

MISE AU POINT/IN-DEPTH REVIEW HYDATID DISEASE: THE LEBANESE CONTRIBUTION

<http://www.lebanesemedicaljournal.org/articles/62-4/review1.pdf>

George F. ARAJ¹, Youmna MOURAD¹

Araj GF, Mourad Y. Hydatid disease: the Lebanese contribution. *J Med Liban* 2014 ; 62 (4) : 217-226.

ABSTRACT • Hydatid disease (HD) or cystic echinococcosis (CE) has been an important zoonotic disease causing medical, economic and public health problems in many parts of the world, including South America, North Africa, Turkey, and Middle Eastern countries. Humans as well as animals, primarily sheep and cattle, are infected by the ingestion of food, usually leafy vegetables, contaminated with the eggs (oncospheres) of the dog tapeworm *Echinococcus granulosus*. Hydatid cysts, which are the larval stage of the parasite, are located mostly in the liver and lungs of the infected host. Because of its chronic endemicity in Lebanon and neighboring countries, this disease has constituted an integral part of research studies conducted by medical doctors and researchers in Lebanon, mostly spearheaded by those at the American University of Beirut (AUB) and its medical center (AUBMC) since the early turn of the last century (1920s). Over 130 wide ranging studies were published; some were innovative e.g. the introduction of the once famous Indirect Haemagglutination (IHA) test for serodiagnosis, and the use of dilute cetrimide as a protoscolicidal agent during surgery. Although the incidence of HD is decreasing in our country, it has acquired increasing public health concern and is considered as an emerging or re-emerging disease in many parts of the world. In this review, we shed light on the numerous studies/publications done in Lebanon as a tribute to those researchers who have impacted the literature of HD in many aspects. The latter include epidemiology and ways of transmission, clinical features and radiological tools for diagnosis, serodiagnosis and immunology, and investigation of different therapeutic modalities for different aspects of the disease. Moreover, consolidating these studies in this review would hopefully represent the historic foundation for interested researchers and investigators, especially in this country, to pursue and build on such studies. The advances in technology, and the availability and utilization of new methodologies will hopefully help find more reliable and efficient ways for the diagnosis, and management of this disease.

Keywords : hydatid disease, Lebanon, echinococcosis, *Echinococcus granulosus*

INTRODUCTION

As a prelude to the contribution of Lebanese researches to hydatid disease (HD) or cystic echinococcosis (CE), an overall refreshing brief summary about this disease is warranted, primarily referring to a couple of publi-

¹Department of Pathology & Laboratory Medicine, American University of Beirut Medical Center, Beirut, Lebanon.

Correspondance: George F. Araj, PhD.
e-mail: garaj@aub.edu.lb

Araj GF, Mourad Y. La contribution libanaise à la maladie hydatique. *J Med Liban* 2014 ; 62 (4) : 217-226.

RÉSUMÉ • La maladie hydatique ou l'échinococcose kystique est une maladie zoonotique causant des problèmes médicaux, économiques et de santé publique dans différentes parties du monde, y compris l'Amérique du Sud, l'Afrique du Nord, la Turquie et les pays du Moyen-Orient. Les hommes aussi bien que les animaux, surtout les moutons et les chiens, sont infectés suite à l'ingestion de légumes feuilles, contaminés par les œufs (oncosphères) de l'*Echinococcus granulosus*. Les kystes hydatiques, qui sont l'étape larvaire du parasite, sont surtout localisés dans le foie et les poumons de l'hôte infecté. Du fait de son endémicité chronique au Liban et dans les pays voisins, cette maladie a longtemps été au cœur des recherches effectuées par des médecins et chercheurs au Liban, surtout ceux de l'Université américaine de Beyrouth (AUB) et son centre médical (AUBMC). Dès le début du siècle dernier, dans les années 20, plus de 130 études ont été publiées ; certaines étaient novatrices, comme par exemple l'introduction du célèbre test d'hémagglutination indirecte pour le sérodiagnostic et l'utilisation de cétrimide dilué comme agent protoscolicide au cours de la chirurgie. Bien que l'incidence de la maladie hydatique soit en décroissance au Liban, elle est considérée comme un problème de santé publique ; c'est aussi une maladie émergente ou ré-émergente dans plusieurs parties du monde. Dans cette revue des nombreuses études et/ou publications réalisées au Liban nous rendons hommage à ces chercheurs et à l'impact de leurs travaux dans la connaissance de plusieurs aspects de la maladie hydatique. Ces derniers incluent l'épidémiologie, les moyens de transmission, les caractéristiques cliniques, radiologiques, sérologiques, et immunologiques nécessaires pour le diagnostic ainsi que les investigations de différentes modalités thérapeutiques. La compilation de ces études constitue une référence de base pour les chercheurs et enquêteurs intéressés à poursuivre des recherches sur ce sujet, en particulier au Liban. Les avancés technologiques ainsi que la disponibilité et l'utilisation de nouvelles méthodologies aideront probablement à trouver des moyens plus fiables et efficaces pour le diagnostic, le traitement et le contrôle de cette maladie.

cations: one regional and the other international [1-2].

Globally, HD is caused by several *Echinococcus* spp. (cestodal tapeworm). In Lebanon and in the Middle East, however, it is caused by *E. granulosus*, the adult worm of which inhabits the dog's intestine. Ingestion of food or water contaminated by eggs shed in feces from infected dogs can infect humans and a wide range of animals including sheep, cattle, horses, and canines. The eggs develop into embryos within the human intestine. Subsequently, they travel through major blood vessels to different body sites/organs primarily the liver and/or lungs.

The embryos begin to form cysts within the infected organs causing damage as they enlarge over many years or decades. Hydatid cysts contain a germinal layer that allows asexual budding to form daughter cysts (protoscoleces) within the primary cyst.

The symptoms of HD is primarily due to the pressure/damage exerted by the enlarging cyst on the adjacent sites e.g. obstruction of blood vessels, lymphatics, and/or bile ducts. Moreover, leakage of fluid (containing antigens) from the cyst by either spontaneous or accidental rupture of the cyst, can result in a spectrum of immunologic reactions ranging from asthma and membranous nephropathy to potentially severe, life-threatening anaphylaxis.

Diagnosis of CE is carried out by different methodologies: imaging, serology, histopathology and nucleic acid detection assays.

Treatment of HD is primarily based on surgical removal of the cyst, followed by therapy with albendazole for 1 to 5 months.

This review is intended to shed light on the numerous studies/publications done in Lebanon on hydatid disease in a consolidated presentation. Moreover, reflecting on these overall scientific contributions is intended to be a tribute to those researchers in this country who have impacted the literature of HD. It is also anticipated that consolidating these studies in this review would represent historic foundation for interested researchers and investigators, especially in this country, to pursue and build on such studies. The advances in technology, and the availability and utilization of new methodology will hopefully help find more reliable and efficient ways for the diagnosis, treatment and control of this disease.

