Journal of the Egyptian Society of Parasitology, Vol.49, No. 2, August 2019
J. Egypt. Soc. Parasitol. (JESP), 2019 (2), 423- 438

OPPORTUNISTIC PARASITIC PULMONARY INFECTIONS IN HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTED PATIENTS: WITH REFERENCES TO EGYPTIAN PARASITES

By
ASHRAF A. ABOU-BAKR[1], NASHWA ALSAYED IBRAHIM[1]
And TOSSON A. MORSY[2]
Military Medical Academy, Cairo11291[1] and Faculty of Medicine, Ain Shams University, Cairo 11566[2], Egypt

Abstract

Prior to the era of potent antiretroviral therapy, parasitic pulmonary infections were more commonly seen than they are today. However, the clinician needs to be aware of the presenting symptoms and signs of these uncommon infections, which may still occur in the immuno-suppressed patient with untreated or drug-resistant HIV infection. The commonest pulmonary parasites are protozoa (toxoplasmosis, amebiasis, cryptosporidiosis and microsporidiosis) and helminthes (paragonimiasis, hydatidosis ancylostomiasis, stronyloidiasis and toxocariasis). It is important to consider parasitic infections in the differential diagnosis of such lung diseases. If parasites are identified early, most parasitosis affect lung is curable with medical or surgical treatments.

Key words: Pulmonary infections, HIV, Toxoplasmosis, Stronyloidiasis, Cryptosporidiosis, Microsporidiosis, Toxocariasis, Echinococcosis/Hydatidosis.

Introduction

Prior to the era of potent antiretroviral therapy, parasitic pulmonary infections were more commonly seen than they are today. However, the clinician still needs to be aware of presenting symptoms and signs of these uncommon infections, which may still be diagnosed in the immunosuppressed patient with untreated or drug-resistant HIV infection. The acquired immunodeficiency syndrome (AIDS) was first recognized among homosexual men in the United States in 1981 (CDC, 1981). While initially limited, infection with the human immunodeficiency virus (HIV) has literally exploded over the past two decades to become the worst epidemic of the twentieth century. With more than 35 million fatalities, the AIDS epidemic now ranks alongside the influenza pandemic of the early 1900s and the Bubonic plague of the fourteenth century in terms of fatalities (CDC, 2006). The epidemic has reached every country and nearly all populations throughout the world. Spread of the disease has been particularly alarming in developing countries, especially sub-Saharan Africa and Southeast Asia, but continues to threaten other populations in Eastern Europe, Latin America, and the Caribbean. In the more developed countries, which have also witnessed dramatic increases in HIV/ AIDS over the past two decades, marked advances in HIV antiretroviral therapy have resulted in significant changes in the survival rate and quality of life of HIV-infected individuals. Current treatments are effective, allowing HIV-infected individuals to live longer, healthier lives, but at the same time have resulted in complacency and a resurgence in high-risk behavior among some populations. This recidivism has resulted in a resurgence of STDs and a recent increase in HIV incidence among populations where HIV prevention had been so effective in past years (WHO, 2006).

Origin of HIV Epidemic: a- zoonosis, in Africa, there are species of chimpanzees that are infected with lentiviruses, similar to the HIV, Molecular phylogenetic studies suggest that HIV evolved from simian immunodeficiency virus (SIV), which was found in two of four subspecies of chimpanzees in the Cameroon (Heeney *et al*, 2006). Similarities in the viral genome were between SIV & HIV, prevalence in the natural host, geographic association between the animal reservoir and emergence of human cases, and plausible route of transmission. b- Transmission and dynamics of the epidemic: The major modes of the acquiring HIV infection are

(Piot, 2006): Sexual transmission, including heterosexual and homosexual contact, parenteral transmission, predominantly among injection drug users (IDU), and perinatal transmission. Nosocomial transmission must be considered (Ganczak and Barss, 2008).

The impact of this disease on human suffering, cultures, demographics, economics, and even politics has been felt in nearly every society across the globe. Opportunistic parasitic infections (OIs) are one of the existing identified causes that aggravate the condition of HIV-infected patients. The spectrum of parasitic opportunistic infections (POIs) affecting HIV-infected individuals is divided into protozoa and helminthes, which play an important role and are one of the commonest causes of the morbidity and mortality in the HIV/AIDS patients (Nissapatorn and Sawangjaroen, 2011).

Pulmonary parasitic infections in HIV patients are *Toxoplasma gondii, Strongyloides stercoralis, Cryptosporidium parvum, Microsporidium* spp. *Paragonimus westermani, Echinococcus*/hydatidosis, *Entamoeba histolytica, Ancylostoma duodenale, Toxocara canis* (Kunst *et al*, 2011).

Review and Discussion

1- Toxoplasmosis: *Toxoplasma gondii* is a ubiquitous intracellular protozoan and one of the worldwide zoological and geographical common parasites (Pappas *et al*, 2009). Although *T. gondii* can infect a wide range of vertebrates, feral and domestic cats are the definitive hosts. The organism undergoes its complete life cycle in the cat, resulting in the production of oocytes, which are passed with the feces into soil. Oocytes may remain infective for over one year. If ingested, *Toxoplasma* can invade tissue and reproduce. Two or three weeks after the first infection, the *Toxoplasma* divides more slowly and a protective membrane forms around the parasite cells. The cyst containing the parasites is called a zoitocyst and the cells inside the cyst are called bradyzoites. The tissue cysts are formed primarily in brain, eye, heart muscle, and skeletal muscle. Bradyzoites persist in tissues for many years, possibly for the life of the host. In cats, the two routes of transmission to humans are (Pomeroy and Filice, 1992): either acquired by eating food or undercooked sporulated oocytes contaminated meat, exposure from infected cat feces, or congenital from mother-to-child during pregnancy. Also, *T. gondii* is an occupational, and/or hospital acquired disease (Saleh *et al*, 2016) from infected blood donors (Sarwat *et al*, 1993) or by needle stick injury (Abdel-Motagaly *et al*, 2017).

Clinical epidemiology: *T. gondii* is generally believed to cause subclinical infection in most immunocompetent hosts, but one review found that one-third of the reported cases of active pneumonia were in patients with no underlying immunosuppressive illness. Of the remaining two-thirds, 61% had AIDS (Mariuz *et al*, 1994) and 39% had other forms of immunosuppression. Most active cases of toxoplasmosis are due to reactivation of latent infection. Approximately one-third of adults in the United States are IgG seropositive for *T. gondii* (Evans and Schwartzman, 1991). In HIV-infected individuals who are sero-positive for *T. gondii*, it is estimated that approximately 30% would develop toxoplasmic encephalitis within two years of the initial diagnosis of AIDS without antiretroviral therapy; another 1% who are seronegative will develop primary toxoplasmosis (Holliman, 1990).

Although encephalitis is overwhelmingly the most common manifestation of *T. gondii* infection in AIDS patients, pneumonitis has become its second most common presentation. The incidence of pneumonitis is unknown, but the number of case reports is increasing. One report estimated the prevalence of *T. gondii* pneumonia in France to be 5%, based upon a prospective study of bronchoalveolar lavage (BAL) specimens in the 169 AIDS patients (Derouin *et al*, 1990). Rates in the United States were much lower, which might be due to the lower rates of dormant infection or to under-diagnosis. Active pulmonary toxoplasmosis does not usu-

ally occur in HIV-infected patients until the CD4+ count falls below 100cells/mm^3 (Bonilla and, Rosa, 1994).

Clinical presentation: *Toxoplasma* pneumonitis generally presents with fever, nonproductive cough, and dyspnea. The chest radiographs generally showed diffuse bilateral interstitial and alveolar infiltrates. Other abnormalities include single or bilateral pulmonary nodules, cavitary infiltrates, lobar pneumonia, and pleural effusions.

Pulmonary toxoplasmosis may be clinically indistinguishable from PCP, tuberculosis, cryptococcosis, or histoplasmosis. Serologic tests for IgG, IgM, IgA, & IgE to *T. gondii* are available, but the results are usually not helpful in the profoundly immunosuppressed patient. However, the absence of IgG antibody to *T. gondii* made the diagnosis much less likely, since most active disease is due to reactivation of latent infection. Reports of gallium scans in patients with *T. gondii* pneumonitis are rare, but diffuse intense uptake was reported, and serum LDH levels might be markedly elevated (Pugin *et al*, 1992). However, in HIV patients, common manifestations are pneumonia for *P. jirovecii* and brain abscess for *T. gondii*. Nevertheless, co-infection remains rare, and pulmonary toxoplasmosis is scarce, or may be underestimated due to the close similarity with *Pneumocystis jirovecii* pneumonia (Rey *et al*, 2017).

