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## Clinical Echinococcosis

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In 221 patients (0.48% of hospital admissions) with hydatid disease (122 female and 99 male), 81% had single and 19% multiple organs involved. Lungs, liver and spleen as single sites of echinococcosis together represented 83.24% of cases and the liver alone represented 95.24% of instances with multiple organ involvement. One hundred seventy-nine single and 74 multiple cysts (ratio of 2.42/1) represented a total of 363 cysts (1.64 cysts/patient). The incidence of intact cysts was 51.52% and 48.48% had ruptured. Ruptures numbered highest in the lungs (73.44%) and greater in multiple (79.66%) than in single cysts (68.12%). In the liver, 27.14% of single and 54.55% of multiple cysts (40.44% of all liver cysts) had ruptured. Cysts varied in size from 0.8 to 35 cm diameter. Single cysts averaged significantly higher (14.16 cm) and multiple ones lower (5.71 cm) as did intact (6.75 cm) versus ruptured cysts (4.33 cm). Except for 10 silent and 15 symptomatic cysts treated medically, all the rest were treated surgically by removal of the endocyst or resection of both endo and exocysts including 205 first, 31 second and 5 third procedures (1.75% of all major operations). Complications occurred in 28.57%. Surgical mortality (3.57%) was markedly lower than with conservative treatment (60%) and significantly less than that of the whole group (14.48%).

**H**YDATID DISEASE is still a major health problem in infested areas of the world.<sup>4,5,8,10,12</sup> It can involve any organ and mimic almost any pathologic condition.<sup>1</sup> Its clinical manifestations concern practically all the medical and surgical specialists but namely the general surgeon because of the multiplicity and magnitude of the general surgical problems so often associated with human echinococcosis. Further studies are therefore needed to improve our understanding of the various clinical problems caused by this parasite in general, and more specifi-

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cally, to reassess the surgical nature, complications and fatality of this disease in order to apply a more appropriate surgical treatment to clinical echinococcosis. In this investigation we have evaluated the clinical scope and surgical prevalence of hydatidosis in a retrospective study particularly covering organ distribution, multiplicity and pathology of this parasite.

### Materials and Methods

This retrospective study covered a period of 7 years at the Saadi Hospital of Pahlavi University in Shiraz, Iran, from March 1964 to March 1971. We reviewed records of all patients admitted for more than 24 hours in the hospital. Special attention was paid to the surgical protocols but anesthesia tables, available x-rays and autopsy protocols were also studied separately from their respective files. Comparing informations obtained from various sources with those from the patients' records and final regrouping of these data prevented errors of omission or duplication.

### Incidence

Hydatid disease involved various organs in 236 cases according to the hospital records but only in 221 patients was the diagnosis confirmed by either surgical exploration, post-mortem examination or both. During the study period, total hospital admissions numbered 46,449. Thus 221 or 0.48% of hospital admissions represented proved cases of hydatid disease.

### Age and Sex

This series includes 122 female and 99 male patients with a mean age of  $31.80 \pm 11.72$  years. Female patients were imperceptibly younger in the average (mean of

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TABLE 1. Age Distribution

Age per decade	Number of Patients	
	Male	Female
1-10	0	0
11-20	14	28
21-30	28	34
31-40	40	38
41-50	15	9
51-60	1	7
61-70	1	6
Total	99	122

31.36 ± 13.32) than male patients (mean of 32.34 ± 9.41) but the difference had no statistical significance (P>0.05). The fourth decade was the age of highest incidence in both male and female patients but the latter showed a comparative preponderance in the fifth, sixth and seventh decades (Table 1).