MATERIALS & METHODS

The gathering of information pertaining to this review relied on several search sources. These included Pubmed, Medline and the Lebanese corner at Saab Medical Library search using “cystic echinococcosis,” “hydatid” combined with “epidemiology,” “diagnosis,” “treatment,”

“radiology,” “immunology,” “prevention” and “Lebanon” as keywords. Additional articles were obtained by contacting specific Lebanese authors who were pioneers in this field. We also contacted the librarian at Saint-Joseph University, Faculty of Medicine, in order to search for any thesis or non published article on this subject by their students and doctors.

We found 134 Lebanese studies/publications done in Lebanon about hydatidosis including original research studies, case reports, reviews, theses, and a book.

RESULTS

I. GENERAL ASPECTS OF THE LEBANESE CONTRIBUTION TO HYDATID DISEASE

The numerous studies/publications done on hydatid disease in Lebanon have impacted the literature of this disease in many aspects. The latter include epidemiology and ways of transmission, clinical features, radiological tools for diagnosis, serodiagnosis and immunology, and investigation of different therapeutic modalities for different aspects of the disease. Although several authors from Lebanon published general information on hydatid disease in adults and children [3-9] this consolidated review is set to present the overall 134 studies under the aforementioned categories as noted below.

II. EPIDEMIOLOGY

WAYS OF TRANSMISSION

In Lebanon, HD is not an obligatory reportable disease; that's why official statistics are lacking. Most of the studies on the prevalence of this disease were based on hospital medical records review. They started during the early part of the last century [6, 10-16]. An estimated 3.82 cases per 100,000 population was reported [11]. A change in gender prevalence between males and females was reported. In 1965, no gender difference was reported by Abou-Daoud KT [13], while a higher rates in females was reported by Frayha G *et al.* [16]. The highest rates occurring between ages 20 and 60, with a predominance

TABLE I LEBANESE CONTRIBUTION TO LOCALIZED ORGAN INVOLVEMENT

Location involvement	Study aspects/Authors	References
Hepatic (most involved 45%-50%)	Description of localization in lobes (77% in right), dissemination, complication upon rupture, risk of infection and bacterial types, mostly reported by Daher M (87 cases) & Haddad MC.	[24-30]
Pulmonary 2 nd most involved 30%-35%)	Reviews and large case series by Haddad S, Srouji (62 cases), Dahan (70 cases), Saade (512 cases), Aubert (8384 cases), mostly unilateral (70%), and 21% in children.	[23, 31-36]
Skeletal (vertebral, spine)	Several case series of vertebral and extra vertebral, spine involvement as primary hydatidosis, confused with malignancy, has unfavorable prognosis, mostly reported by Murray R & Haddad F, Bulos S & Nasser N, Haddad FS & Bitar E.	[37-40]
Brain	Several case series reported about the confusing clinical presentation, challenges and difficulty in diagnosis, recurrences, role of radiologic diagnosis, mostly addressed by Haddad FS.	[41-48]
Cardiac	Mostly appear in adults, affect left heart chamber, misleading presentation, unfavorable prognosis	[22,49-53]
Other body sites	Rare case reports on involvement of pancreas, peritoneum and mesocolon, female pelvis, eye orbit, kidney and thigh muscle.	[54-62]

among Christians (2:1 Christians to Moslems); the highest rates were found in the Mohafazat of Beirut and Mount Lebanon, and were more common among dog owners. No preference was observed among different social classes [11-12,16].

Concerning animals, the incidence of *Echinococcus granulosus* was reported as: 20%-33% in dogs (carry the adult worm), 41.5% in cows, 45% in cattle, 6.6%- 22.1% in sheep and goats (all these are intermediate hosts that carry the larval form, like humans) [10, 16-18]. Others, also published about animal infections of hydatid disease in Lebanon and Syria [19-20].

Concerning prevention of HD in Lebanon, a prophylactic program was published by Joseph Asmar in 1958 [21]. It included education of citizens, reduction of canine pets, better conditions in abattoirs, and good cooperation with regional countries to eradicate the disease.

III. LOCALIZED ORGAN INVOLVEMENT

Organ involvement by hydatid cysts have been reported by several authors with emphasis on liver and lung [6, 22-23]. Though liver (45-50%) and lungs (30-35%) are the main involved organs in humans, the infection can affect also a wide range of organs: kidneys (5.8%), spleen (4.7%), soft tissues (3.5%), and peritoneum (2.7%) in addition to many other rare locations.

Table I lists the studies addressing different organs by Lebanese authors.

IV. RADIOLOGY

Numerous studies were generated by many Lebanese authors on radiologic description and aspects of hydatid disease since 1958, see Table II. They reported on a variety of imaging features that vary according to growth stage, associated complications, affected organs, cyst findings

TABLE II LEBANESE CONTRIBUTION TO RADIOLOGY IN HYDATID DISEASE

METHODS	Study aspects	Authors/References
RADIOGRAPHY		
Bronchography	Follow-up of some pulmonary hydatidosis cases treated by internal suture of the pericyst to look for either residual cavitation or localized bronchiectasis.	Srouji M et al. 1958 [23]
Conventional radiography	For liver hydatidosis, replaced by US and CT scan	Rizk G et al. 1971 [63]
Angiography	For diagnosing and localizing liver and spleen hydatid cysts	Rizk G et al. 1971 [63]
Plain chest radiography	Screening for pulmonary hydatidosis	Saksouk F et al. 1980 [64]
Melography	An old invasive procedure for spinal hydatidosis but contraindicated because the risk of disseminating the disease intradurally	Fahl M et al. 1994 [65]
Spinal radiography	Nonspecific for spinal hydatidosis and may show bone destruction and sometimes abnormal soft tissue masses in the paravertebral regions	Fahl M et al. 1994 [65]
ULTRASONOGRAPHY		
Abdominal	It confirms the presence of hydatid lesions in the abdomen mainly the liver as well as the internal structure of the cyst and distinguishes simple, calcified and infected hydatid cysts from other fluid filled lesions	Saksouk F et al. 1980 [64] Haddad M 1999 [9, 66] Haddad M et al. 2001 [27-28, 67] Naffaa L et al. 2003 [68]
Echocardiography	Coupled with CT scan to diagnose cardiac hydatidosis	Maalouf J et al. 1985 [69] Tedy G et al. 1995 [53].
Echoguided percutaneous treatment	Image-guided treatment of complex hepatic hydatid cyst.	Haddad MC et al. 2000 [70] Haddad MC et al. 2001 [67]
COMPUTED TOMOGRAPHY		
Cerebral	For intracerebral and extradural intracranial hydatid cysts.	Baassiri A & Haddad FS 1984 [45]
Thoracic	For pulmonary hydatid cysts.	Saksouk F et al. 1986 [71]
Spinal	Shows clearly the bony destructive changes as well as the paraspinal soft tissue involvement	Fahl M et al. 1994 [65]
MAGNETIC RESONANCE IMAGING		
Spinal	It demonstrates the cysts and their extent in the spinal and paraspinal spaces/canal	Fahl M et al. 1994 [65] Haddad M et al. 2001 [67]
Abdominal	Hydatid cyst of the pancreas	Haddad M 2003 [55]
Functional MRI using DW & MRS	For differentiating parasitic from non parasitic cysts	Haddad M et al. 2011 [72]
US: ultrasonography CT: computed tomography MRI: magnetic resonance imaging DW: diffusion weighted.....MRS: proton MR spectroscopy		

and pre-/postoperative assessment of disease. As noted in Table II, different radiologic methodologies were applied including chest radiography, ultrasonography (US), echocardiography, angiography, computed tomography (CT) and magnetic resonance (MR) imaging.