Diagnosis: Bronchoscopy with bronchoalveolar lavage (with or without transbronchial biopsy) is the preferred method of diagnosis, but its sensitivity and specificity are unknown (Oksenhendler *et al*, 1990). The diagnosis is confirmed by observing the tachyzoite form of the organism in the BAL fluid or transbronchial biopsy. The reliable methods of detection are Giemsa staining or eosin/methylene blue staining. Tachyzoite is 5 to 7 microns and crescent-shaped. Immunofluorescence staining with a monoclonal antibody, inoculation of mice followed by traditional culture, or PCR technology may increase the yield of BAL, but most of these methods were not readily available (Derouin *et al*, 1989).

If bronchoscopy is not diagnostic, then an open lung biopsy can be performed, either by video-assisted thoracoscopic surgery (VATS) or traditional thoracotomy. Pathologically, the fibrinous exudate can be seen in the bronchi and alveoli, with an inflammatory cell interstitial infiltrate and areas of parenchymal necrosis. The organism may be seen within alveolar macrophages or freely floating within the alveoli. Unfortunately, the diagnosis of *Toxoplasma pneumonitis* is usually made by postmortem examination of the lungs, because it is often not considered premortem and the special stains that are needed to make diagnosis are not requested. Even with antemortem diagnosis, one review estimates the mortality to be 40% in immunosuppressed hosts (Burg *et al*, 1989).

Treatment: The combination of pyrime thamine and sulfadiazine is the regimen of choice for treatment of extrapulmonary toxoplasmosis. The same regimen is used for pulmonary toxoplasmosis since there are no controlled studies specifically designed for lung involvement. A 200mg loading dose of pyrimethamine is given initially and is followed by 50 to 75mg/day, while sulfadiazine is given at 4 to 6grams/ day (McCabe and Oster, 1989). Leucovo- rin calcium (10 to 20mg/day orally) is usually given to reduce the hematologic toxicity of these drugs. Clindamycin (at a dose of 600mg every six hours) could be used in combination with pyrimethamine in patients with sulfa intolerance (Dannemann *et al*, 1992).

The exact duration of therapy for *Toxoplasma* pneumonitis is unknown; however, at least three to six weeks should be given, depending upon the severity of the disease and the response rate. Unfortunately, adverse reactions are common to all of these drugs. Other drugs that may be considered include atovaquone azithromycin clarithromycin, dapsone, pyrimrthamine, or trimethoprim-sulfamethoxazole alone or in combination with other agents.

Secondary prophylaxis or maintenance therapy was prudent because relapses of toxoplasmosis were reported in up to 80% of patients after successful therapy (Lane *et al*, 1994): 1- The lowest relapse rate for *Toxoplasma* encephalitis was reported with pyrimethamine (25 to 75mg/day) and sulfadiazine (1.0 to 1.5gm four times daily) with leucovorin (15mg/day). 2- Clindamycin® with pyrimethamine can be used in sulfa intolerant patients. There was, however, a high relapse rate with the low doses of clindamycin; as a result, 1200mg/day in divided doses was suggested if tolerated by the patient (Luft and Remington, 1992).

According to guidelines issued from the Centers for Disease Control and Prevention, the United States Public Health Service and the Infectious Diseases Society of America, discontinuation of the secondary prophylaxis may be considered if (Benson *et al*, 2005): a- Patient completed treatment successfully, b- Patient was asymptomatic, or c- CD4 count was maintained above 200 cells/micro L for six months

Primary prophylaxis against *Toxoplasma* encephalitis should be considered in patients with CD4+ counts below 100cell/ mm^3 and positive *T. gondii* serology (Maguire *et al*, 1986). TMP/SMX is the recommended first-line prophylactic agent, as it also offered prophylaxis against PCP. The other effective prophylactic drugs include pyrimethamine as a single agent, Pyrimethamine-dapsone, Fansidar, or possibly Clarithromycin, Azithromycin, & Atovaquone.

The seronegative persons who were not taking a PCP prophylactic agent with the known activity against toxoplasmosis should be retested for IgG antibody when CD4+ count dropped below 100cells/mm^3. They should receive the appropriate prophylaxis if they have seroconverted (CDC, 1995). If the CD4 count rose to above 200cells/micro L for three months, primary prophylaxis for toxoplasmosis might be discontinued (Furrer *et al*, 2000).

In Egypt, toxoplasmosis were reported in man as children with neurological manifestations (Wishahy *et al*,1971;1972), adults and children with malignancy (El Shazly *et al*, 1996), blood donors (elsheikha *et al*, 2009) and childbearing females (Saleh *et al*, 2014), also edible animals (Rifaat *et al*, 1971), farm animals (Rifaat *et al*, 1977), camels (Michael *et al*, 1977), draught horses (Haridy *et al*, 2009), donkeys and their milk (Haridy *et al*, 2010), stray dogs (El Behairy *et al*, 2013), carnivores animals as well as rodents (Mikhail *et al*, 2017)

2- Strongyloidiasis: *Strongyloides stercoralis* is an intestinal parasite that has a worldwide distribution but is predominantly found in tropical and subtropical areas as well as the southeastern United States.

The primary mode of transmission occurs when larvae from contaminated feces penetrate the skin, although infection can also occur via the fecal-oral route and from sexual transmission (Celedon *et al*, 1994).

Most infected persons remain either asymptomatic or have low grade abdominal symptoms. Some patients, particularly those who are immunosuppressed, can develop disseminated strongyloidiasis or the hyperinfection syndrome, both of which are considered "systemic strongyloidiasis" (Satoh *et al*, 2003).

In contrast to other helminthic parasites, *S. stercoralis* can complete its life cycle entirely within the human host (Siddiqui *et al*, 2006). As a result, the burden of adult worms in infected humans can increase substantially through a cycle of autoinfection. During autoinfection, the rhabditiform larvae mature into filariform larvae within the gastrointestinal tract. The filariform larvae can then penetrate the perianal skin or colonic mucosa to complete the cycle of autoinfection. Larval transformation within the gastro-intestinal tract may also be accelerated by constipation, diverticula, other conditions that reduce bowel motility, and steroid use. Although autoinfection is limited by an intact immune response, a low level of autoinfection may permit the organism to persist

for decades and cause clinical manifestations long after the initial infection (Chu *et al*, 1990). This has been observed in prisoners of war who were found to be infected more than 40 years after exposure in Thailand (Pelletier *et al*, 1988). However, in patients with depressed cell-mediated immunity, autoinfection may give rise to potentially fatal hyperinfection with disseminated disease (Keiser and Nutman, 2004).

Eosinophilia is not universally present in strongyloidiasis, but may be the only clue that the patient harbors a parasitic infection. A report, for example, evaluated 128 Indochinese patients with eosinophilia, the cause of which was not apparent by routine screening (Nutman *et al*, 1987). Intestinal parasitism with one or more organisms was responsible for the eosinophilia in 122; hookworm (55%) and *S. stercoralis* (38%) were the most common organisms. However, eosinophilia may be suppressed or absent in disseminated disease because of concomitant pyogenic infection or steroid administration (Arsic-Arsenijevic *et al*, 2005). The serum IgE concentration is often elevated in these settings (Robinson *et al*, 1994).

The cycle of autoinfection can lead to the hyperinfection syndrome by greatly increasing the parasite burden. Autoinfection within the gastrointestinal tract begins when rhabditiform larvae transform into filariform larvae, which penetrate the intestinal wall to enter the bloodstream. The massive dissemination of filariform larvae to the lungs, liver, heart, central nervous system, and endocrine glands induces inflammation that may result in symptomatic dysfunction of these organs and even septic shock (Cebular *et al*, 2003).

The disseminated strongyloidiasis occurs when the organism, in the larval form, is found outside the usual migration pattern. Hyperinfection is an augmentation of the life cycle, resulting in a heavy infestation of worms in the lungs.

The most common manifestations of the hyperinfection syndrome include (Lam *et al*, 2003): Fever Nausea and vomiting Anorexia Diarrhea Abdominal pain Dyspnea Wheezing Hemoptysis Cough. Chest radiograph reveals pulmonary infiltrates; consisting of foci of hemorrhage, pneumonitis, and edema. Adult parasites rarely localize in the bronchial tree and lay eggs that develop into larvae in the airway. Bronchospasm frequently accompanied these hyperinfection manifestations (Nowkolo and Imohiosen, 1973).

Clinical epidemiology: Surprisingly, there have only been scattered cases of the systemic strongyloidiasis in HIV-infected patients (Lessnau *et al*, 1993). The only associated risk factor in the HIV-infected population is previous or current residence in an endemic area. Risk factors for the development of strongyloidiasis in the general population include (Davidson *et al*, 1984): a- race (white), b- sex (male), c- Use of steroids, d- Hematologic malignancy. Prior gastric surgery, the presence of schistosomiasis and/or ascariasis may be an additional risk factor relevant in rural, underdeveloped countries where these infections are common (Nucci *et al*, 1995).