### Diagnosis

As a high index of suspicion for echinococcosis is inherent to the medical practice in our area, a Casoni test, multiple x-ray examinations and organ scanning are considered practically in every patient suspected to be a possible host for hydatid cyst. In addition to this basic screening, angiography, tomography and bronchography have definitely helped to diagnose hepatic and pulmonary echinococcosis when plain x-rays have failed to demonstrate a characteristic pattern. Casoni skin test showed a positive yield from 62.5 to 100 per cent. These data are summarized in Table 2. Clinically, only hepatic echinococcosis showed a consistently recognizable pattern with abdominal mass and/or hepatomegaly, abdominal pain and sometimes jaundice. On the other hand, pulmonary hydatid cysts presented a diagnostic pattern in 91.49% of plain chest x-rays but greatly varying clinical manifestations. However, expectoration of hydatid fluid or cyst debris, or even bile rarely but firmly established the diagnosis of pulmonary echinococcal disease in cases of thoracobilia.<sup>2</sup> (Table 3) Diagnostic confirmation was finally reached by surgery in 189 patients, autopsy in 25 and both operation and post-mortem examination in 7 cases.

### Organs Involved

Of 221 patients, 179 (81%) had single organ involvement and 42 (19%) showed multiple organs or sites in-

TABLE 2. Casoni Test in Hydatid Cysts

Organs	Total Casoni tests	Casoni positive	%
Lungs	62	48	77.42
Liver	25	23	92.00
Liver and peritoneal cavity, sites unspecified	8	5	62.50
Spleen	5	5	100

TABLE 3. Diagnosis of Echinococcosis

Diagnostic means	Total	Number diagnostic	%
Casoni test, all organs	100	81	81.00
Plain chest x-ray	94	86	91.49
Plain abdominal x-ray	65	6	9.23
Thoracic tomogram	8	7	87.50
Expectoration of cyst fluid, debris or bile	5	5	100
Hepatic scan	4	3	75.00
Hepatic angiogram	2	2	100
Bronchogram	1	1	100

involved by hydatid disease. Lungs, liver and spleen were the most common single sites of pathology having single or multiple cysts. In fact 149 patients (83.24%) harbored cysts of these three organs. Among multiple organs involved simultaneously, liver was outstanding and outnumbered all other organs or sites by containing single or multiple cysts in 40 of 42 patients (95.24%). Other organs and sites of single or multiple involvements are shown in Table 4 and 5.

### Single versus Multiple Cysts

We found 179 single (one cyst per organ) and 74 multiple cysts (more than one cyst in one organ). Thus single to multiple cysts presented a ratio of 2.42/1. In 6 patients multiple cysts were so numerous that an exact count could not be made by the surgeon. These cases were all abdominal and presumably included dozens of smaller cysts in the peritoneal cavity in addition to the known number involving other abdominal organs. Counting only the known numbers recorded by the operating surgeons, the 74 instances of multiple cysts per organ included a definite minimum of 184 individual cysts which together with 179 single cysts made up a total of 363 hydatid cysts in 221 patients (1.64 cysts per patient) (Table 6).

TABLE 4.

Single Organs Involved	Number of patients	%
Lungs	83	46.36
Liver	57	31.84
Spleen	9	5.02
Small bowel	7	3.90
Stomach	3	1.68
Pancreas	3	1.68
Kidney	3	1.68
Brain	3	1.68
Peritoneum	2	1.12
Prostate gland	2	1.12
Gall Bladder	1	0.56
Mesentery of Small Bowel	1	0.56
Omentum	1	0.56
Large Bowel	1	0.56
Heart	1	0.56
Femur	1	0.56
Urinary Bladder	1	0.56
Total	179	100

### Intact and Ruptured Cysts

The total of 363 cysts included 187 (51.52%) intact and 176 (48.48%) ruptured ones. The greatest number of ruptured cysts were seen in pulmonary echinococcosis representing 94 of 128 cysts of lungs (73.44%). The proportion of ruptured single cysts was 47 of 69 (68.12%) and of multiple cysts 47 of 59 (79.66%). Liver cysts were less often ruptured. Of 136 liver cysts only 55 (40.44%) were recorded as ruptured. Ruptured single cysts were 19 out of 70 (27.14%) and multiple cysts 36 out of 66 (54.55%).

