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Antiparasitic Drug

Related terms:

Chagas disease, Epileptic seizure, Cyst, Albendazole, Trypanosoma cruzi, Benznidazole, Nifurtimox, Cryptosporidiosis, Lesion

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Antiparasitic drugs

Stephen W Page, in Small Animal Clinical

INTRODUCTION
Helminth, arthropod and protozoal infect
cause significant morbidity and mortality
a zoonotic hazard with public health impl
despite the availability and use of a numb
antiparasitic drugs (Table 10.1). This highl
of drug selected, the way in which drugs a
approaches to parasite control is critical to
of parasite infection. This chapter provide
pharmacology of the major antiparasitic d
most important epidemiological and publ
the parasites of dogs and cats.

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Diagnostic Criteria for Neurocysticercosis

Hector H. Garcia, ... A. Clinton White, in Tropical Infectious Diseases (Third Edition), 2011

Antiparasitic Drugs
The role of antiparasitic drugs in the treatment of NCC has been controversial. The first randomized controlled trials were published in the 1990s, and consensus on optimal management is only now emerging.[140–142]

Praziquantel is absorbed well after oral administration, but has extensive first-pass metabolism, which is accelerated

by antiepileptic drugs (carbemazepine, phenytoin, and probably phenobarbital) as well as by corticosteroids.[143,144] This induction can be inhibited by cimetidine (e.g., 400 mg PO tid). Coadministration increases levels of praziquantel, but the

Taenia Solium and Neurocysticercosis

Linda Siti Yancey, A. Clinton White, in Immigrant Medicine, 2007

Antiparasitic drugs

The role of antiparasitic drugs in the treatment of neurocysticercosis has been controversial.[18] Praziquantel and later albendazole were recognized as antiparasitic agents that could kill the parasites. Praziquantel was approved for use in the US in the early 1980s and albendazole became available in the early 1990s. However, the first controlled trial on their use in neurocysticercosis was published in 1995 and it showed no effect. Subsequent trials and expert meetings are beginning to clarify the role of antiparasitic therapy in cysticercosis. Much of the controversy has stemmed from poor study design, including grouping patients with markedly different forms of disease and failure to account for the natural history. There is an emerging consensus among experts about the proper role of antiparasitic drugs in management of neurocysticercosis. All experts agree that neurocysticercosis represents a spectrum of diseases that not only differ in clinical manifestations, but also differ in pathogenesis and optimal management.[18] Thus, the major different forms will be discussed separately, as parenchymal and extra-parenchymal.

Parenchymal neurocysticercosis

Single enhancing lesions

The most common presentation of neurocysticercosis among immigrants to the US is with seizures and a single enhancing lesion on neuroimaging studies. Overall, the seizures usually respond to a single antiepileptic medication.[20] In the absence of antiparasitic therapy, the lesions usually resolve over months to years.

Controlled trials of antiparasitic therapy in patients with single enhancing lesions have given variable results. However, most studies show more rapid radiologic resolution with antiparasitic drugs. Recurrent seizures tend to occur at the time of resolution. Thus, they occur earlier in patients receiving antiparasitic medications. By contrast, the proportion of patients who go on to develop chronic calcifications does not appear to be affected. The role of steroids in reducing inflammation around lesions is better defined with several recent studies showing clear benefit in reduction of seizure activity and faster resolution of lesion on CT when steroids were used in conjunction with antiepileptic medications.

Overall, the major focus of management of patients with seizures and single enhancing lesions should be on optimizing antiseizure medications. There is also likely a small benefit from antiparasitic drugs (e.g. albendazole 15 mg/kg/day for 8 days, as listed in Tables 27.1 and 27.2) and a short course of corticosteroids.

Multiple parenchymal lesions

Patients presenting with seizures with multiple cysticerci will usually have at least one cysticercus in the process of degenerating (e.g. edema or contrast enhancement on imaging studies). Other cysticerci may be in the viable stage. Thus, patients are at risk for sequential de
prolonged seizure risk. A recent placebo-c
but statistically significant reduction in ge
with albendazole.[19] The difference was m
medications. However, there was no decr
calcifications. While this trial mainly focus
cysticercus thought to be viable, most exp
with only enhancing lesions. Thus, patien
should usually be treated with a course of
mg/kg/day for 8 days or praziquantel 50–
27.1 and 27.2). They should also generally
at the same time.