All authors concluded that the simultaneous reliance on radiologic and serologic findings can generally help establish the diagnosis of hydatid disease. Sometimes, a hydatid cyst in an unusual location with atypical imaging findings may complicate the differential diagnosis. Nevertheless, familiarity with imaging findings, especially in patients living in endemic regions, is advantageous in this context.

V. SEROLOGIC AND IMMUNOLOGIC STUDIES

Serodiagnosis is one of the most studied aspects in hydatid disease in Lebanon, reflected in more than 20 published articles, primarily lead by Garabed Garabedian, and Robert Matossian (Table III). Most clinically relevant was the introduction of a new sensitive and specific Indirect Hemagglutination (IHA) test by Garabedian G that is still used today in our routine laboratories.

The immunologic and serologic studies are presented under different categories as shown in Table III.

VI. TREATMENT OPTIONS FOR HYDATOSIS

➤ Experimental approaches in search for anti-hydatid agents

Several studies from AUB targeted revealing the interaction of *E. granulosus* ova with the environment as well as the different aspects of hydatid cell wall and cyst metabolism. Berberian D 1936 and 1957 [104-105] demonstrated the susceptibility of cement substance around ova of *E. granulosus* to alkaline but not acidic conditions. This explained why the ovum passes unaffected through the stomach to the duodenum where the oncosphere (embryo) is liberated.

Schwabe C and colleagues [106-111], as of 1959, carried out several in vitro and in vivo experiments about the cell wall permeability regulation, metabolic, immunologic, therapeutic aspects, and the inhibitory role of acetylcholinesterase.

Kilejian A *et al.* [112-113] studied the distribution of glycogen, acid and alkaline phosphatases, and DNA in both the larval and adult stages of *E. granulosus*, as well as the characteristic of lecithin and cholesterol on hydatid cyst tissues.

Meymerian E and Schwabe C 1962 [114] studied the resistance of the ova of *E. granulosus* to germicides.

TABLE III LEBANESE AUTHORS CONTRIBUTION TO SEROLOGIC AND IMMUNOLOGIC ASPECTS OF HYDATID DISEASE (HD)

CONTRIBUTION TO SEROLOGY & IMMUNOLOGY ASPECTS	Authors/References
Presentation and assessment of different hydatid antigens for use in different serologic tests Different types of antigenic preparations (Crude hydatid fluid filtered, nonfiltered; Purified fluid or extracts of scolices; and Cyst fluid fractions) were studied and compared for the best yield in IHA and complement fixation (CF) tests.	Turner E <i>et al.</i> 1935; Emery D 1937 Hariri M <i>et al.</i> 1965; Garabedian G 1971 Garabedian G & Zekian-Arslanian B 1976 [73-77]
Garabedian first introduction of indirect haemagglutination (IHA) test for the serodiagnosis of hydatid disease It used RBC treated with tannic acid and coated with hydatid antigen and proved high reliability.	Garabedian G <i>et al.</i> 1957; 1957; 1959; 1960 [78-81]
Modifications in Garabedian's method Using pyrovic aldehyde and chrome chloride for coating of antigen and prolonging activity of reagents	Matossian R & Kane G 1971; Mamo 1974 Matossian R <i>et al.</i> 1976 [82-84]
Evaluation of different techniques/tests Looking for the most reliable diagnosis of HD especially in relation to liver and pulmonary involvement.	Matossian R <i>et al.</i> 1979 Matossian R 1981; 1990 [85-87]
Humoral immunity in humans and mice Determination of total and specific immunoglobulins (IgG, IgM, IgA, IgE) and assessment of their sequential evolution and role versus cyst development, and as relates to hepatic and pulmonary involvement.	Kane G <i>et al.</i> 1971; Matossian R <i>et al.</i> 1972 Matossian R & Araj G 1975; Araj G <i>et al.</i> 1977 Matossian R <i>et al.</i> 1976; Matossian R 1977 Haddad E 1990 [88-94]
Serologic follow-up and prognostic values Different tests were used to assess the evolution of antibody detection in humans post-surgery or after medical treatment with albendazole.	Matossian R & Araj G 1975; Kanaan S 1984 Awar G <i>et al.</i> 1991; Matossian R 1992 Matossian R <i>et al.</i> 1992. [90, 95-97]
Cell mediated immunity (CMI) Studying sequential evolution/response of CMI post infection in mice.	Araj G <i>et al.</i> 1976 [98]
Cytology to diagnose pulmonary hydatidosis	Tomb J, Matossian R 1976 [99]
Immunization approaches In search of protection from HD infection.	Turner E <i>et al.</i> 1933; 1936 Araj G <i>et al.</i> 1976 [98, 100-102]
Study immunologic aspects & HLA genetic association among HD patients from different Lebanese sects	Kanaan S 1984 [95]
Update on laboratory diagnosis of HD	Araj G 2003 [103]

Frayha G in 1968 [115-116] revealed the de novo synthesis of cholesterol present in the hydatid cyst wall, effect of sex hormone on the growth of the cyst in albino mice.

On another aspect, Rickard M *et al.* 1977 [117] studied the effect of normal serum on protoscoleces and the involvement of the alternate complement pathway in the lysis of these protoscoleces.

➤ **Management of hepatic and abdominal cysts**

Several studies pertaining to hydatid disease therapy have been published by Lebanese authors starting as early as 1940.

To facilitate clarification of these contributions to therapy of hydatid disease, the WHO 2010 classification will be adopted incorporating the Lebanese studies accordingly.

The WHO guidelines are based on image and stage specific approach, which is helpful for choosing one of the following therapeutic options: Surgery (open and laparoscopic surgery) to remove cysts completely; Percutaneous treatment [PAIR (puncture, aspiration, injection, re-aspiration) technique and the PEVAC (percutaneous evacuation) technique]; Anti-infective drug therapy benzimidazole based (BMZ); and finally, Watch and wait approach.

