-xilosus*).

In human medicine also, recent advances seem to confirm an implication of *Staph* in syndromes characterized by chronic fatigue and muscular pain.

Further multidisciplinary studies are necessary for an adequate solution of the problem since, up to date, every accepted symptomatic and antibacterial treatment for CFS have obtained, at best, a slight improvement in function.

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