### Size of Echinococcal Cysts

Descriptions giving dimensions of the cysts were only available in 110 single and 21 multiple hydatid cysts. The greatest size (35 cm diameter) and the smallest (0.8 cm diameter) were both observed in liver cysts. However, the smallest cyst with 0.8 cm diameter was only an autopsy finding and showed 1.2 cm difference from the smallest 2 cm size cyst observed clinically. Therefore this cyst is not included in the series for calculating the mean size of the clinically recorded diameters. The mean size (diameter) for single cysts was  $14.16 \pm 3.68$  cm whereas it was  $5.71 \pm 3.21$  cm for multiple cysts with a statistically significant difference ( $P < 0.05$ ). Single cysts with available information as to their size comprised 61 intact and 49 ruptured cysts and multiple ones included 12 intact and 9 ruptured hydatid cysts. The mean size of intact single cysts ( $15.02 \pm 6.28$  cm) compared to that of the ruptured ones ( $14.06 \pm 4.73$  cm) showed no statistically significant difference ( $P > 0.05$ ). However, in the multiple cysts, intact structures had a mean size of  $6.75 \pm 3.67$  cm against that of  $4.33 \pm 1.87$  cm for the ruptured cysts with a statistically significant difference ( $P < 0.05$ ).

### Pathology

All patients except one had *Echinococcus Granulosus*. Although gross appearance of several multiple cysts simulated *Echinococcus Multilocularis* infestation, except in one instance no such diagnosis was made by the pathologist.

Grossly, infection accompanied all the ruptured cysts according to surgical protocols but valid bacteriologic proof was not established in any case because a primary culture was never obtained initially from the surgically sterile specimen. In fact bacteriologic reports either concerned cyst materials contaminated after surgery or discharges from surgically drained hydatid cysts or from surgical wounds. Thus surgeons' descriptions were to be relied upon as the only valid indication for the very early condition of the cyst being noted as infected or free from infection. Intact cysts were generally described as not being infected and only a few intact hepatic cysts were grossly suspected to have infection.

TABLE 5.

Multiple organs or sites involved	Number of patients	%
Liver and peritoneal cavity, sites unspecified	10	23.81
Liver and lungs	9	21.43
Liver and gastrohepatic omentum	6	14.29
Liver and spleen	3	7.14
Liver and porta hepatis	3	7.14
Liver and extrahepatic biliary ducts	2*	4.76
Liver, lung and peritoneum	1*	2.38
Liver, pancreas, spleen	1	2.38
Liver, omentum, pelvic peritoneum	1	2.38
Liver, diaphragm, mesentery of colon, peritoneum	1	2.38
Liver and stomach	1	2.38
Liver and diaphragm	1	2.38
Liver, Peritoneum, retroperitoneum, pelvic peritoneum	1	2.38
Lung, rib, vertebrae	1**	2.38
Pleura and rib	1**	2.38
Total	42	100

\*One cyst per site or organ

\*\*Involved by a single hydatid cyst

The exocyst, formed by the host organ, and the endocyst, proper to the parasite, presented two distinct structures in all patients. Even in ruptured and overtly infected hydatid cysts these two parts could be grossly distinguished. In only one pulmonary hydatid cyst no endocyst could be found at surgery. In this patient retrospective questioning revealed that the cyst should

TABLE 6.

Organs	Single hydatid cysts	Multiple hydatid cysts (2 to 9 cysts) per organ	Total number of cysts
Liver	70	66	136
Lungs	69*	59*	128
Spleen	7	12	19
Peritoneum and pelvic peritoneum	6	33	39
Small bowel	5	5	10
Stomach	3	2	5
Kidney	3	0	3
Brain	3	0	3
Pancreas	3	2	5
Prostate gland	2	0	2
Diaphragm	1	2	3
Mesentery of small bowel	1	1	0
Omentum	1	3	4
Large bowel	1	0	1
Gall bladder	1	0	1
Heart	1	0	1
Femur	1	0	1
Urinary bladder	1	0	1
Total	179	184	363

\*Include two bilateral involvements

have been eliminated through expectoration prior to surgical exploration.