Diagnosis: The organisms may be identified through examination of wet preparations of the stool, sputum, or bronchoalveolar lavage fluid. The diagnosis may also be made serologically, but the tests are not widely available: ELISA gave a sensitivity of 85 to 90% and a specificity approaching 90%. However, there were false positive tests in patients with other parasitic infections (Igra-Siegman *et al*, 1981)

For diagnosis, at least two concentrated stool specimens must be examined for the presence of rhabditiform larvae as well as serologic testing. If these diagnostic tests are negative and clinical suspicion of strongyloidiasis remains, either examination of duodenal fluid for larvae or empiric ivermectin therapy. Ivermectin is recommended to treat the uncomplicated strongyloidiasis with typical dose of ivermectin is 200mcg/kg administered in two single doses, usually given two weeks apart. In patients with disseminated disease (hyperinfection syndrome) ex-

tended dosing of ivermectin with typical dose schedule of 200mcg/kg daily for 5 to 7 days minimum. Ivermectin can be combined with albendazole (Biggs *et al*, 2009).

Daily stool examinations should be performed during treatment to determine the effect on larval burden, and ongoing daily treatment until symptoms resolve and stool tests have been negative for at least two weeks is often recommended (El Masry and O'Donnell, 2005). In patients with eosinophilia that persists for more than three months despite therapy, indicated treatment failure or other causes of eosinophilia. Remissions induced by the multi-dose regimen of ivermectin have been maintained for up to three years (Torres *et al*, 1993).

Empiric therapy: Prophylaxis must be considered in patients from endemic areas, especially those with unexplained eosinophilia. Ivermectin may be given either as a single dose (200mcg/kg/day) or in a multi-dose schedule (200mcg/kg/day for four days).

In Egypt, so many authors dealt with the strongyloidiasis in many governorates particularly in the Nile Delta (Abdul-Fattah *et al*, 1995; El Shazly, *et al*, 2006; El Badry *et al*, 2018; Ahmed *et al*, 2019 and others).

3- *Cryptosporidium* species and *Microsporidium* species*: Cryptosporidium* spp. and *Giardia duodenalis* are common etiol ogical agents in humans and animals globally (Checkley *et al*, 2015) *Cryptosporidium* is second only to rotavirus in causing diarrhea and death in children in developing countries, responsible for 2.9 million cases annually in children aged<24 months in the Sub-Saharan Africa (Sow *et al*, 2016). Currently, over 30 *Cryptosporidium* species have been recognized, but humans are mostly infected with *C. parvum* and *C. hominis* with the former mostly transmitted anthroponotically while the latter can be transmitted either anthroponotically or zoonotically (Naguib *et al*, 2018). *Cryptosporidium* and Microsporidium are causative agents of gastrointestinal disease in HIV-infected patients. There are a few case reports of pulmonary disease due to these organisms in the early AIDS era, before effective antiretroviral therapy (Weber *et al*, 1993). Fever and cough were the dominant symptoms (Mannheimer and Soave, 1994). Cabral-Marques *et al.* (2014) in Brazil reported the first cases of pneumonia caused by *Mycoplasma pneumoniae*, *Serratia marcescens* or *Aspergillus* sp. and diarrhea caused by *Microsporidium* sp. or *Isospora* belli. Prevention of exposure is presently the preferred method of prophylaxis, particularly in the patient with advanced immunosuppression.

In Egypt, the cryptosporidiosis endemicity was reported in man, mainrly children, farm and stray animals, and the infective stages in food and water sources by many authors as (El-Sherbini and Mohammad, 2006: Youssef *et al*, 2008; Shoukry *et al*, 2009; Abouel-Nour *et al*, 2015; 2016; Ahmed and Karanis, 2018). Also, in Egypt, *Microsporidium* species (Pleistophoridae) and/or *M.* spores were detected in children and fish (Rizk and Soliman, 2001; El-Shazly *et al*, 2006: Morsy *et al*, 2015; El-Shazly *et al*, 2015).

4- Toxocariasis (also called visceral larva migrans or VLM) refers to human infection caused by roundworms that are not natural human parasites. Toxocariasis occurs as a result of human infection with the larvae of the dog ascarid, *Toxocara canis*, or, less commonly, the cat ascarid, *Toxocara cati*. Another form of VLM is caused by human ingestion of eggs of the pig ascarid, *Ascaris suum*. Clinical presentations consist of VLM and ocular larva migrans (OLM); infection may also be subclinical (Won *et al*, 2008). The toxocariasis occurs worldwide. Infection tends to occur more frequently in tropical regions than in temperate regions, and more frequently among rural populations than urban populations. *Toxocara* larvae can develop at temperatures <50 degrees Fahrenheit although efficiency decreases as the temperature increases (Azam *et al*, 2012). In the United States, the seroprevalence of *Toxocara* has been estimated at 13.9%; rates

are increased among individuals living in poverty and among certain minority groups (especially the African Americans). Prevalence rates of 40% or more were reported in Indonesia and Brazil (CDC, 2011). In North America, it was estimated that about 5% of dogs and puppies are infected (Mohamed *et al*, 2009). In Egypt, like other developing countries, the risk of zoonotic infection related to domiciled, as well as stray dogs is high due to keeping of the livestock and pets animals in the houses in nearly all the rural areas (Youssef and Uga, 2014)

In the environment, shed eggs embryonate and become infective after about three weeks and humans acquire infection as accidental hosts. Following ingestion of infective eggs by dogs or cats, they hatch to larvae (0.5mm) penetrate the gut wall and migrate through the lungs, bronchial tree, and enter the esophagus; adult worms develop in the small intestine, where they lay eggs that are shed in the stool. In most of the older animals, larvae penetrate gut wall and subsequently larvae encyst in tissues. Encysted larvae can reactivate in female dogs during late pregnancy and infect puppies via transplacental and trans-mammary routes; adult worms can subsequently become established in the small intestines of puppies. *Toxocara* can also be transmitted through ingestion of paratenic hosts. Eggs ingested by small non-canine mammals (such as rabbits) can hatch and larvae can penetrate the gut wall with subsequent migration into various tissues where they encyst. The life cycle is completed when dogs eat larvae encysted in the tissues of these paratenic hosts and the larvae develop into egg-laying adult wor-ms in the small intestine of the host(s).

Humans are accidental hosts who become infected by ingesting infective eggs in contaminated soil or encysted larvae in the tissues of infected paratenic hosts (Despommier, 2003). Direct contact with infected puppies and kittens is not classically considered to be a risk factor for human infection since the eggs must embryonate before being infective, although sometimes pets carry embryonated eggs in their fur (El-Tras *et al*, 2011). Following ingestion, the eggs hatch and larvae penetrate the intestinal wall and are carried by the circulation to various tissues (liver, heart, lungs, brain, muscle, eyes). The larvae do not undergo any further development in these sites, but the host inflammatory response against the migrating larvae can cause both the mechanical and immunopathological damage to the tissues, which leads to severe local reactions that are the basis of toxocariasis. VLM is principally a disease of young children, especially those with exposure to playgrounds and sandboxes contaminated by dog or cat feces (Carvalho and Rocha, 2011). Infection can also be acquired by eating of raw liver or other undercooked meat from an infected intermediate host (rabbit, chicken, cattle, or swine) containing encapsulated larvae (Lim, 2008).

The clinical manifestations of the visceral larva migrans (VLM) are a consequence of both the damage caused by migrating larvae and the host eosinophilic granulomatous response. Migration of larvae can cause eosinophilic infiltration, granuloma formation, or eosinophilic abscesses. VLM occurs most commonly in young children and results in hepatitis and pneumonitis as the larvae migrate through the liver and lungs, respectively. The heavy infection may result in fever, anorexia, malaise, irritability, hepatomegaly, respiratory symptoms, pruritic urticaria-like cutaneous lesions and eosinophilia (Beshear Hendley, 1973).

Larvae frequently localize in the liver; hepatic manifestations may include hepatomegaly or nodular lesions. Pulmonary involvement may cause dyspnea, wheezing, and a chronic nonproductive cough in 20 to 80% of patients (Snyder, 1961). Rales are common on physical examination. The chest radiograph demonstrates abnormalities in ≥40% of patients with symptomatic illness (Walsh, 2011). Bilateral peribronchial infiltration is most common; parenchymal infiltrates can also occur (Sakai *et al*, 2006). The

computed tomography (CT) may demonstrate the multifocal subpleural nodules with halo or ground-glass opacities and ill-defined margins (Ota *et al*, 2009). Severe respiratory tract picture is an uncommon complication of heavy infection (Enko *et al*, 2009).