1. Surgery

Open surgery was the only treatment available for hydatid disease before the 1990's [72, 118-119]. With the availability of effective chemotherapy, percutaneous treatment and laparoscopy became the mainstay in the treatment of non complicated and accessible abdominal hydatid cysts more than 5 cm in size [72].

a. Open surgery

In 1940, Haddad S and Khairallah A [120] were the first to publish about the surgical excision of hydatid cyst and its management. In the 1950s onward Jidejian Y [6, 118, 121-122] spearheaded the studies on HD by publishing several articles describing different surgical techniques according to the location of the hydatid cysts. Later on, he edited a landmark book covering his own surgical experience and other aspects of hydatid disease [6]. In 1971, Haddad FS [123] described a new simple surgical procedure for the removal of hepatic hydatid cysts without opening the cysts and spilling their content into the surrounding tissues.

b. Laparoscopy

The first laparoscopic excision of a hepatic hydatid cyst in Lebanon was reported by Khoury G *et al.* at AUBMC in 1994 [124]. Thereafter, other Lebanese surgeons used this surgical technique for the excision of hydatid cysts from liver and spleen with successful follow-up and outcome [125-126].

c. Surgical complications

The risks of the open, percutaneous or laparoscopic surgical methods include those associated with any surgical intervention, anaphylactic reactions, and secondary cystic echinococcus (CE) due to spillage of viable para-

site material. A couple of publications on such complications and managements were reported [24, 127-129].

To prevent CE due to spillage of viable parasites, surgeons have been using cetrimide (see below, under anti-parasitic drugs) as a key protoscolicidal agent, injected into the cyst prior to its excision [72, 130-131].

d. Liver transplantation

Liver transplantation, which is only rarely needed, was also performed at the AUBMC for a severe case of multiple hydatid cysts of the liver [132].

2. Percutaneous treatment and complications

In 2000, Haddad M *et al.* [70, 129] reported on the percutaneous approach as a minimally invasive technique used in the treatment of cysts in the liver, or rarely at other abdominal locations. It is indicated for inoperable patients and those who refuse surgery or relapse after surgery. In addition to using cetrimide, percutaneous treatment is always accompanied by adjunctive chemotherapy using albendazole for 3-7 days prior to the procedure and one month after [128].

The main risks associated with the percutaneous treatment are cyst cavity infection, fistulae and rarely anaphylactic shock [72]. One rare and serious complication was a life-threatening liver laceration with arterial hemorrhage reported in 2008 by Loutfi S *et al.* [133].

The analysis of clinico-radiological findings and different therapeutic modalities of 61 patients with HEC was reported by Haddad M *et al.* [27]. They concluded that HEC are best treated by nonsurgical minimally invasive techniques combined with adjuvant antihelminthic chemotherapy, while surgery should be reserved for complicated HEC by intraperitoneal rupture.

Cystic echinococcosis complicated by rupture into the biliary tree causing biliary obstruction with or without cholangitis is usually treated by endoscopy combined with surgery or percutaneous approach [72].

➤ **Anti-parasitic drugs & Chemotherapy**

1. Protoscolicidal agents

The experimental search for a protoscolicidal agent was carried out by Meymerian E *et al.* in 1963 [130]. They were the first to introduce the use of an effective and safe cetrimide (cethyl-trimethyl-ammonium-bromide) as a protoscolicidal agent during surgery of hydatidosis to prevent viable protoscoleces from forming secondary hydatidosis. This was demonstrated and concluded after investigating several agents e.g. alcohol, formalin and hypertonic saline solutions, sodium hypochlorite, hydrogen peroxide, iodine and cetrimide. In Lebanon, most surgeons still use cetrimide solution at 0.1%-0.5% for injecting the cysts before surgical excision. Some, however, use 20% hypertonic saline as recommended by the WHO-OIE, 2001 [72].

2. Agents for systemic use

During late 1960s and early 1970s, Frayha G led with collaborators [4, 115-116, 131, 134] the continued search for systemic hydatid agents (through screening 64 chemicals, 13 exhibited high activity) by studying the meta-

bolic aspect of the parasite. They noted that acetate (feric and cupric acetylacetonate) was incorporated into the lipids of *E. granulosus* displaying effective scolical activity after 10 min of exposure. These studied chemicals were organic and thus amenable to structural modifications, leading the way to developing drugs useful in systemic treatment and prophylaxis of hydatid disease. Today, the benzimidazoles (BMZ) such as albendazole and mebendazole (high dose) are commonly used for the medical therapy of echinococcosis, often as supplementary therapy with either surgery or percutaneous treatments [72].

Schantz P and Nassar N 1982 [135] published about chemotherapy for hydatidosis in animals and humans. Nassar N in 1987 [136] presented the AUBMC experience and the data on 41 patients with inoperable HEC over a six-year period. The results presented in this paper provide strong support in favor of medical treatment with an expected overall success rate of 70% in an otherwise inoperable patient group.

3. Watch and wait approach

Some asymptomatic cysts are discovered incidentally on imaging examinations. These cysts do not require any treatment if uncomplicated or inactive and cysts may undergo spontaneous degeneration [72].

➤ Management of cysts in extra-hepatic sites and specific situations

Several publications addressed management of infection in different body sites:

1. Lung

For pulmonary echinococcosis, there is no uniform recommended treatment. BMZ's are mainly used for small, uncomplicated lung cysts. However, surgery and radical procedures are needed for extended parenchymal involvement.

Shabb *et al.* in 1995 [137], and Taha *et al.* in 1996 [138] published about surgical treatment of pulmonary hydatidosis. They reported on postoperative complications. They studied 53 patients treated surgically over a period of 10 years who underwent different procedures including evacuation after chemical sterilization, imbrication, marsupialization, lobectomy and segmentectomy. Both imbrication and marsupialization were found to be equally effective methods for treatment of pulmonary hydatid cysts. Anatomic resection was rarely required.

Other surgical techniques were also reported by Lebanese authors. For example, Srouji M *et al.* 1958 [23] described a treatment option for pulmonary hydatidosis by internal suturing of the pericyst after careful removal of the parasite. In 1963, Yacoubian and Dajani [139] described a new technique of handling the pericyst space after removal of a hydatid cyst of the lung. The technique was applicable to both intact and ruptured cysts and does not compromise normal lung tissue and therefore gives good functional results. Thoracoscopy was used by Shabb B *et al.* to successfully treated two cases of infected pulmonary hydatid cysts. [137].

2. Bone

Hydatidosis of the bone is the most difficult form of cystic echinococcosis to treat due to multiple recurrences and complications [37-38, 40, 43, 140]. Radical resection of the affected bone is the most effective treatment but rarely feasible. Multiple recurrences with repeated surgical procedures and a high risk of serious complications such as spinal involvement, fistulae, acute and chronic osteomyelitis is a very common scenario.

3. Heart

For heart echinococcosis, surgery is the treatment of choice. Venous filters are used to prevent dissemination, if complete removal of the cyst is impossible. In most cases, and after surgical healing, the prognosis is good with a low rate of recurrence [22, 51, 69]. Ghanem *et al.* reported on hydatid cyst affecting ventricles [50].

4. Pancreas

Pancreatic hydatid cysts are also best treated surgically regardless of their location. The recurrence rate has been reported to be around 10%. For this reason, long-term follow-up is recommended and medical therapy with BMZ's is needed in most cases too. Faraj W *et al.* in 2006 [56] used the laparoscopic technique to excise pancreatic hydatid cysts.