Complete or incomplete calcification of hydatid cysts was noted in 8 patients (3.62% of all patients). These cysts were all single and represented 2.20% of the total number of cysts. They involved the liver four times (4.12% of patients with liver cysts and 2.94% of liver cysts), the lungs twice (2.13% of patients with lung cysts and 1.55% of pulmonary cysts), once the spleen (7.69% of patients with cysts of the spleen and 5.26% of splenic cysts) and once the only cardiac cyst included in this series.

### Silent Cysts

Clinically unsuspected and silent hydatid cysts, discovered at autopsy, were only found in patients suffering from other major pathology. In 10 such cases in this series, miliary tuberculosis had caused death in three, bronchopneumonia in another three, malignancy in two, postnecrotic cirrhosis in one and pulmonary embolism in the last patient. None of these patients had a pulmonary hydatid cyst and except two, one with retroperitoneal and another with splenic involvement, the remaining 8 patients had single or multiple hepatic echinococcosis, 4 of whom also showed splenic involvement.

### Surgical Prevalence

During the 7 years of this study period 11, 712 major surgical operations were performed excluding procedures done under local anesthesia. This number included 205 primary procedures in 196 patients as the initial treatment and 36 reoperations (31 second and 5 third procedures) for complications of echinococcosis. Thus, the first surgical attempt to treat hydatid disease represented 1.75% of all major operations and surgery for completing the treatment or treating complications of echinococcosis accounted for 0.31% of the major procedures and 36 of 196 or 18.37% of surgically treated patients. Together the initial and the subsequent procedures counted 241 or 2.06% of all major operations. From another point of view, as only two patients in this study revealed to have abdominal hydatid cysts at exploratory laparotomy performed for recurrent abdominal pain and suspicion of neoplasm, echinococcosis justified surgery initially in 194 patients (98.98%) and ultimately in two (1.02%).

### Surgical Treatment

A detailed account of the surgical treatment of our cases is beyond the scope of this paper but our review showed that the principle of surgical therapy, total excision of the cyst or cysts inasmuch as compatible with ease and safety, was adhered to by all 38 surgeons and senior residents who performed the operations. Further-

more, for rather simple cases of single small or average size cysts, results did not vary with technical preferences of the operating surgeons. Application of cryosurgical methods as already reported from this center<sup>9</sup> was very successful in small cysts. Plain surgical dissection and excision was also equally good in small and average cysts in general but less so in larger cysts as with cryosurgery. Concerning the two major organs, liver and lungs, resectability was nearly 100% for single cysts. However, for multiple liver cysts, resectability was only about 40% whereas it still approached 100% in the few multiple and bilateral lung cysts included in this series which were treated by single or staged operations. Resection of liver cysts resulted in a remaining cavity after removal of the endocyst which necessitated drainage for an average of 7 to 12 days postoperatively but usually much longer. Lung cysts however required the usual postoperative pleural drainage as for all thoracic operations. The cavity remaining in the lung parenchyma after excision of the cyst was generally closed by endoplication after suturing of individual bronchial openings. In a few instances the remaining cavity was left open and gradually became expanded and ultimately leveled with the rest of the normal lung as evidenced on postoperative x-rays. Only a few large cysts of more than 10 cm diameter left a persistent cavity behind several months after excision as seen on x-rays taken in the outpatient clinics.

### Complications

Postoperative complications ranged from simple superficial wound infection to hemorrhage, anaphylactic shock, peritonitis, subphrenic abscesses, draining sinuses after resection and drainage of hepatic hydatid cysts and wound dehiscence in abdominal echinococcosis. In thoracic cases, persistent pneumothoraces, empyemas and bronchopleural fistulas, thoracobilia, wound infections and persistent partial atelectasis constituted the postoperative complications. Grossly 56 patients (28.57%) showed one or more postoperative complications, 36 of whom required reoperation and seven died.

Of the 25 non-surgical patients, 10 were clinically silent but 9 of the 15 symptomatic patients had fatal complications. These complications consisted of spontaneous or traumatic rupture of abdominal hydatid cysts with generalized peritonitis in three and subphrenic abscesses in two. The other four patients had pylephlebitis, portal hypertension caused by liver echinococcosis with esophageal variceal bleeding, ruptured liver hydatid cyst with choledochal obstruction and ruptured cardiac hydatid cyst with cardiac tamponade.