Cysticercal encephalitis (numerous cysticerci w

A minority of patients with multiple cystic
from the inflammatory response to the pa

International Review of Cell and Molecular Biology

Joachim Müller[1], Andrew Hemphill, in International Review of Cell and Molecular Biology, 2013

3.1.1

DNA Intercalating Agents

Among the first antiparasitic drugs are compounds that directly intercalate into DNA. The acridine derivative quinacrine, an early antimalarial and the first antigiardial drug, interacts with DNA, and thereby inhibits

treated with anti-inflammatory drugs such
are contraindicated because of the potent
response and cerebral edema. In most cas
spontaneously with anti-inflammatory me
would treat these patients with antiparasit
resolved.

Calcifications

Parenchymal calcifications caused by neur
10% of residents of some endemic areas.
calcifications is a significant risk factor for
with seizures associated with a calcified le
other focal epilepsy. Treatment of a calcifi
not indicated. Anti-inflammatory drugs h
no clear evidence whether they provide ar
calcified focus has been used in some cas
however, are easily managed with a single

Extra-parenchymal neurocysticercosis

Ventricular neurocysticercosis

When hydrocephalus due to obstruction o
the intracranial pressure. Historically, ven
open craniotomy, but this was associated
With advances in the use of neuroendosco
be carried out using minimally invasive pr
morbidity. The method of choice at this ti
Endoscopic foramenotomy can often be u
Antiparasitic medications should not be g
cause the cysticerci to be friable or to adh
often rupture during removal, but this ha
when accompanied by intraprocedural irri

Neuroendoscopy is not available in all cer
treated emergently. These patients can us
diversion (usually via placement of a ventr

replication and RNA and protein biosynthesis (Ciak and Hahn, 1967). Like other acridine derivatives, quinacrine is an intercalating agent binding to DNA with a preference for (A+T)-rich regions and thereby blocking DNA replication and RNA biosynthesis. One of the most commonly known intercalating agents, ethidium bromide, has been used since the 1950s as antitrypanosomal drug in African cattle (Roy Chowdhury et al., 2010).

The binding affinities of pentamidine derivatives (Bell et al., 1991) and bis-benzimidazoles (Bell et al., 1993) to calf thymus DNA are strongly correlated to their efficacies against *G. lamblia*. Pentamidine-derivatives such as diamidines and arylimidamides are effective not only against *G. lamblia* but also against a variety of other parasites (Torres-Gómez et al., 2008) including trypanosomatids (Shapiro and Englund, 1990; Soeiro et al., 2008, 2005) and apicomplexa, namely *N. caninum* in vitro (Leepin et al., 2008; Schorer et al., 2012) and in vivo (Debache et al., 2011), and *T. gondii* in vitro (Kropf et al., 2012). Since DNA

Toxoplasmosis Primary

failure is high in patients treated only with
failure rate appears to be lowered by the a
antiparasitic drugs. Case series have ident
chemotherapy and steroids. However, this
discouraged since it carries a substantial r
hydrocephalus from cysticerci and/or acc
obstruction of the foramina.

Subarachnoid neurocysticercosis

Cysticerci in the basilar cistern can cause
obstruction, communicating hydrocephal
before antipara sitic drugs were available,
By contrast, more recent case series have
rates.[14,18,23] Expert consensus recommen
antiparasitic drugs, anti-inflammatory dru
procedures. Nevertheless, there are few g
for medication. Most experts recommend
mg/kg/day in divided doses for at least 28
course of albendazole. Repeated courses,
switching to praziquantel have been tried
reports of improved responses with endos
parasites, but this approach has not yet be

In some cases, however, the residual symp
inflammatory response to cysticercal antig
cysticerci. Thus, inflammation seems to d
optimal management has not been define
day) or dexamethasone (doses up to 24 m
antiparasitic drugs. After 2–4 weeks, the d
require more prolonged steroid therapy, r
sparing agent.

Giant subarachnoid neurocysticercosis

Some cysticerci, particularly in the sylvian
to over 5 cm in diameter. In contrast to m

Preventive Measures

María-Jesús Pinazo, ... Joaquim Gascon, in Infectious Diseases (Fourth Edition), 2017

Management

The choice of antiparasitic drug will depend upon the HAT form and whether the CNS is infected or not. Pentamidine in *T.b. gambiense* or suramin in *T.b. rhodesiense* can be used when the CNS is spared from infection. Pentamidine dosage is 4 mg/kg/day, intramuscular or intravenous, for 7 days.[52] *T. b. rhodesiense* and some strains of *T. b. gambiense* do not respond to pentamidine. Suramin dosage is 20 mg/kg/day (maximum 1500 mg), one intravenous injection every 5 days for 25 days (five total doses).