5. Brain

Haddad FS pioneered the neurosurgery in this location since 1950s, and reported that brain hydatidosis is best treated surgically and cysts should be best removed intact to avoid recurrence or anaphylaxis [42-44, 141]. Najjar M *et al.* in 2007 [44] reported one case and Fares Y *et al.* in 2011 [46] reported 9 cases of successfully managed brain hydatidosis.

A review on the management of hydatid cyst of the brain was published by Haddad GF & Haddad FS in 2000 [141].

CONCLUSION

The Lebanese scientific contribution to hydatid disease started at the turn of the last century. Despite political turmoils, their activities in addressing different aspects of this disease has been sustained till to date, warranting deserving recognition. The numerous studies and investigations carried out on this disease by the Lebanese scientists covered a wide spectrum of disciplines including epidemiology, clinical features, radiological tools for diagnosis, serodiagnosis and immunology, and investigation of different therapeutic modalities for different aspects and/or sites of the disease.

Consolidating these studies in this review reflects not only a tribute and recognition to those Lebanese scientists, but also represents the historic foundation for interested researchers and investigators, especially in this country, to pursue and build on such foundations. The advances in technology, and the availability and utilization of new methodologies will hopefully help find more reliable and efficient ways for the diagnosis, treatment, and control of this disease.

ACKNOWLEDGMENTS

The authors are grateful to Drs. George Frayha, Michel Daher, Fouad S. Haddad and Maurice C. Haddad for their valuable and constructive comments.

REFERENCES

- Seimenis A. Overview of the epidemiological situation on echinococcosis in the Mediterranean region. *Acta Tropica* 2003; 85: 191-5.
- Moro P, Schantz P. Echinococcosis: a review. *Intl J Infect Dis* 2009; 13: 125-33.
- Khoury M. Kystes hydatiques au Liban. *J Med Liban* 1962; 15: 377-89.
- Frayha G. Studies on hydatid disease in Lebanon. *J Med Liban* 1970; 23: 135-50.
- Slim M, Jidejian Y, Khayat G, Nasr A. Hydatid disease in childhood. *J Pediatr Surg* 1971; 6: 440-8.
- Jidejian Y. *Hydatid Disease*, 1st ed, Beirut: Catholic University Press, 1979.
- Matossian R, Rickard M, Smyth J. Hydatidosis: a global problem of increasing importance. *Bull World Health Organ* 1977; 55: 499-507.
- Fuleihan F. Hydatid disease. *Med Educ (Int)* 1982; 1: 1043-4.
- Haddad M, Abu Fakher F, Al Awar G, Al Awar O, El Hajj I, Hajjar B. Hydatid disease. *J Med Liban* 1999; 47: 243-5.
- Turner E. The incidence of hydatid disease in Syria. *Trans R Soc Trop Med Hyg* 1936; 30: 225-8.
- Schwabe C, Abou Daoud K. Epidemiology of echinococcosis in the Middle East: Human infection in Lebanon, 1949 to 1959. *Am J Trop Med Hyg* 1961; 10: 374-81.
- Abou-Daoud K, Schwabe W. Epidemiology of echinococcosis in the Middle East. 3. A study of hydatid disease patients from the city of Beirut. *Am J Trop Med Hyg* 1964; 13: 681-5.
- Abou-Daoud KT. The epidemiology of hydatid disease in Lebanon. *J Med Liban* 1965; 18: 159-68.
- Luttermoser G, Koussa M. Epidemiology of echinococcosis in the Middle East: Incidence of hydatid infection in swine in Lebanon and its significance. *Am J Trop Med Hyg* 1963; 12: 22-5.
- Awn J. Hydatid disease in Lebanon as reflected by some Lebanese hospitals. A thesis presented in partial fulfillment of the requirements for the degree of Master of Science, Department of Microbiology, American University of Beirut, Beirut, Lebanon, May 1986.
- Frayha G, Awn J, Nabbut N. Hydatid disease in Lebanon: its prevalence during the last 25 years. *Leb Sci Bull* 1989; 5: 53-64.
- Goodale R, Krischner H. Biological tests for hydatid disease: A comparison of the Casoni and Weinberg tests. *Am J Trop Med* 1930; 10: 71-6.
- Pipkin A, Rizk E, Balikian G. Echinococcosis in the Near East and its incidence in animal hosts. *Trans Roy Soc Trop Med Hyg* 1951; 45: 253-60.
- Dailey M, Sweatman G. The taxonomy of *Echinococcus granulosus* in the donkey and dromedary in Lebanon and Syria. *Ann Trop Med Parasitol* 1965; 59: 463-7.
- Dailey M, Schacher J, Sweatman G. Animal reservoirs of hydatid disease (*Echinococcus granulosus*) in Lebanon and Syria with a review of the world literature on *E. granulosus* infections in foxes. *J Med Liban* 1966; 19: 225-34.
- Asmar J. Echinococcosis in Lebanon: Measures for the prevention of echinococcosis in Lebanon. *Rev Med Moyen Orient* 1958; 15: 216-21.
- Kurban A, Attar S, Dragatsi G, Shafik A. Echinococcosis of the heart. *Am Heart J* 1953; 46: 764-71.
- Srouji M, Mulhim R, Wilson J. Hydatid cyst of the lung with bronchographic evaluation of treatment by internal suture of the pericyst. *J Thorac Surg* 1958; 35: 779-94.
- Dagher I, Hovnanian A. Intra-biliary rupture of hydatid cyst of the liver. *Ann Surg* 1955; 141: 263-67.
- Matossian R. Hydatid cyst of the liver. *Helminthologia* 1986; 23: 283-94.
- Daher M, Abi-Akl A, Rassi Z, Souraty P, el-Khazen M, Khalife P. Diagnosis and treatment of hydatid cysts of the liver. Apropos of 87 cases operated on between 1980 and 1992. *J Med Liban* 1996; 44: 121-8.
- Haddad M, Awar G, Huwajjah S, Al-Kutoubi A. Echinococcal cysts of the liver: a retrospective analysis of clinicoradiological findings and different therapeutic modalities. *Clin Imaging* 2001a; 25: 403-8.
- Haddad M, Al-Awar G, Sammak B et al. Echinococcal cysts of the liver: Epidemiology, imaging classification, diagnosis and management. *J Med Liban* 2001b; 49: 146-56.
- Farah M, Atallah N, Gedeon E, Khoury N, Chemali A, Yared B. Sclerosing cholangitis secondary to fistulisation of hepatic hydatid cysts into the biliary tree: presentation of 6 cases. Pathogenic considerations and proposal for an operative protocol. *J Med Liban* 1987; 37: 16-25.
- Matossian R, Najjar F. Suppurative salmonellosis in human hepatic hydatid cysts. *Ann Trop Med Parasitol* 1968; 62: 143-6.
- Haddad S. Hydatid disease of the lungs. *Orient Hosp Annu Rep* 1948; 1: 49-53.
- Dahan E. A propos de 70 opérés de kystes hydatiques pulmonaires: Intérêt des examens de laboratoire. *J Med Liban* 1962; 15: 401-4.
- Saadé B, Ashoush R, Chiniara S. Réflexion à propos de cinq cent douze cas de kystes hydatiques du poumon. *Ann Chir* 1983; 37: 92-4.
- Aubert M, Viard P. Étude statistique sur l'hydatidose pleuro-pulmonaire dans le bassin méditerranéen en 1982: à propos de 8384 cas. *Ann Chir* 1983; 37: 74-7.
- Nahas H. An unusual case of pulmonary hydatid cyst. *J Med Liban* 1962; 15: 396-400.
- Balikian J, Dagher I, Idriss I. Hydatid tension pneumothorax: report of a case. *J Med Liban* 1974; 27: 551-6.
- Bulos S, Nassar N. Hydatid disease of the spine. *Arab J Med* 1985; 4: 8-12.
- Fares Y, Khazim R, El Zaatari MM, Haddad GF, Barnes PR. Spinal hydatid disease and its neurological complications. *Scand J Infect Dis* 2003; 35: 394-6.
- Murray RO, Haddad FS. Hydatid disease of the spine. *J Bone Joint Surg [Br]* 1959; 41B: 499-506.
- Haddad FS, Bitar E. Primary hydatid disease of the spine: report of 14 cases and review of the literature. *Pan Arab Journal of Neurosurgery* 1997; 1: 46-52.
- Goodale R. Hydatid cyst of the brain. *Am J Trop Med* 1931; 11: 61-4.
- Haddad FS. Hydatid disease of the brain: some considerations of its recurrence. *Arch Int Hidatid* 1957; 16: 445-7.
- Haddad FS, Haddad GF. Overview of brain hydatid and