### Morbidity and Mortality

The hospital stay of our patients ranged from 8 to 110 days with a mean of  $18.71 \pm 14.92$ . For the 196 surgical

patients the mean hospital stay was  $17.98 \pm 15.36$  which was not statistically different from that of the whole group ( $P > 0.05$ ) but was significantly shorter than the calculated means of  $24.48 \pm 9.28$  days for the 25 non-surgical patients and of  $29.40 \pm 12.17$  days calculated separately for the 10 patients with silent echinococcoses ( $P < 0.05$ ). On the other hand 156 surgical patients who had only one operation showed a mean hospital stay of  $13.19 \pm 3.26$  days which was much shorter ( $P < 0.05$ ) than those of 35 patients with 2 operations ( $30.17 \pm 21.50$  days) and another 5 with 3 operations ( $78.80 \pm 20.39$  days). When means for postoperative periods were calculated it was shown that the 205 primary procedures were associated with a mean of  $10.78 \pm 5.08$  postoperative days but the 36 reoperations presented a mean of  $17.11 \pm 15.58$  days and the difference was significant ( $P < 0.05$ ). Also, considering patients who had one operation and those who had two and three procedures (nine with primary two procedures and 31 with secondary operations), the postoperative means were significantly shorter for the first group compared with the second and the second group compared with the third (Table 7). Thus, the length of hospital stay was directly proportional to the complexity of cases implying longer preoperative work-up and more significant complications and to the number of operations.

The mortality in this series was represented by 32 deaths in 221 patients (14.48%). However, only 7 deaths occurred in the 196 surgical patients postoperatively which indicates a total surgical mortality of 3.57%. Causes of deaths were operative and postoperative uncontrollable bleeding in two patients with massive liver resection, thoracobilia with aspiration of bile in another two, postcraniotomy cerebral edema, dehiscence of bronchial suture with bronchopleural fistula and anaphylactic shock after operative rupture of an abdominal cyst in the remaining three patients.

Deaths in patients with one, two and three operations respectively numbered four, two and one, representing a mortality of 2.56%, 5.71% and 20%. On the other hand, non-surgical patients included 10 cases of silent hydatid disease only discovered at autopsy and 15 others with

clinical manifestation but also proved by autopsy. This identifies 25 non-surgical patients with an apparent mortality of 100%. However, as initially 236 patients justified the clinical diagnosis of hydatid disease, in addition to 221 patients who had a confirmed diagnosis, 15 others could have harbored the disease with diagnostic confirmation. Therefore a minimum of 40 patients (25 autopsy proved and 15 unconfirmed) may be considered to represent total non-surgical cases with a mortality of 25/40 or 62.5%. On the other hand, considering that fatal complications caused by or directly related to echinococcosis occurred in 9 of the 15 symptomatic patients a more realistic non-surgical mortality would be 9/15 or 60%.

### Discussion

This study confirms that echinococcosis is still a major clinical problem and in spite of recent advances in diagnostic and therapeutic means, hydatid cysts may still present a considerable morbidity and a significant mortality. That hydatidosis is primarily a surgical disease, is shown in our study beyond any doubt. In fact if treated surgically both morbidity and mortality should considerably drop as seen by comparing surgical and non-surgical results in this series. The most interesting difference is between the non-surgical mortality of about 60% and less than 4% for our surgical cases and for a closely similar figure reported by others.<sup>8</sup> A definite point of emphasis revealed by this study is the highly fatal evolution among hospital patients with symptomatic hydatidosis treated non-operatively.

There is a period of silent growth in the natural history of this parasite when no clinical manifestation should occur e.g. in the 10 silent cases in this study and as reported in another recent study.<sup>5</sup> These instances would not have been discovered were it not for another major disease invariably present and causing death in all our silent cases. This may implicate an increased susceptibility to hydatid infestation caused by a major debilitating disease. Nevertheless, and irrespective of the factors involved, after the silent period is over, beginning of clinical manifestations forms a decisive turning point with a changing prognostic significance that if not treated

TABLE 7.