Melarsoprol and eflornithine are effective for both hemolymphatic and neural stages but because of their toxicity or administration requirements they are mostly used in the late-stage of the disease, where the CNS is involved.

Both drugs can be used in *T.b. gambiense* infection, but only melarsoprol is useful in *T.b. rhodesiense*

can cause mass effect and midline shift, e
If the mass effect cannot be quickly revers
surgical decompression may be required.
aspiration of the cyst fluid or removal of t
symptomatic from mass effect, however, g
other subarachnoid cysticerci.

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infection because it is innately resistant to eflornithine.

Melarsoprol, a trivalent arsenical derivative, has been the treatment of choice for patients who have had CNS involvement for five decades. Arsenic-related encephalopathy syndrome occurs in 5–8% of cases and the mortality rate of this complication is up to 50%.[52,54] The treatment of this adverse effect is corticoids (dexamethasone 0.5–0.6 mg/kg/day, q12h or q8h), symptomatic treatment and supportive care. Melarsoprol

Haemonchus contortus and Haemonchosis – Past, Present and Future Trends

C.E. Lanusse[1], ... A.L. Lifschitz, in Advances in Parasitology, 2016

4.2
Modulation on drug transport and efficacy against resistant *Haemonchus contortus*

Currently, resistance to antiparasitic drugs is recognized as a problem in small ruminant and bovine production systems (Kaplan and Vidyashankar, 2012; Prichard, 1994). The drug–drug interactions at the efflux transporter protein level are not

only important in the host but also at the target nematodes. P-gp has been described not only in mammals but also in parasites, such as *Onchocerca volvulus* (see Kwa et al., 1998) and *H. contortus* (see Prichard and Roulet, 2007). Drug efflux mediated by P-gps in different parasites has been proposed as a potential resistance mechanism for different drugs (Xu et al., 1998). Increased scientific evidence supporting this concept has

American Trypanosomiasis (Chagas Disease)*

Louis V. Kirchhoff, in Tropical Infectious Diseases (Third Edition), 2011

Treatment of Clinical Chagas Disease

Beyond the possible use of antiparasitic drugs, the treatment of both acute and chronic Chagas disease is symptomatic. Patients with severe acute chagasic myocarditis should be supported as would any patient with acute congestive cardiomyopathy. In patients with symptomatic chronic Chagas heart disease, therapy is directed at ameliorating symptoms through the use of the cardiotropic drugs and anticoagulants generally used in patients with cardiomyopathies due to other causes.[78,152–155] Pacemakers have been shown to be useful in patients with ominous bradyarrhythmias or heart block.[156] The usefulness of autologous bone marrow cells to ameliorate symptoms associated with Chagas cardiomyopathy is being studied.[157]

Cardiac transplantation is an option in patients with endstage Chagas heart disease, and more than 150 *T. cruzi*-infected patients have undergone the procedure in Brazil and the United States.[158–160] Reactivated acute Chagas disease occurred often in the patients transplanted initially in Brazil due to the postoperative immunosuppression, but this has been less of a problem in the last decade or so as smaller doses of cyclosporine have been used.[159,161,162] Of

concern, the usual parasitologic methods for detecting acute *T. cruzi* infection were not sensitive detectors of the reactivations. Moreover, the occurrence of posttransplant malignant neoplasms is an additional problem.[163] Patients who have had a heart transplant for Chagas disease occasionally develop cutaneous lesions containing large numbers of parasites,[164] and this has been observed in *T. cruzi*-infected patients with renal transplants and HIV/acquired immunodeficiency syndrome (AIDS) as well.[97,102] The efficacy and toxicity of long-term prophylaxis with either nifurtimox or benznidazole in *T. cruzi*-infected patients after cardiac transplantation have not been assessed. In spite of these problems, the long-term survival of Chagas patients with heart transplants is greater than that of individuals receiving heart transplants for other reasons, most likely because the lesions of chronic *T. cruzi* infection are generally limited to the heart.[165] The frequency with which *T. cruzi*-infected immigrants in the United States are considered for cardiac transplantation will increase over time as this group increases in size and ages.