- its surgical management: personal experience with cyst delivery. *Pan Arab J Neurosurgery* 2003; 7: 33-41.
44. Haddad FS, Haddad GF. Hydatid disease of the central nervous system. Personal experience: Its appearance, management, and outcome in the brain and the spine. *Neurosurg Q* 2005; 15: 33-41.
 45. Baassiri A, Haddad FS. Primary extradural intracranial hydatid disease: CT appearance. *Am J Neuroradiol* 1984; 5: 474-5.
 46. Najjar M, Rajab Y, El-Beheiri Y. Intracranial hydatid cyst. Dilemma in diagnosis and management. *Neurosciences (Riyadh)* 2007; 12: 249-52.
 47. Kanj A, Fares Y, Yehya R, Hamzeh F. Unusual appearance of a cerebral hydatid cyst as a hemorrhagic infarct. *Neurosciences (Riyadh)* 2010; 15: 275-6.
 48. Fares Y, El-Zaatari M, Haddad G, Kanj A. Cerebral hydatid cyst: Successfully managed. *Pan Arab J Neurosurg* 2011; 15: 9-11.
 49. Abdel Razek M, Nassif S, Rizk G, Slim M. Hydatid cysts of the heart and liver in a child: case report and review of the literature. *Z Kinderchir Grenzgeb* 1975; 16: 273-81.
 50. Ghanem E, Khoury J, Hatem J. Kyste hydatique du ventricule droit. *Archives de Maladies du Cœur et des Vaisseaux* 1991; 84: 865-7.
 51. Shukri R, Melhem R. Intracardiac hydatid cyst: Concise communication. *J Thorac Imaging* 1993; 8: 79-80.
 52. Sarkis A, Ashoush R, Alawi A, Haddad A, Jebara V, Checrallah E. Hydatid cyst of the heart simulating coronary ischemia. *Ann Cardiol Angeiol (Paris)* 2001; 50: 206-10.
 53. Tedy G, Maamari S, Khoury J, Heraoui E et al. Pericardial hydatid cysts. Value of magnetic resonance imaging. A propos of a clinical case. *Ann Cardiol Angeiol (Paris)* 1995; 44: 280-3.
 54. Serhal S, Mestiri S, Sebai F. Kyste hydatique du pancréas: à propos de 3 observations. *J Chir* 1987; 124: 542-4.
 55. Haddad M. Hydatid cyst of the pancreas as a cause of pancreatic cystic lesions. *Am J Roentgenol* 2003; 18: 885-6.
 56. Faraj W, Selmo F, Khalifeh M, Jamali F. Laparoscopic resection of pancreatic hydatid disease. *Surgery* 2006; 139: 438-41.
 57. Hannouch D, Hakime H. Kystes hydatique des mesos (à propos de 3 cas). *J Med Liban* 1964 ; 17: 421-7.
 58. Bickers W. Hydatid disease of the female pelvis. *Am J Obstet Gynecol* 1970; 107: 477-83.
 59. Baghdassarian S, Zakhariya H. Report of three cases of hydatid cyst of the orbit. *Am J Ophthalmol* 1971; 71: 1081-4.
 60. Haines G. Echinococcal cyst of the kidney. *J Urol* 1977; 117: 788-9.
 61. Abi Saad G, Musallam K, Korban Z, Reslan O, Mneimne M. Solitary hydatid cyst of the thigh: A challenging diagnosis. *Vector Borne Zoonotic Dis* 2009; 9: 743-5.
 62. Wani RA, Wani I, Malik AA, Parray FQ, Wani AA, Dar AM. Hydatid disease at unusual sites. *J Case Reports and Images* 2012; 3:1-6.
 63. Rizk G, Tayyarah K, Ghandur-Mnaymneh L. The angiographic changes in hydatid cysts of the liver and spleen. *Radiology* 1971; 99: 303-9.
 64. Saksouk F, Rizk G, Ghassan K, Tu'meh S. Ultrasonography of liver hydatid cysts. *J Med Liban* 1980; 31: 103-23.
 65. Fahl M, Haddad FS, Huballah M, Kana'an S, Husheimi I, Azizi T. Magnetic resonance imaging in intradural and extradural spinal echinococcosis. *Clin Imaging* 1994; 18: 179-83.
 66. Haddad MC, Sammak BM, Al-Karawi M. Hepatic hydatid cyst with exophytic component: a cautionary sign. *Br J Radiol* 1999; 72: 519.
 67. Haddad M, Birjawi G, Khouzami R, Khoury N, El-Zein Y, Al-Kutoubi A. Unilocular hepatic echinococcal cysts: sonography and computed tomography findings. *Clin Radiol* 2001; 56: 746-50.
 68. Naffaa L, Birjawi G, Mourany B, Rouhana G, Haddad M. Imaging of hepatic cystic lesions. *J Med Liban* 2003; 51: 100-16.
 69. Maalouf J, Alam S, Dagher I, Rizk G, Saksouk F. Hydatid cyst of the heart: Diagnosis by two-dimensional echocardiography and computed tomography. *Am Heart J* 1985; 109: 605-7.
 70. Haddad M, Sammak B, Al-Karawi M. Percutaneous treatment of heterogenous predominantly solid echopattern echinococcal cysts of the liver. *Cardiovasc Interven Radiol* 2000c; 23: 121-5.
 71. Saksouk FA, Fahl MH, Rizk GK. Computed tomography of pulmonary hydatid disease. *J Comput Assist Tomogr* 1986; 10: 226-32.
 72. Haddad M, Awar G, Jalbout R et al. New trends in the management of hepatic *Echinococcus granulosus*. *J Med Liban* 2011; 59: 154-9.
 73. Turner E, Berberian D, Dennis E. The value of the Casoni test in dogs. *J Parasitol* 1935; 21: 180-2.
 74. Emery D. A stable concentrated purified antigen for the immunological study of hydatid disease. *J Parasitol* 1937; 23: 62-7.
 75. Hariri M, Koussa M, Schwabe C. Host-parasite relationships in echinococcosis: The antigen of the indirect hemagglutination test for hydatid disease. *Am J Trop Med Hyg* 1965; 14: 592-604.
 76. Garabedian G. Evaluation of the reactivity of hydatid whole-scolex antigen in hydatid disease serology. *Ann Trop Med Parasitol* 1971; 65: 385-91.
 77. Garabedian G, Zekian-Arslanian B. The influence of Seitz filtration on the activity of hydatid fluid antigen. *Ann Trop Med Parasitol* 1976; 70: 435-7.
 78. Garabedian G, Matossian R, Djanian AY. An indirect hemagglutination test for hydatid disease. *J Med Liban* 1957; 10: 275-82.
 79. Garabedian G, Matossian R, Djanian AY. Serologic diagnosis of hydatid disease by indirect hemagglutination. *J Immunol* 1957; 78: 269-72.
 80. Garabedian G, Matossian R, Suidan F. A correlative study of immunological tests for the diagnosis of hydatid disease. *Am J Trop Med Hyg* 1959; 8: 67-71.
 81. Garabedian G, Malakian A, Matossian R. A simple haemagglutination drop test for human hydatidosis. *Ann Trop Med Parasitol* 1960; 54: 233-5.
 82. Matossian R, Kane G. The use of stable freeze dried erythrocytes as antigens in hydatid diagnosis. *J Med Liban* 1971; 24: 227-30.
 83. Matossian R, Mamo A, Dakroub R. Slide hemagglutination test in hydatid disease: a correlative study of diagnostic procedures. *J Clin Pathol* 1976; 29: 39-41.
 84. Mamo A, Dakroub R. Un test rapide d'hémagglutination indirecte dans le diagnostic de la maladie hydatique. *J Med Liban* 1974; 27: 223-8.
 85. Matossian R, Draper C, McLaren M et al. The serodiag-