Hospitalization Time and Mortality	Surgical patients			
	196 patients	156 with 1 operation	35 with 2 operations	5 with 3 operations
Preop stay (days)	$3.65 \pm 2.93$	$3.30 \pm 2.56$	$4.34 \pm 2.89$	$9.6 \pm 6.39$
Postop stay (days)	$11.76 \pm 7.89^*$	$9.97 \pm 2.37$	$13.19 \pm 11.39^{**}$	$23.73 \pm 12.83^\dagger$
Total hospital stay (days)	$17.98 \pm 15.36$	$13.19 \pm 3.26$	$30.17 \pm 21.50$	$78.80 \pm 20.39$
Mortality	7 (3.57%)	4 (2.56%)	2 (5.71%)	1 (20%)

\* in 241 operations

\*\* in 70 operations

† in 15 operations

by surgical extirpation the disease is no longer a harmless condition and may carry a forbiddingly high rate of fatal complications.

Predominance of single pulmonary involvement over single liver hydatidosis in this series matches similar findings by others reporting on echinococcosis in Iran<sup>7</sup> and makes one consider that the lungs could act as a primary filter if some special conditions prevail. Such environmental factors as scarcity of rainfalls and dusty atmosphere in the south could make an air-borne respiratory infestation possible which would explain the southern preponderance of pulmonary hydatid cysts as opposed to the northern majority of hepatic echinococcosis in Iran. Reports from mediterranean countries and other regions of geographic environment similar to northern Iran also indicate a uniformly greater hepatic infestations.<sup>8,10,11</sup>

Complexity and variability of clinical echinococcosis are characteristic features of this disease. Except in pulmonary and hepatic echinococcosis, finding a definite pattern is impossible and often diagnosis is only established by surgical exploration or post-mortem examination. Occasionally the parasite changes the physiologic function of the involved organ significantly and further obscures the diagnosis so that even pulmonary or hepatic diseases, of otherwise typical form, became unrecognizable. Thoracobilia,<sup>2</sup> pulmonary embolism, cavitary lung lesions with hemoptysis and obstructive jaundice and portal hypertension with bleeding esophageal varices are some examples of such complex clinical pictures observed in our study. However, most of the lung and liver hydatids present recognizable features as evidenced in this study (Table 3) and in fact none of the silent cases included a lung cyst and those with liver involvement harbored liver cysts far below the average size. Thus in the silent cases the sine qua non of diagnosis, radiologically visible and clinically palpable cysts of the pulmonary and hepatic locations were absent.

Diagnostic value of the Casoni skin test has been considered as firmly established with an accuracy of about 90%.<sup>6,12</sup> False negatives in our series varied from zero in splenic cysts to 37.5% in cysts of the abdominal cavity involving liver and peritoneum of unspecified sites. False positive Casoni tests could not be ascertained in our study but an approximate figure may be obtained by considering 6 positive intradermal reactions in 7 unconfirmed cases tested, i.e., 6 false positive in a total of 107

patients tested or 5.61%. This is markedly less than a 10-15 per cent false positive tests reported in other studies.<sup>3,6</sup>

Regarding the three major sites, liver, lungs and spleen, the yield of positive Casoni was lowest with pulmonary, higher with liver and highest with splenic echinococcosis. Neither the predominance of multiple over single, nor that of ruptured over intact cysts explained this difference for which the greater immunoactivity of the liver and spleen may be responsible. Other tests such as complement fixation, latex agglutination, passive hemagglutination and indirect fluorescent-antibody<sup>6</sup> were not used in this series.

Cyst size and its correlation with intact versus ruptured status and single versus multiple structures in this series revealed that factors contributing to rupture may include a greater diameter of the cyst but are definitely related to multiplicity of the cysts and pliability or elasticity of their host organ. Thus multiple lung cysts included the largest and single liver cysts the smallest number of ruptures.

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