Megaesophagus associated with Chagas disease should be treated as is idiopathic achalasia.[166,167] The best initial relief of symptoms is achieved by balloon dilatation of the lower esophageal sphincter. Patients with megaesophagus who fail to respond to repeated balloon dilatation may require surgical treatment. The procedure most often used is wide esophagocardiomyectomy of the anterior gastroesophageal junction, combined with valvuloplasty to reduce reflux. Patients with extreme megaesophagus can be treated with esophageal resection with reconstruction using an esophagogastroplasty.[168,169] In developed countries, laparoscopic myotomy is being used with increasing frequency to treat idiopathic achalasia, and this relatively simple procedure may become the method of choice for both idiopathic achalasia and Chagas disease. A possible role for the injection of botulinum toxin is being evaluated.[170]

Patients in the early stages of colonic dysfunction associated with chronic *T. cruzi* infection can be managed with a high-fiber diet and occasional laxatives and enemas. Fecal impaction necessitating manual disimpaction may occur, as can toxic megacolon, which requires surgical intervention.[171] Volvulus is a complication of chagasic megacolon that requires immediate attention. Endoscopic emptying can be done initially in patients without clinical, endoscopic,

or radiographic signs of ischemia in the affected segment. Cases that are complicated should be treated with surgical decompression. In either case, however, surgical treatment of the megacolon is ultimately necessary because of the common recurrence of volvulus. Several surgical procedures have been used to treat advanced chagasic megacolon, and all of them include resection of the sigmoid as well as removal of part of the rectum.[172,173]

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Although a modification of macrocyclic lactone activity after P-gp modulation was confirmed in vitro, in vivo trials performed under field conditions are necessary to evaluate the clinical impact of the P-gp inhibition. The enhanced sensitivity of resistant larvae to ivermectin obtained after its co-incubation with pluronic 85 did not correlate with their in vivo co-administration to sheep (Bartley et al., 2009). In the in vivo trial, the presence of pluronic 85 did not improve the efficacy against resistant *H. contortus* (see Bartley et al., 2012). However, significant increment on ivermectin efficacy against resistant nematodes of sheep together with an enhancement on ivermectin systemic availability was

A worldwide yearly survey of new data in adverse drug reactions

Oscar Ozmund Simooya, in Side Effects of Drugs Annual, 2014

Chloroquine *[SED-15, 722; SEDA-32, 521; SEDA-33, 568; SEDA-34, 441; SEDA-35, 495]*

Chloroquine and hydroxychloroquine are well-recognised antiparasitic drugs. However, they are also prescribed for the treatment of rheumatic diseases such as systemic lupus erythematosus [10R]. Ocular and cardiac toxicities induced by chloroquine are discussed in a review [11R].

A study of 36 patients with rheumatoid arthritis, 26 of whom received chloroquine therapy, showed hyperreflective abnormal particles in the different layers of the cornea in 19 of the 26 patients' eyes studied by confocal microscopy [12C]. These deposits were found in the superficial epithelium (14/19), basal epithelium (8/19) and anterior stroma (5/19). The deposits were associated statistically with cumulative dosage.

Observational Studies

Cardiovascular system: A review discusses chloroquine cardiomyopathy [13R]. Although a rare occurrence, cardiac toxicity includes conduction disturbances (bundle-branch block, atrioventricular block) and cardiomyopathy with hypertrophy, restrictive physiology and co
recommends diagnostic procedures.

Sensory system: Chloroquine-induced *re*
drug reaction. The retinopathy can occur
A case is reported of a 52-year-old womar
chloroquine retinopathy 10 years after sto

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Common Intestinal Roundworms

Paul S. Pottinger, Elaine C. Jong, in The Travel and Tropical Medicine Manual (Fifth Edition), 2017

Pregnant and Lactating Women

There are very few controlled data on the use of antiparasitic drugs in pregnancy and lactation. Both mebendazole and albendazole have been shown to have teratogenic potential in animal models. It would be prudent to withhold therapy during the first trimester and to delay therapy as long as possible, ideally until after

Echinococcus and Echinococcosis, Part A

J. Eckert*[1], R.C.A. Thompson[§], in Advances in Parasitology, 2017

3.4.1.4.1

Chemotherapy with benzimidazoles

Until the mid-1970s, many attempts to find antiparasitic drugs against experimental larval echinococcosis in rodents were unsuccessful. The tide turned in 1974 after Thienpont et al. (1974), researchers at Janssen Pharmaceutica Beerse, Belgium, had detected the efficacy of mebendazole against metacestodes of *T. taeniaeformis* in mice. Scientists in Australia described a high efficacy of this drug against metacestodes of *T. pisiformis* in rabbits and of *Mesocestoides corti* and *E. granulosus* in mice (Heath and Chevis, 1974; Heath et al., 1975). Authors in Russia (Krotov et al., 1974) and the United States of America (Campbell et al., 1975)[6] reported that the tumorous growth of *E. multilocularis* metacestodes in rodents can be inhibited by treatment with increased doses of mebendazole.