- nosis of human hydatid disease: Additional studies on selected sera using indirect haemagglutination (IHA), enzyme linked immunosorbent assay (ELISA) and defined antigen substrate spheres (DASS). *J Helminthol* 1979; 53: 287-91.
86. Matossian R. A simplified radioimmunoassay technique for hydatid disease and human trichinosis. *J Helminthol* 1981; 55: 49-57.
 87. Matossian R. Laboratory and field evaluation of human hydatidosis (larval echinococcosis) in Lebanon: an interim report. *Helminthologia* 1990; 27: 203-10.
 88. Kane G, Matossian R, Batty I. Fluorochrome labelled anti-immunoglobulin fractions used with antigen preparations for the assessment of parasitic diseases. *Ann NY Acad Sciences* 1971; 177: 134-45.
 89. Matossian R, Kane G, Chantler S, Batty I, Sarhadian H. The specific immunoglobulin in hydatid disease. *Immunology* 1972; 22: 423-30.
 90. Matossian R, Araj G. Serologic evidence of the post-operative persistence of hydatid cysts in man. *J Hyg (Lond)* 1975; 75: 333-40.
 91. Matossian R, Alami S, Salti I, Araj G. Serum immunoglobulin levels in human hydatidosis. *Int J Parasitol* 1976; 6: 367-71.
 92. Matossian R. The immunological diagnosis of human hydatid disease. *Trans R Soc Trop Med Hyg* 1977; 71: 101-4.
 93. Araj G, Matossian R, Frayha G. The host response in secondary hydatidosis of mice: Circulating antibodies. *Z Parasitenkd* 1977; 52: 23-30.
 94. Haddad E. Anti-hydatid antibody levels and classes in livestock located in Lebanon. A thesis presented in partial fulfillment of the requirements for the degree of Master of Science, Department of Microbiology, American University of Beirut, Beirut, Lebanon, April 1990.
 95. Kanaan S. Immunological and genetical aspects of patients with hydatid disease in Lebanon. A dissertation submitted to the Faculty of Medical Sciences in partial fulfillment of the requirements for the degree Doctor of Philosophy in Basic Medical Sciences of the American University of Beirut, Beirut, Lebanon, November 1984.
 96. Awar G, Matossian R, Radwan H, Meshefedian G. Monitored medico-surgical approach to the treatment of cystic hydatidosis. *Bull World Health Organ* 1991; 69: 477-82.
 97. Matossian R, Awar G, Radwan H, Craig P, Meshefedian G. Immune status during albendazole therapy for hydatidosis. *Ann Trop Med Parasitol* 1992; 86: 67-75.
 98. Araj G, Matossian R, Malakian A. The host response in secondary hydatidosis of mice: Cell mediated immunity. *Z Parasitenkd* 1977; 52: 31-8.
 99. Tomb J, Matossian R. Diagnosis of pulmonary hydatidosis by sputum cytology. *Johns Hopkins Med J* 1976; 139 (Suppl): 38-40.
 100. Turner E, Berberian D, Dennis E. Successful artificial immunization of dogs against taenia echinococcus. *Proc Soc Exp Biol Med* 1933; 30: 618-19.
 101. Turner E, Berberian D, Dennis E. The production of artificial immunity in dogs against *Echinococcus granulosus*. *J Parasitol* 1936; 22: 14-28.
 102. Turner E, Berberian D, Dennis E. The production of artificial immunity against hydatid disease in sheep. *J Parasitol* 1937; 23: 43-61.
 103. Araj GF. Laboratory diagnosis of hydatid disease. The Lebanese Society of General Surgery, *Surgical News* 2003; 1: 7-9.
 104. Berberian D. Some observations on the effect of digestive juices on scolices of *Echinococcus granulosus*. *J Helminthol* 1936; 14: 21-40.
 105. Berberian D. Host specificity and the effect of digestive juices on ova of *Echinococcus granulosus*. *Orient Hosp Annu Rep* 1957; 10: 33-43.
 106. Schwabe CW. Host-parasite relationships in echinococcosis: observations on the permeability of the hydatid cyst wall. *Am J Trop Med Hyg* 1959; 8: 20-8.
 107. Schwabe CW, Schinazi LA, Kilejian A. Host-parasite relationships in echinococcosis: age resistance to secondary echinococcosis in the white mouse. *Am J Trop Med Hyg* 1959; 8: 29-36.
 108. Farhan I, Schwabe CW, Zobel CR. Host-parasite relationships in echinococcosis: III. Relation of environmental oxygen tension to the metabolism of hydatid scolices. *Am J Trop Med Hyg* 1959; 8: 473-8.
 109. Schwabe CW, Koussa M, Acra AN. Host-parasite relationships in echinococcosis: IV. Acetylcholinesterase and permeability regulation in the hydatid cyst wall. *Comp Biochem Physiol* 1961; 2: 161-72.
 110. Schwabe CW, Koussa M, Hadidian L, . Host-parasite relationships in echinococcosis: IX. In vitro survival of hydatid scolices and the effects of drugs upon scolex respiration. *Am J Trop Med Hyg* 1963; 12: 338-45.
 111. Schwabe CW, Luttermose GW, Koussa M, Ali SR. Serial passage of fertile hydatid cysts of *Echinococcus granulosus* in absence of the definitive host. *J Parasitol* 1964; 50: 260.
 112. Kilejian A, Schinazi LA, Schwabe CW. Host-parasite relationships in echinococcosis. V. Histochemical observations on *Echinococcus granulosus*. *J Parasitol* 1961; 47: 181-8.
 113. Kilejian A, Sauer K, Schwabe CW. Host-parasite relationships in echinococcosis. VIII. Infrared spectra and chemical composition of the hydatid cyst. *Exp Parasitol* 1962; 12: 377-92.
 114. Meymarian E, Schwabe CW. Host-parasite relationships in echinococcosis: VII. Resistance of the ova of *Echinococcus granulosus* to germicides. *Am J Trop Med Hyg* 1962; 11: 360-4.
 115. Frayha G. A study of the synthesis and absorption of cholesterol in hydatid cysts (*Echinococcus granulosus*). *Comp Biochem Physiol* 1968; 27: 875-8.
 116. Frayha G, Dajani R, Lawlor W. *Echinococcus granulosus* in albino mice: effect of host sex and sex hormones on the growth of hydatid cysts. *Exp Parasitol* 1971; 29: 255-62.
 117. Rickard M, Mackinlay L, Kane G, Matossian R, Smyth J. Studies on the mechanism of lysis of *Echinococcus granulosus* protoscolices incubated in normal serum. *J of Helminth* 1977; 51: 221-8.
 118. Jidejian Y. Hydatid disease. *J Med Liban* 1952; 5: 59-63.
 119. Settaf A, Mansori F, Sefrioui A, Slaoui A. Hydatid cysts of the liver. Therapeutic and prognostic classification. *Presse Med* 1994; 23: 362-6.
 120. Haddad S, Khairallah A. Surgical consideration of hydatid disease: report of some unusual cases. *Ann Surg* 1940; 111: 597-604.
 121. Jidejian Y. Hydatid disease. *Surgery* 1953; 34: 155-67.
 122. Jidejian Y. Collective review of hydatid disease. *J Int Coll Surg* 1957; 28: 125-33.