Larvae can also travel via the systemic circulation to muscles, the heart, the eye, or the CNS. Manifestations of the CNS include the eosinophilic meningo-encephalitis, space occupying lesions, myelitis, and cerebral vasculitis causing seizures (Marx *et al,* 2007). Manifestations of the peripheral nervous system include radiculitis, affection of cranial nerves, or musculoskeletal involvement (Jabbour *et al*, 2011). Death due to the myocardial and/or CNS involvement was rarely reported.

Diagnosis: VLM should be suspected in the setting of compatible clinical manifestations, together with leukocytosis, eosinophilia, and hypergammaglobulinemia (elevated serum levels of IgE, IgG, & IgE). Marked leukocytosis with eosinophilia occurs in more than 30% of cases, and elevated titers of anti-A or anti-B isohemagglutinins are the commonly observed in about 50% of patients. An eosinophilic granulomatous hepatitis may develop leading to abnormalities in liver function tests, including elevated transaminases and/or alkaline phosphatase (Hassan and Aziz, 2010). The ELISA sensitivity varied, but PCR helpful (de Visser *et al*, 2008), as well as imaging studies (CT and MRI). For ocular larva migrans (OLM) is considerably lower than for VLM; the diagnosis of OLM generally relies on the findings on ophthalmologic examination

Visceral toxocariasis is treated with antiparasitic drugs. Treatment of ocular toxocariasis is more difficult and usually consists of measures to prevent progressive damage to the eye (CDC, 2013).

In Egypt, toxocariasis, and zoonotic toxocariasis in man particularly children in the rural areas, in stray and pet dogs and cats and renal toxocariasis, urticaria toxocariasis as well as the ocular toxocariasis were reported by many authors (Khalil *et al,* 1976; Morsy *et al,* 1981; Khalil, 1977; Safar, *et al*, 1995; Nada *et al,* 1996; Oteifa and Moustafa, 1997; Ismail and Khalafallah, 2005; Haridy *et al*, 2009; and others).

5- Paragonimiasis is caused by the lung flukes of the genus *Paragonimus* with 50 species and subspecies of *Paragonimus* found in carnivorous animal hosts. About 10 species were reported to cause disease in humans, the most common of which is the oriental lung fluke, *P. westermani*. The adult parasites are reddish-brown, ovoid or coffee-bean shaped, of approximately 10 by 5mm, and is covered with cuticular spines. Adult flukes can produce as many as 20,000 eggs/ day (Johnson *et al,* 1985). There are usually fewer than 20 worms within any individual, but these can survive within humans for more than 20 years. The eggs are brown, ovoid, measure approximately 100µm x 55µm with a thick shell.

Paragonimiasis occurs predominantly in several parts of Central and South America, West Africa, and the Far East. Different species occur in the distinct geographic regions. *P. westermani* is found in the Far East, particularly in India, China, Japan and the Philippines. In the United States, the disease is diagnosed most commonly in immigrants from endemic countries, but a few cases of locally-acquired *P. kellicotti* were reported (Castilla *et al*, 2003). It is estimated that 2.5 million people are infected worldwide. The prevalence of infection increases in areas with numerous human and animal reservoir hosts, an abundance of the first and second intermediate hosts (snails and crabs or crayfish, respectively), and with the prevailing social customs of eating raw or undercooked seafood.

Paragonimiasis can be acquired by ingesting raw meat from carnivorous animal hosts, such as wild boars containing young flukes. Transmission has also been reported via the contaminated utensils such as the knives and/or chopping boards (Choo *et al*, 2003). The chronic cerebral paragonimia sis com-

bined with aneurysmal subarachno id hemorrhage. Outbreaks of paragonimiasis were documented (Cui *et al*, 1988).

Humans acquire the infection by ingesting the raw, salted, or wine-soaked fresh water crabs or crayfish that harbor the metacercarial stage of the parasite. Eggs in human sputum or feces contaminate water, releasing miracidia that infect snails. From these infected snails, cercariae arise and infect crabs or crayfish. After human ingestion of infected undercooked crabs or crayfish, the metacercariae excyst in the duodenum, penetrate the gastrointestinal wall, and migrate within the peritoneal cavity. Although few young flukes may migrate to extrapulmonary sites, most of the developing flukes penetrate the diaphragm to migrate within the pulmonary parenchyma (Yang *et al*, 1959).

The flukes become surrounded by an infiltrate of eosinophils and neutrophils, and later mononuclear leukocytes. Local necrosis of pulmonary parenchyma occurs, followed by the development of a fibrous capsule around the maturing flukes. By the seventh or eighth week of infection, the completely matured flukes begin egg production within the capsule which may enlarge and rupture, often into a bronchiole.

Unlike many parasites, in which pulmonary involvement is secondary to the damage or inflammatory response elicited by organisms that are destined for non-respiratory sites, pulmonary localization is a primary event in paragonimiasis. The paragonimiasis manifestations differ in the early and late phases of the infection (Nwokolo, 1972).

The second phase of infection refers to the time when mature flukes inhabit the lungs. This stage may last for a decade before the flukes gradually die. Recurrent hemoptysis is the most common complaint during this phase. The expectorated material typically has a characteristic chocolate color; composed of a mixture of blood, inflammatory cells, and *Paragonimus* eggs released when the capsules around mature flukes ruptures into a bronchiole. Although the patient may experience some malaise, fever is generally absent. The patient often does not feel or appear ill despite the recurrent hemoptysis. Blood eosinophilia is minimal or absent. Generally, one or more lesions at the sites of localized encysted flukes or their burrowing tracts are recognized on chest x-ray (Suwanik and Harinsuta, 1959), although no abnormalities are detected in about 20% of cases (Ogakwu and Nwokolo, 1973). When abnormalities are visible on plain film or with tomography, one or more may be seen.

Treatment of paragonimiasis with triclabendazole has also been found to be effective. One study involving 62 patients; compared the efficacy of three different triclabendazole doses (5mg/kg/daily for three days, or 10 mg/kg twice on one day, or 10mg/kg single dose) versus praziquantel (dose of 25mg/kg thrice daily for three days). Clinical tolerance was superior in all triclabendazole regimens to that of praziquantel. Clinical symptoms resolved at a comparable rate in all four treatment groups, and a more rapid parasitological response to treatment was seen in patients treated with triclabendazole (Calvopina *et al*, 1998). In Egypt, Barduagni *et al*. (2008) recommended Triclabendazole, a systemic anthelmintic, safe and very effective against many trematodes including *Paragonimus* spp.

In Egypt, Awadallah and Salem (2015) in Sharkia Governorate reported *Paragonimus* spp. (1.33%) in school children.

6- Echinococcosis/Hydatidosis: Echinococcal disease is caused by infection with the metacestode stage of the tapeworm *Echinococcus*, which belongs to the family Taeniidae. Four *Echinococcus* species infect man, which are *E. granulosus & E. multilocularis* are the commonest, causing cystic echinococcosis & alveolar echinococcosis respectively. The other two species, *E. vogeli* & *E. oligarthrus*, cause polycystic echinococcosis but rarely been associated with human (Bhatia, 1997). *E. granulosus* its initial phase is always asymptomatic. Many infections are acquired in childhood but do not cause clinical manifestations until adult-

hood. Latent periods of more than 50 years before symptoms arise have been reported. While approximately 50% of detected cases occur in asymptomatic patients, many more cases remain undiagnosed or are found incidentally at autopsy (McManus *et al*, 2003).

Clinical picture of *E. granulosus* infection depends upon the cysts' site and size. Small and/or calcified cysts may remain asymptomatic indefinitely. But, symptoms due to the mass effect within organs, obstruction of the blood or lymphatic flow, or complications such as rupture or secondary bacterial infections can result. Cysts typically increase in diameter at a rate of one to five centimeters per year. Hydatid cysts may be found in almost any site of the body, either from primary inoculation or via secondary spread. The liver is affected in approximately two-thirds of patients, the lungs in approximately 25%, and other organs including the brain, muscle, kidney, bone, heart, and pancreas in a small proportion of patients. Up to 90% of *E. granulosus* patients have single-organ involvement, and more than 70% have only one cyst (Ali-Khan an Rausch, 1987). The affected sites are: A- Liver is asymptomatic, right lobe is affected in 60 to 85% of cases. Significant symptoms are unusual before reached at least 10cm in diameter. If cysts become large, hepatomegaly with or without associated right upper quadrant pain, nausea and vomiting can result. Liver cysts can rupture into the biliary tree causing biliary colic, obstructive jaundice, cholangitis, or pancreatitis (Frider *et al*, 1999). B- Lung, pulmonary involvement led to a variety of symptoms, including chronic cough (sometimes with accompanying hemoptysis or evacuation of cyst material), chest pain, pleuritis or dyspnea. Rupture of a cyst into a bronchus may lead to hemoptysis, respiratory distress, and the asthma-like symptoms. If cysts rupture into the pleural space, a pleural effusion or empyema may develop. Lung abscesses can also occur. C- Other organs infected are the heart can result in mechanical rupture with widespread dissemination or pericardial tamponade. The CNS involvement can lead to seizures or signs of raised intracranial pressure; infection of the spinal cord can result in spinal cord compression. Cysts in the kidney can cause hematuria or flank pain (Gogus *et al*, 2003). The immune complex-mediated disease, glomerulonephritis leading to the nephrotic syndrome, and secondary amyloidosis were reported (Gelman *et al*, 2000). Bone cysts are usually asymptomatic until a pathologic fracture develops; spine, pelvis and long bones are most frequently affected (Mazyad *et al*, 1999). Ocular cysts occur and may be presented with headache gradually worsening, right eye swelling increased and visual deterioration (Al-Muala *et al*, 2012).