Further detailed experimental studies revealed that prolonged oral treatment of rodents with albendazole, fenbendazole, flubendazole and mebendazole significantly (mostly >90%) inhibited the proliferation of *E. multilocularis* metacestodes, damaged the parasite structure, prevented metastasis formation and prolonged the survival time of the treated animals, but usually did not kill the parasites. On the other hand, in the same model, cysts of *E. granulosus* could be killed (Eckert and Pohlenz, 1976; Eckert et al., 1978; Burkhardt, 1981; Schantz et al., 1982; Eckert, 1986). Concurrently, pharmacological studies on the bioavailability of high oral doses of benzimidazoles and the presumably effective serum drug levels were performed in experimental animals and humans (Witassek et al., 1981; Luder et al., 1986). The results formed the basis for monitoring of serum drug levels in patients and adaptation of the oral doses.

Among the early reports on the use of high oral mebendazole doses against AE in humans were those of Akovbiantz et al. (1977) in Switzerland and Wilson et al. (1978) in Alaska, and against CE communications of Bekhti et al. (1977) in Belgium, Danis et al. (1977) in France, Beard et al. (1978) in Australia and Al-

Moslih et al. (1978) in Iraq (for further references, see Schantz et al., 1982). In 1980 an international workshop on 'Chemotherapy of Larval Echinococcosis in Animals and Humans' was organized by the Janssen Foundation at Janssen Pharmaceutica, Beerse, Belgium, which was particularly supported by Dr Paul A. Janssen and his coworkers (Schantz et al., 1982). Since most of the early studies included only single or small numbers of patients and had given rather inconsistent results, the Swiss Study Group on Echinococcosis (steering committee members: A. Akovbiantz, R. Ammann, J. Bircher, J. Eckert) suggested that the WHO Parasitic Disease Programme (WHO/PDP) at WHO in Geneva coordinate international studies on the treatment of human echinococcosis with benzimidazoles (WHO/PDP, 1981). The project was supported by Dr A. Davis (Director, PDP), Dr Z. Matyas (Chief, Veterinary Public Health [VPH]) and Dr Z. Pawlowski (Senior Medical Officer, PDP) and launched in 1981, based on a uniform protocol (WHO/PDP, 1981, 1984). In 1986 the first results of a multicentric trial were published, which included 85 CE and 54 AE patients treated with mebendazole, albendazole or flubendazole at clinical centres in Anchorage, Beirut, Besançon, Paris, Rome, Sofia and Zurich. Pharmaceutical companies (Janssen Pharmaceutica, Smith, Kline & French) and several University institutes and hospitals cooperated in the studies (Davis et al., 1986). In the following years, various aspects of chemotherapy of human CE and AE were subjects of discussions at workshops or conferences and numerous publications (reviewed in Schantz et al., 1982; Eckert, 1986; Sato et al., 1993; Ammann and Eckert, 1995; Horton, 1997; WHO, 2001a; Horton, 2003; Eckert and Deplazes, 2004; Kern, 2004, 2006; Junghanss et al., 2008, and others). The continuous interest of WHO (Dr F.-X. Meslin, Dr T. Fujikura, Dr Z. Pawlowski, Dr L. Savioli) into echinococcosis and the international cooperation of research groups within the framework of 'WHO Informal Working Groups on Echinococcosis' (see below) proved to be stimulating and important for the further development of chemotherapy. Methods and results were discussed and evaluated at several international meetings, for example, 1983 in Geneva, Switzerland (WHO, 1984a); 1990 in Anchorage, Alaska; 1992 in Besançon, France (WHO/CDS/VPH, 1992); 1993 in Beijing, China (WHO/VPH, 1993); 1994 in Al-Ain, United Arab Emirates (WHO, 1996) and 1995 in Hokkaido,

Japan. In 1996 these efforts resulted in the publication of 'Guidelines for treatment of cystic and alveolar echinococcosis in humans' prepared by numerous experts of the WHO-IWGE (WHO, 1996). An updated guideline was published in 2010 (Brunetti et al., 2010). Results on the benefits and problems of chemotherapy of human CE and AE have been reviewed in various articles (e.g., Ammann et al., 1999; Pawlowski et al., 2001; Eckert and Deplazes, 2004; Kern, 2006, 2010; Eckert et al., 2011; chapter "Clinical management...", this volume).

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