123. Haddad FS. A new simple surgical procedure in the management of celes and cysts. *Orient Hosp Annu Rep* 1971; 24: 21-35.
124. Khoury G, Geagea T, Hajj A, Jabbour-Khoury S, Baraka A, Nabbout G. Laparoscopic treatment of hydatid cysts of the liver. *Surg Endosc* 1994; 8: 1103-4.
125. Khoury G, Bikhazi K, Jabbour-Khoury S. Results of laparoscopic treatment of hydatid cysts of the liver. *Surg Endosc* 1996; 10: 57-9.
126. Khoury G, Abiad F, Geagea T, Nabout G, Jabbour S. Laparoscopic treatment of hydatid cysts of the liver and spleen. *Surg Endosc* 2000 Mar; 14: 243-5.
127. Khoury G, Jabbour-Khoury S, Soueidi A, Nabbout G, Baraka A. Anaphylactic shock complicating laparoscopic treatment of hydatid cysts of the liver. *Surg Endosc* 1998; 12: 452-4.
128. Haddad M, Huwajjah S, Mourad F, Sharara A, Al-Kutoubi A. Adjuvant therapy in the treatment of complications following surgery for hepatic echinococcal cysts. *Cardiovasc Intervent Radiol* 2000; 23: 406-9.
129. Haddad M, Huwajjah S, Al-Kutoubi A. The safe use of cetrimide and hypertonic saline for percutaneous ablation of hepatic echinococcal cysts complicated by intrabiliary rupture. *Cardiovasc Intervent Radiol* 2000; 23: 412-4.
130. Meymerian E, Luttermoser GW, Frayha GJ, Schwabe CW, Prescott B. Host-parasite relationships in echinococcosis. X. Laboratory evaluation of chemical scolicides as adjuncts to hydatid surgery. *Ann Surg* 1963; 158: 211-15.
131. Frayha, G, Dajani R, Saheb S. Systematic search for a systemic hydatid scolicide. I. In vitro screening of chemicals against the scolices of hydatid cysts (*Echinococcus granulosus*). *Chemotherapy* 1971c; 16: 371-9.
132. Faraj W, Mukherji D, Fakh H, Majzoub N, Khalife M. Liver transplantation in Lebanon: A hard lesson to learn. *Ann Transplant* 2010; 15: 25-9.
133. Loutfi S, Arabi M, Safadi B, Haddad M. Life-threatening liver laceration with arterial hemorrhage complicating percutaneous treatment of hepatic hydatid cyst. *J Med Liban* 2008; 56: 185-8.
134. Frayha G. Comparative metabolism of acetate in the taeniid tapeworms *Echinococcus granulosus*, *E. multilocularis* and *Taenia hydatigena*. *Comp Biochem Physiol [B]* 1971a; 39: 167-70.
135. Schantz P, Nassar N. Chemotherapy for larval echinococcosis in animals and humans: report of a workshop. *Z Parasitenkd* 1982; 67: 5-26.
136. Nassar N. Chemotherapy of human echinococcosis (*E. granulosus*) with benzimidazole carbamates six years experience. *Ther Infect Dis* 1987; 2: 101-9.
137. Shabb B, Khoury G, Taha A. Thoracoscopic treatment of two patients with infected hydatid cyst. *Mediterranean J Infect Parasit Dis* 1995; 10: 236-43.
138. Taha A, Shabb B, Nassar H. Surgical therapy for pulmonary hydatidosis. *Int Surg* 1996; 81: 187-8.
139. Yacoubian H, Dajani T. Preliminary report on a new method of surgical management of hydatid cysts of the lung. *Ann Surg* 1963; 157: 618-24.
140. Haddad FS, Haddad FS, Haddad SI. La malignité de l'aechinococose. *Rev Med Moyen Orient* 1963; 20: 270- 5.
141. Haddad GF, Haddad FS. Management of hydatid cyst of the brain. *Contemporary Neurosurgery* 2000; 22: 1-6.