Diagnosis: A combination of imaging and serology diagnosis of both cystic and alveolar echinococcosis, although serologic assays are more sensitive and specific for *E. multilocularis*. Diagnosis is by ultrasound imaging in combination with serologic testing with ELISA. When ultrasound reveals in-folding of the inner cyst wall, separation of the hydatid membrane from the wall of the cyst, or hydatid sand, a diagnosis of hydatid disease is probable. Serologic testing can confirm the diagnosis. For *E. multilocularis*, lesions on ultrasound may have an irregular contour and may be difficult to differentiate from tumor. In these cases, the patient may appear well; however. the serological testes were recommended to be pursued for diagnostic confirmation. The likelihood of a positive serology depends on cyst location and viability. Patients with cysts in the liver are more likely to be seropositive than patients with cysts in the lung. Serologic assays are less likely to be positive if the cyst is calcified or nonviable. In these cases, diagnostic judgment may need to take into account the serologic testing limitations. Percutaneous aspiration or biopsy should be reserved for situations when other diagnostic methods are inconclusive because of the potential for anaphylaxis and secondary spread of the infection. If aspiration is required, it should be performed under ultrasound or CT guidance, and concurrent administration of benzimidazole therapy to decrease the risk of complications.

In Egypt, many authors dealt with the definitive host, mainly dogs, cattle, slaughtered an-

imals and human infection as well as the medical and surgical treatment (Handousa, 1951; Haridy *et al*, 1998; 2000, 2008; El Shazly *et al*, 2007a; b; Aaty *et al*, 2012; Hassanain *et al*, 2016; Aldahmashi *et al*, 2016; and others)

Conclusion

It is important to consider parasitic infections in the differential diagnosis of such lung diseases. If identified early, most parasitic diseases that affect the lung are curable with medical or surgical treatments.

No doubt, the opportunistic helminthes and protozoa parasites do recognized and affected the HIV before he and/or she recognized themselves as HIV patients.

Undoubtedly, the early diagnosis and the proper treatment of these opportunistic parasites minimize risky life of HIV patients.

The HIV is a retrovirus, which means that each viral particle contains genetic material on 2 strands of RNA, as well as enzymes that are necessary for completion of the viral life cycle. Viral RNA must be reverse-transcribed into DNA to allow viral reproduction. Each HIV viral particle contains an enzyme called reverse transcriptase to facilitate this process. HIV infection begins with binding of the virus to the CD4 protein present on some human T cells. HIV must also bind with another "coreceptor" on the cell surface to gain entry into the cell. Once inside the cell, the virus*'* reverse transcriptase enzyme transcribes the viral RNA into DNA. Viral DNA then enters the cell nucleus and becomes integrated into the human DNA by way of the integrase enzyme.

Recommendation

Prior to starting any medications, the healthcare worker should undergo HIV test to ensure that he or she is HIV negative. If PEP is warranted, either 2 or 3 available anti-retroviral drugs must be recommended, based on the combination of the exposure severity and the patient status. The antiretroviral drugs are taken for 28 days.

Healthcare workers started on PEP should have close follow-up with an HIV expert to monitor for adverse drug reactions. The HIV antibody testing should be performed at 6 weeks, 12 weeks, and 6 months after the exposure.

There has been growing interest in the use of the PEP for nonoccupational exposures to HIV (nPEP), including unanticipated sexual exposures (either consensual or involving survivors of sexual assault) or injection-drug use exposures.

References

Aaty, HE, Abdel-Hameed, DM, Alam-eldin, Y H, El-Shennawy, S, Aminou, HA, *et al,* 2012: Molecular genotyping of *Echinococcus granulosus* in animal and human isolates from Egypt. Acta Trop.121:125-8.

Abdel-Motagaly, AME, Ibrahim, AMA, Morsy, TA, 2017: An intervention program on blood protozoa acquired by needle stick injury and infection control. J. Egypt. Soc. Parasitol. 47, 2:309-22.

Abdul-Fattah, MM, Nasr, ME, Yousef, SM, Ibraheem, MI, Abdul-Wahhab, SE, *et al,* 1995: Efficacy of ELISA in diagnosis of strongyloidiasis among the immune-compromised patients. J. Egypt. Soc. Parasitol. 25, 2:491-8.

Abouel-Nour, MF, El-Shewehy, DMM, Hamada, SF, Morsy, TA, 2015: The efficacy of three medicinal plants: garlic, ginger and mirazid and a chemical drug metronidazole against *Cryptosporidium parvum.* i- Immunologic response. J. Egypt. Soc. Parasitol. 45, 3:559-70.

Abouel-Nour, MF, El-Shewehy, DMM, Hamada, SF, Morsy, TA, 2016: The efficacy of three medicinal plants; garlic, ginger and mirazid and a chemical drug metronidazole against *Cryptosporidium parvum*: ii- Histological changes. J. Egypt. Soc. Parasitol. 46, 1:185-200

Ahmed, SA, El-Moselhy, A, El-Moammaly, A, El-Shewy, K, 2019: *Strongyloides stercor-alis* in patients on corticosteroids therapy using enzyme-linked immunosorbent assay and gelatin particles indirect agglutination tests: A diagnostic approach. Acta Parasitol. May 8. doi: 10.-2478/s11686-019-00060-w.

Ahmed, SA, Karanis, P, 2018: An overview of methods/techniques for the detection of *Cryptosporidium* in food samples. Parasitol. Res. 117, 3:629-53.

Aldahmashi, M, Alassal, M, Kasb, I, Elrakhawy, H, 2016: Conservative Surgical management for pulmonary hydatid cyst: Analysis and

outcome of 148 cases. Canad. Respir. J. 2016: 8473070. doi: 10.1155/2016/8473070.

Ali-Khan, Z, Rausch, RL, 1987: Demonstration of amyloid and immune complex deposits in renal and hepatic parenchyma of Alaskan alveolar hydatid disease patients. Ann. Trop. Med. Parasitol. 81:381-6.

Al-Muala, HD, Sami, SM, Shukri, MA, Hasson, HK, Alaboudy, AT, 2012: Orbital hydatid cyst. Ann. Maxillofac. Surg. 2, 2:197-9.

Arsic-Arsenijevic, V, Dzamic, A, Dzamic, Z, *et al*, 2005: Fatal *Strongyloides stercoralis* infection in a young woman with lupus glomerulonephritis. J. Nephrol.18:787-90.

Awadallah, MA, Salem, LM, 2015: Zoonotic enteric parasites transmitted from dogs in Egy-pt with special concern to *Toxocara canis* infection. Vet. World 8, 8:946-57

Azam, D, Ukpai, OM, Said, A, *et al*, 2012: Temperature and the development and survival of infective *Toxocara canis* larvae. Parasitol. Res. 110:649-52.

Barduagni, P, Hassanein, Y, Mohamed, M, Wakeel, AE, Sayed, ME, *et al*, 2008: Use of triclabendazole for treatment of patients co-infected by *Fasciola* spp. and *S. mansoni* in Behera Governorate, Egypt. Parasitol. Res. 102, 4: 631-3.

Benson, CA, Kaplan, JE, Masur, H, *et al*, 2005: Treating opportunistic infections among HIV-infected adults and adolescents: Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association/ Infectious Diseases Society of America. Clin. Infect. Dis. 40:S131-8.

Beshear, JR, Hendley, JO, 1973: Severe pulmonary involvement in visceral larva migrans. Am. J. Dis. Child. 125:599-604.

Bhatia, G, 1997: *Echinococcus*. Semin. Respir. Infect. 12:171-9.

Biggs, BA, Caruana, S, Mihrshahi, S, *et al*, 2009: Management of chronic strongyloidiasis in immigrants and refugees: Is serologic testing useful? Am. J. Trop. Med. Hyg. 80:788-92.

Bonilla, CA, Rosa, UW, 1994: *Toxoplasma gondii* pneumonia in patients with the acquired immunodeficiency syndrome: diagnosis by bronchoalveolar lavage. South Med. J. 87:659-62.

Burg, JL, Grover, CM, Pouletty, P, Boothroyd, JC, 1898: Direct and sensitive detection of a pathogenic protozoan, *Toxoplasma gondii*, by polymerase chain reaction. J. Clin. Microbiol. 27: 1787-91.

Cabral-Marques, O, Klaver, S, Schimke, L F, Ascendino, ÉH, Khan, TA, *et al*, 2014: First report of the Hyper-IgM syndrome Registry of the Latin American Society for Immuno- deficiencies: Novel mutations, unique infectio-ns, and outcomes. J. Clin. Immunol. 34, 2:146-56.

Calvopina, M, Guderian, RH, Paredes, W, *et al*, 1998: Treatment of human pulmonary paragonimiasis with triclabendazole: Clinical tolerance and drug efficacy. Trans. R. Soc. Trop. Med. Hyg. 92:566-72.

Carvalho, EA, Rocha, RL, 2011: Toxocariasis: Visceral larva migrans in children. J. Pediatr. (Rio J). 87, 2:100-10.

Castilla, EA, Jessen, R, Sheck, DN, Procop, GW, 2003: Cavitary mass lesion and recurrent pneumothoraces due to *Paragonimus kellicotti* infection: North American paragonimiasis. Am. J. Surg. Pathol. 27:1157-9.

CDC, 1981: *Pneumocystis* Pneumonia; Los Angeles. MMWR Morb/ Mortal Wkly. Rep.30:250-8.

CDC, 1995: USPHS/IDSA Guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: a summary. MMWR Recomm. Rep. 44:1-10.

CDC, 2006: The Global HIV/AIDS pandemic, 2006. MMWR Morb. Mortal. Wkly. Rep. 55: 841-6.

CDC, 2011: Ocular toxocariasis; United States, 2009-2010. MMWR Morb. Mortal. Wkly. Rep. 60:734-9.

CDC, 2013: Parasites-Toxocariasis (also known as Roundworn infection).

Cebular, S, Lee, S, Tolaney, P, Lutwick, L, 2003: Community-acquired pneumonia in immuno-compromised patients: Opportunistic infections to consider in differential diagnosis. Postgrad. Med. 113:65-9.

Celedon, **JC, Mathur-Wagh, U, Fox, J, *et al*, 1994:** Systemic strongyloidiasis in patients infected with the human immunodeficiency virus: A report of 3 cases and review of the literature. Medicine (Baltimore); 73:256-70.

Checkley, W, White, AC, Jr, Jaganath, D, Arrowood, MJ, Chalmers, RM, *et al*, 2015: A review of the global burden, novel diagnostics, therapeutics, and vaccine targets for *Cryptosporidium*. Lancet Infect. Dis. 15:85-94

Choo, JD, Suh, BS, Lee, HS, *et al*, 2003: Chronic cerebral paragonimiasis combined with aneurysmal subarachnoid hemorrhage. Am. J. Trop. Med. Hyg. 69:466-70.

Chu, E, Whitlock, WL, Dietrich, RA, 1990: Pulmonary hyperinfection syndrome with *Strongyloides stercoralis*. Chest 97:1475-8.

Cui, J, Wang, ZQ, Wu, F, Jin, XX, 1988: An outbreak of paragonimiosis in Zhengzhou City, China. Acta Trop. 70:211-4.

Dannemann, B, McCutchan, JA, Israelski, D, *et al*, 1992: Treatment of toxoplasmic encephalitis in patients with AIDS; A randomized trial comparing pyrimethamine plus clindamycin to pyrimethamine & sulfadiazine: California Collaborative Treatment Group. Ann. Intern. Med. 116:33-8.

Davidson, RA, Fletcher, RH, Chapman, LE, 1984: Risk factors for strongyloidiasis: A case-control study. Arch. Inter. Med. 144:321-8.

de Visser, L, Rothova, A, de Boer, JH, *et al*, 2008: Diagnosis of ocular toxocariasis by establishing intraocular antibody production. Am. J. Ophthalmol. 145:369-74.

Derouin, F, Sarfati, C, Beauvais, B, *et al*, 1989: Laboratory diagnosis of pulmonary toxoplasmosis in patients with acquired immunodeficiency syndrome. J. Clin. Microbiol. 27: 1661-6.

Derouin, F, Sarfati, C, Beauvais, B, *et al*, 1990: Prevalence of pulmonary toxoplasmosis in HIV-infected patients. AIDS 1990; 4:1036.

Despommier, D, 2003: Toxocariasis: Clinical aspects, epidemiology, medical ecology, and molecular aspects. Clin. Microbiol. Rev. 16:265-70.

El Behairy, AM, Choudhary, S, Ferreira, L R, Kwok, OC, Hilali, M, *et al*, 2013: Genetic characterization of viable *Toxoplasma gondii* isolates from stray dogs from Giza, Egypt. Vet. Parasitol. 193, 1/3:25-9.

El Masry, HZ, O'Donnell, J, 2005: Fatal *Strongyloides* hyperinfection in heart transplantation. J. Heart/Lung Transplant. 24:1980-9.

El Shazly, AM, Afify, EM, Morsy, TA, 1996: Antibodies against *Toxoplasma* in children and adults with malignancy. J. Egypt. Soc. Parasitol. 26, 3:781-7.

El Shazly, AM, Awad, SE, Sultan, DM, Sadek, GS, Morsy, TA, 2006: Intestinal parasites in Dakahlia governorate, with different techniques in diagnosing protozoa. J. Egypt. Soc. Parasitol. 36, 3:1023-34.

El-Badry, AA, Hamdy, DA, Abd El Wahab, WM, 2018: *Strongyloides stercoralis* larvae found for the first time in tap water using a novel culture method. Parasitol. Res. 117, 12: 3775-80.

Elshazly, AM, Attia, G, El-Ghareeb, AS, Belal, US, 2011: Clinical varieties of Toxocariasis *canis* in Children's Hospital, Mansoura University: Is it an underestimated problem? J. Egypt. Soc. Parasitol. 41, 2:263-74.

El-Shazly, AM, Awad, SE, Abdel Tawab, A H, Haridy, FM, Morsy, TA, 2007a: Echinococcosis (zoonotic hydatidosis) in street dogs in urban and rural areas, Dakahlia Governorate, Egypt. J. Egypt**.** Soc. Parasitol. 37, 1:287-98.

El-Shazly, AM, Awad, SE, Hegazy, MA, Mohammad, KhA, Morsy, TA, 2007b: Echinococcosis *granulosus*/hydatidosis an endemic zoonotic disease in Egypt. J**.** Egypt. Soc**.** Parasitol. 37, 2:609-22.

El-Shazly, LB, El-Faramawy, AA, El-Sayed, NM, Ismail, KA, Fouad, SM, 2015: Intestinal parasitic infection among Egyptian children with chronic liver diseases. J. Parasit. Dis. 39, 1:7-12.

Elsheikha, HM, Azab, MS, Abousamra, N, Rahbar, M, 2009: Seroprevalence of and risk factors for *Toxoplasma gondii* antibodies among asymptomatic blood donors in Egypt. Parasitol. Res. 104, 6:1471-6.

El-Sherbini, GT, Mohammad, KA, 2006: Zoonotic cryptosporidiosis in man and animal in farms, Giza Governorate, Egypt. J. Egypt. Soc. Parasitol. 36, 2:S49-58.

El-Tras, WF, Holt, HR, Tayel, AA, 2011: Risk of *Toxocara canis* eggs in stray and domestic dog hair in Egypt. Vet. Parasitol. 178, 3/4:319-23

Enko, K, Tada, T, Ohgo, KO, *et al*, 2009: Fulminant eosinophilic myocarditis associated with visceral larva migrans caused by *Toxocara canis* infection. Circ J 2009; 73:1344.

Evans, TG, Schwartzman, JD, 1991: Pulmonary toxoplasmosis. Semin. Respir. Infect. 6:51-8.

Frider, B, Larrieu, E, Odriozola, M, 1999: Long-term outcome of asymptomatic liver hydatidosis. J. Hepatol. 30:228-34.

Furrer, H, Opravil, M, Bernasconi, E, *et al*, 2000: Stopping primary prophylaxis in HIV-1-infected patients at high risk of *Toxoplasma* encephalitis: Swiss HIV Cohort Study. Lancet 355:2217-9.

Ganczak, M, Barss, P, 2008: Nosocomial HIV infection: Epidemiology and prevention, a global perspective. AIDS Rev. 10, 1:47-61.

Gelman, R, Brook, G, Green, J, *et al*, 2000: Minimal change glomerulonephritis associated with hydatid disease. Clin. Nephrol. 53:152-6.

Gogus, C, Safak, M, Baltaci, S, Turkolmez, K,

2003: Isolated renal hydatidosis: Experience with 20 cases. J. Urol. 169:186-90.
Handousa AB, 1951: Proptosis caused by hydatid disease. Br. J. Ophthalmol. 35:607-13.
Haridy, FM, Abdel Gawad, AE, Ibrahim, B B, Hassan, AA, El Sherbini, GT, *et al*, 2008: Zoonotic hydatidosis in donkeys: Post-mortum examination in the zoo, Giza, Egypt. J. Egypt. Soc. Parsitol. 38, 1:305-12
Haridy, FM, Hassan, AA, Hafez, AO, El-Sherbini, GT, Morsy, TA, 2009: External and intestinal parasites of pet dogs with reference to zoonotic toxocariasis. J. Egypt. Soc. Parasitol. 39, 1:321-6.
Haridy, FM, Ibrahim, BB, Morsy, TA, 1998: Studies on hydatidosis in slaughtered camels in Egypt. J. Egypt. Soc. Parasitol. 28, 3:673-81.
Haridy, FM, Ibrahim, BB, Morsy, TA, 2000: Sheep-dog-man: The risk zoonotic cycle in hydatidosis. J. Egypt. Soc. Parasitol. 30, 2:423-9.
Haridy, FM, Shoukry, NM, Hassan, AA, Morsy, TA, 2009: ELISA-sero-prevalence of *Toxoplasma gondii* in draught horses in Greater Cairo, Egypt. J. Egypt. Soc. Parasitol. 39, 3:821-6.
Haridy, FM, Saleh, NM, Khalil, HH, Morsy, TA, 2010: Anti-*Toxoplasma gondii* antibodies in working donkeys and donkey's milk in Greater Cairo, Egypt. J. Egypt. Soc. Parasitol. 40, 2: 459-64.
Hassan, SE, Aziz, MMA, 2010: Detection of antibodies to excretory-secretory antigen of *Toxocara vitulorum* infective larvae in the buffalo calves by ELISA. Glob. Vet. 4, 1:97-102.
Hassanain, MA, Shaapan, RM, Khalil, FA, 2016: Sero-epidemiological value of some hydatid cyst antigen in diagnosis of human cystic echinococcosis. J. Parasitol. Dis. 40, 1:52-6.
Heeney, JL, Dalgleish, AG, Weiss, RA, 2006: Origins of HIV and the evolution of resistance to AIDS. Science 313:462.
Holliman, RE, 1990: Serological study of the prevalence of toxoplasmosis in asymptomatic patients infected with human immunodeficiency virus. Epidemiol. Infect. 105:415-8.
Igra-Siegman, **Y, Kapila, R, Sen, P, *et al*, 1981:** Syndrome of hyperinfection with *Strongyloides stercoralis*. Rev. Infect. Dis. 3:397-400.
Ismail, MA, Khalafallah, O, 2005: *Toxocara canis* and chronic urticaria in Egyptian patients. J. Egypt. Soc. Parasitol. 35, 3:833-40
Jabbour, RA, Kanj, SS, Sawaya, RA, *et al*, 2011: *Toxocara canis* myelitis: clinical features, magnetic resonance imaging (MRI) findings, and treatment outcome in 17 patients. Medicine (Baltimore) 90:337-44.
Johnson, RJ, Jong, EC, Dunning, SB, *et al*, 1985: Paragonimiasis: diagnosis and the use of praziquantel in treatment. Rev. Infect. Dis. 7: 200-6.
Keiser, PB, Nutman, TB, 2004: *Strongyloides stercoralis* in the immunocompromised population. Clin. Microbiol. Rev. 17:208-12.
Khalil, HM, 1977: Toxocariasis in Egypt. J. Egypt. Publ. Hlth. Assoc. 52, 5:330-43
Khalil, HM, Rifaat, MA, Abdel-Aal, TM, Khaled, ML, Sadek, MS, *et al*, 1976: Toxocariasis in the humans and dogs of Siwa Oasis, Qena and Aswan Governorates, A.R.E. J. Egypt. Publ. Hlth. Assoc. 51, 5:289-96
Kunst, H, Mack, D, Kon, OM, Banerjee, A K, chiodini, P, *et al*, 2011: Parasitic infections of the lung: a guide for the respiratory physician. Thorax 66, 6:528-36
Lam, CS, Tong, MK, Chan, KM, Siu, YP, 2006: Disseminated strongyloidiasis: A retrospective study of clinical course and outcome. Eur. J. Clin. Microbiol. Infect. Dis. 25:14-8.
Lane, HC, Laughon, BE, Falloon, J, *et al*, 1994: NIH conference. Recent advances in the management of AIDS-related opportunistic infections. Ann. Intern. Med. 120:945-50.
Lessnau, KD, Can, S, Talavera, W, 1993: Disseminated *Strongyloides stercoralis* in human immunodeficiency virus-infected patients: Treatment failure and a review of the literature. Chest 104:119-24.
Lim, JH, 2008: Toxocariasis of the liver: Visceral larva migrans. Abdom. Imag. 33:151-6.
Luft, BJ, Remington, J, 1992: Toxoplasmic encephalitis in AIDS. Clin. Infect. Dis. 15:211-8.
Maguire, GP, Tatz, J, Giosa, R, Ahmed, T, 1986: Diagnosis of pulmonary toxoplasmosis by bronchoalveolar lavage. N.Y. State J. Med. 86: 204-6.
Mannheimer, SB, Soave, R, 1994; Protozoal infections in patients with AIDS: Cryptosporidiosis, isosporiasis, cyclosporiasis, and microsporidiosis. Infect. Dis. Clin. North Am. 8:483-8.
Mariuz, P, Bosler, EM, Luft, BJ, 1994: Toxoplasmosis in individuals with AIDS. Infect. Dis. Clin. North Am. 8:365-70.
Marx, C, Lin, J, Masruha, MR, *et al*, 2007: Toxocariasis of CNS simulating acute disseminated encephalomyelitis. Neurology 69:806-8.
Mazyad, MAM, Morsy, TA, Habib, KhSM, 1999: Vertebral unilocular hydatidosis in a she-

pherd and his wife. J. Egypt. Soc. Parasitol. 29, 2:547-50.

McCabe, RE, Oster, SA, 1989: Current recommendations and future prospects in the treatment of toxoplasmosis. Drugs 38:973-6.

McManus, DP, Zhang, W, Li, J, Bartley, P B, 2003: Echinococcosis. Lancet 362:1295.

Mikhail, MW, Hasan, AH, Allam K, Mohammed, NM, 2017: Seroprevalence of *Toxoplasma gondii* among commensal rodents from Giza Governorate, Egypt. J. Egypt. Soc. Parasitol. 47, 1:145-50

Michael, SA, El Refai, MA, Morsy, TA, 1977: Incidence of *Toxoplasma* antibodies among camels in Egypt. J. Egypt. Soc. Parasitol. 7, 2:129 -32.

Mohamed, AS, Moore, GE, Glickman, LT, 2009: Prevalence of intestinal nematode parasitism among pet dogs in the United States (2003-2006). J. Am. Vet. Med. Assoc. 234:631-5.

Morsy, K, Abdel-Ghaffar, F, Mehlhorn, H, Bashtar, AR, Abdel-Gaber, R, 2012: Ultrastructure & molecular phylogenetics of a new isolate of *Pleistophora pagri* sp. nov. (Microsporidia, Pleistophoridae) from *Pagrus pagrus* in Egypt. Parasitol. Res. 111, 4:1587-97.

Morsy, TA, Sadek, MS, Abdel Hamid, MY, 1981: Intestinal parasites of stray cats in Cairo, Egypt. J. Egypt. Soc. Parasitol. 11, 2:331-45.

Nada, **SM, Abazza, BE, Mahmoud, LA, Habeeb, YS, Hussein, HF, *et al*, 1996:** Toxocariasis as a cause of renal disease in children in Sharkia Governorate, Egypt. J. Egypt. Soc. Parasitol. 26, 3:709-17.

Naguib, D, El-Gohary, AH, Roellig, D, Mohamed, AA, Arafat, N, *et al*, 2018: Molecular characterization of *Cryptosporidium* spp. and *Giardia duodenalis* in children in Egypt. Parasit. Vectors Jul 11; 11(1):403. doi: 10.1186/ s13071-018-2981-7.

Nissapatorn, V, Sawangjaroen, N, 2011: Parasitic infections in HIV infected individuals: Diagnostic & therapeutic challenges. Indian J. Med. Res. 134, 6:878-97.

Nucci, M, Portugal, R, Pulcheri, W, *et al*, 1995: Strongyloidiasis in patients with hematologic malignancies. Clin. Infect. Dis. 21:675-8.

Nutman, TB, Ottesen, EA, Ieng, S, *et al*, 1987: Eosinophilia in Southeast Asian refugees: Evaluation at a referral center. J. Infect. Dis. 155: 309-12.

Nwokolo, C, 1972: Endemic paragonimiasis in Eastern Nigeria: Clinical features and epidemiology of the recent outbreak following the Nigerian civil war. Trop. Geogr. Med. 24:138-44.

Nwokolo, C, Imohiosen, EA, 1973: Strongyloidiasis of respiratory tract presenting as "asthma". Br. Med. J. 2:153-8.

Ogakwu, M, Nwokolo, C, 1973: Radiological findings in pulmonary paragonimiasis as seen in Nigeria: A review based on one hundred cases. Br. J. Radiol. 46:699-703.

Oksenhendler, E, Cadranel, J, Sarfati, C, *et al*, 1990: *Toxoplasma gondii* pneumonia in patients with the acquired immunodeficiency syndrome. Am. J. Med. 88:N18-22.

Ota, KV, Dimaras, H, Héon, E, *et al*, 2009: Toxocariasis mimicking liver, lung, and spinal cord metastases from retinoblastoma. Pediatr. Infect. Dis. J. 28:252-8.

Oteifa, NM, Moustafa, MA, 1997: The potential risk of contracting toxocariasis in Heliopolis District, Cairo, Egypt. J. Egypt. Soc. Parasitol. 27, 1:197-203.

Pappas, G, Roussos, N, Falagas, ME, 2009: Toxoplasmosis snapshots: Global status of *Toxoplasma gondii* seroprevalence and implications for pregnancy and congenital toxoplasmosis. Int. J. Parasitol. 39, 12:1385-94

Pelletier, LL, Jr, Baker, CB, Gam, AA, *et al*, 1988: Diagnosis and evaluation of treatment of chronic strongyloidiasis in ex-prisoners of war. J. Infect. Dis. 157:573-6.

Piot, P, 2006: AIDS: from crisis management to sustained strategic response. Lancet 368: 526-8.

Pomeroy, C, Filice, GA, 1992: Pulmonary toxoplasmosis: a review. Clin. Infect. Dis. 14: 863-6.

Pugin, J, Vanhems, P, Hirschel, B, *et al*, 1992: Extreme elevations of serum lactic dehydrogenase differentiating pulmonary toxopl- asmosis from Pneumocystis pneumonia. N. Engl. J. Med. 326: 1226-9.

Rey, MF, Mary, C, Sanguinetti, D, Ranque, S, Bartoli, C, *et al*, 2017: Successful treatm- ent of pulmonary and cerebral toxoplasmosis associated with *Pneumocystis* pneumonia in an HIV patient. Diseases 5(4); pii: E35. doi: 10. 3390/ diseases5040035.

Rifaat, MA, Morsy, TA, Sadek, MS, Azab, ME, Safar, EH, *et al*, 1977: Serological surveys for toxoplasmosis among farm animals in Egypt. J. Egypt. Soc. Parasitol. 7, 2:229-33

Rifaat, MA, Morsy, TA, Salem, S.A, Sadek, M SM, 1971: Toxoplasmosis in buffaloes and cat-

tle in U.A.R. Pakis. Med. Rev.5:209-10.

Rizk, H, Soliman, M, 2001: Coccidiosis among malnourished children in Mansoura, Dakahlia Governorate, Egypt. J. Egypt. Soc. Parasitol. 31, 3:877-86.

Robinson, RD, Lindo, JF, Neva, FA, *et al*, 1994: Immunoepidemiologic studies of *Strongyloides stercoralis* and human T lymphotropic virus type I infections in Jamaica. J. Infect. Dis. 169:692-6.

Safar, EH, Abdel Ghaffar, FM, Saffar, SA, Makled, KM, Habib, KS, *et al*, 1995: Incidence of *Toxoplasma* and *Toxocara* antibodies among out-patients in the Ophthalmic Research Institute, Egypt. J. Egypt. Soc. Parasitol. 25, 3: 839-52.

Sakai, S, Shida, Y, Takahashi, N, *et al*, 2006: Pulmonary lesions associated with visceral larva migrans due to *Ascaris suum* or *Toxocara canis*: Imaging of six cases. Am. J. Roentgenol. 186: 1697-702.

Saleh, AMA, Ali, HA, Ahmed, SAM, Hosny, SM, Morsy, TA, 2014: Screening of *Toxoplasma gondii* infection among childbearing age females and assessment of nurses' role in prevention and control of toxoplasmosis. J. Egypt. Soc. Parasitol. 44, 2:329- 342

Saleh, AMA, Al-Agroudi, MA, Morsy, TA, 2016: Occupational, nosocomial or hospital acquired toxoplasmosis. J. Egypt. Soc. Parasitol. 46, 2:407-418.

Sarwat, MA, Ahmed, AB, Zamzami, OM, Fawzy, AFA, Morsy, TA, 1993: *Toxoplasma go\ndii* in Saudi blood donors: A serological study using 3 tests. J. Egypt. Soc. Parasitol. 23, 3:751-7.

Satoh, M, Kiyuna, S, Shiroma, Y, *et al*, 2003: Predictive markers for development of strongyloidiasis in patients infected with both *Strongyloides stercoralis* and HTLV-1. Clin. Exp. Immunol. 133:391-6.

Shoukry, NM, Dawoud, HA, Haridy, FM, 2009: Studies on zoonotic cryptosporidiosis *parvum* in Ismailia Governorate, Egypt. J. Egypt. Soc. Parasitol. 39, 2:479-88.

Siddiqui, AA, Genta, RM, Berk, SL, 2006: Strongyloidiasis. In: Trop. Infectious Diseases: Principles, Practices and Pathogens. Guerrant, RL, Walker, DH, Weller, PF (Eds.). Church-hill Livingstone Elsevier, Philadelphia.

Snyder, C, 1961: Visceral larva migrans: Ten years' experience. Pediatrics 28:85-92.

Sow, SO, Muhsen, K, Nasrin, D, Blackwelder, WC, *et al*, 2016: The burden of *Cryptosporidium* diarrheal disease among children < 24 months of age in moderate/high mortality regions of Sub-Saharan Africa and South Asia, utilizing data from Global Enteric Multicenter Study (GEMS) PLoS Negl Trop Dis. 10:e0004729. doi: 10.1371/journal.pntd.0004729/

Suwanik, R, Harinsuta, C, 1959: Pulmonary paragonimiasis; an evaluation of roentgen findings in 38 positive sputum patients in an endemic area in Thailand. Am. J. Roentgenol. Radi. Ther. Nu-cl. Med. 81:236-9.

Torres, J, Isturiz, R, *et al*, 1993: Efficacy of ivermectin in treatment of strongyloidiasis complicating AIDS. Clin. Infect. Dis. 17:900-4.

Walsh, MG, 2011: *Toxocara* infection and diminished lung function in a nationally representative sample from the United States population. Int. J. Parasitol. 41:243-8.

Weber, R, Kuster, H, Visvesvara, GS, *et al*, 1993: Disseminated microsporidiosis due to *Encephalitozoon hellem*: Pulmonary colonizat-ion, microhematuria, & mild conjunctivitis in a patient with AIDS. Clin. Infect. Dis. 17:415-9.

WHO, 2006: Antiretroviral therapy for HIV infection in adults & adolescents in resource-limited settings towards universal access. Geneva.

Wishahy, AO, Rifaat, MA, Morsy, TA, El Naggar, BA, 1971: Some observations on toxoplasmosis in Egyptian children. J. Egypt. Soc. Parasitol. 2 /3:149-150.

Wishahy, AO, Rifaat, MA, Morsy, TA, El Naggar, B.A, 1972: Toxoplasmosis in children with some neurological manifestations. J. Trop. Med. Hyg. 75, 12:255-6.

Won, KY, Kruszon-Moran, D, Schantz, PM, Jones, JL, 2008: National seroprevalence and risk factors for zoonotic *Toxocara* spp. infection. Am. J. Trop. Med. Hyg. 79:552-6.

Yang, SP, Huang, CT, Cheng, CS, Chiang, L C, 1959: The clinical and roentgenological courses of pulmonary paragonimiasis. Dis. Chest 36: 494-8.

Youssef, AI, Uga, S, 2014: Review of parasitic zoonosis in Egypt. Trop. Med. Hlth. 42, 1:3-14.

Youssef, FG, Adib, I, Riddle, MS, Schlett, CD, 2008: A review of cryptosporidiosis in Egypt. J. Egypt. Soc. Parasitol. 38, 1:9-28.