Available online at www.scientiaresearchlibrary.com

Scientia Research Library

ISSN 2348-0416
USA CODEN: JASRHB

Journal of Applied Science And Research, 2017, 5 (3):88-96

(*http://www.scientiaresearchlibrary.com/arhcive.php*)

Interest of the Adenosine deaminase assay in the ascites fluid in the diagnosis of peritoneal tuberculosis

K.KRATI*, H.OUARRACH*,S.OUBAHA, Z.SAMLANI ***

*Service de gastroentérologie CHU Mohammed VI .Marrakech

** Laboratoire de physiologie, Université cadi Ayad.Faculté de Medecine et de Pharmacie Marrakech .

ABSTRACT

Tuberculosis is a public health problem in Morocco, the prevalence of which is increasing in recent years, despite diagnostic and therapeutic advances. Peritoneal tuberculosis is the most frequent form of digestive tuberculosis, and its diagnosis of certainty is either microbiological or histological, but there are some recent methods that are particularly important, such as the measurement of adenosine deaminase (ADA) The activity has a very good diagnostic value with high specificity and sensitivity according to the studies at a threshold value of 30 IU / l. In order to determine the practical value of the ADA assay in the ascites fluid in the diagnosis of peritoneal tuberculosis, a retrospective study was carried out within our department over a period of 8 years.

Keywords : Peritoneal tuberculosis, ascites, Adenosine *deaminase*, peritoneal biopsies

---

INTRODUCTION

Peritoneal tuberculosis, a public health problem, is by far the most common peritoneal pathology in Morocco [1]. The clinical and biological presentation of peritoneal tuberculosis is polymorphic and non-specific [1,2]. Diagnosis involves several non-invasive and invasive means [2]. Nevertheless, there are some recent methods which are particularly important, such as the ADA, whose measurement of the activity has a very good diagnostic value with high specificity and sensitivity according to the studies at a threshold value of 30 IU / L, thus avoiding the use of laparoscopy or laparotomy for peritoneal biopsy, which remains the best diagnosis but burdened with morbidity and non-negligible mortality [1,2].

Adenosine deaminase (ADA) is a key enzyme of purine metabolism that catalyzes the deamination of adenosine and 2'-deoxyadenosine to inosine and deoxyinosine by forming ammonia. It participates in the proliferation and differentiation of lymphocytes. The elevation of this enzyme to a threshold value of 30 IU / L in the peritoneal fluid has a sensitivity and specificity of (100% and 97%, respectively) for the diagnosis of peritoneal tuberculosis in the absence of cirrhosis [3]. However, the only increase in the ADA will not make it possible to retain the diagnosis and indicate the treatment of peritoneal tuberculosis, false positives being possible in case of cancer, ascites

linked to cirrhosis

The objective of our study is to determine the practical relevance of the ADA assay in the ascites fluid in the diagnosis of peritoneal tuberculosis.

MATERIAL AND METHODS

A retrospective study was conducted within our department over a period of 8 years (January 2009 to January 2017), including all patients diagnosed with peritoneal TBK. All patients received a biological, radiological assessment and an exploratory ascitic aspiration with ADA. All patients received anti-tuberculosis treatment with regular follow-up throughout the treatment period

The inclusion and exclusion criteria:

We included in the study all female or male patients regardless of age who were diagnosed with peritoneal tuberculosis.

We excluded:

- Cirrhotic patients
- Patients with other etiologies of exudative ascites
- Patients whose records do not provide sufficient information.

RESULTS AND DISCUSSION

In our study, we collected 142 cases of peritoneal tuberculosis during the study period, with an average age of 44.3 years (range from 16 years to 85 years). And the age group most affected was: 36-45 years.

The sex ratio M / F was 0.39.

Background analysis revealed BCG vaccination in all patients, active and passive smoking in 50 cases (ie 35.2% of patients), an ATCD of ethylism in 10 cases (7.04% of patients case).

The personal ATCD of tuberculosis was noted in 20 patients (14.08% of cases) including: 2 cases of peritoneal TBK; 10 cases of pleuropulmonary TBK; 4 cases of multifocal TBK, 2 cases of intestinal TBK, 2 cases of lymph node TBK. For tuberculosis familial TBCD, tuberculosis was found in 18 patients (12.6% of cases).

For comorbidities: 2 patients were on short-term immunosuppressive therapy (1.4% of cases), 30 patients were immunosuppressed (21.1% of cases), including 24 diabetic cases, 4 cases of hemodialysis, 2 cases with HIV disease

Reason for hospitalisation:

The pattern of hospitalization was dominated by abdominal distension in 94.3% of cases (134 patients), abdominal pain in 29.5% cases (42 patients), altered general status in 18.3% of cases Patients), an Anasarca state in 1.4% of the cases (2 patients).

Associated in some patients had dry cough in 14.08% of cases (20 patients), dyspnea in 4.22% of cases (6 patients), chronic diarrhea in 7.04% of cases (10 patients), amenorrhea in 4.22% of patients (6 patients), rectal bleeding in 1.04% (2 patients), hematemesis in 1.04% of the patients (2 patients).

Clinical signs :

Clinical signs were dominated by ascites in all patients, general impairment in 130 patients (91.54%), abdominal pain in 92 patients (64.78% of cases), Febrile syndrome in 76 patients (53.52% of cases), night sweats in 72 patients (49.65% of cases).

In our series, the ascitic fluid aspirate performed in all patients showed a citrin yellow appearance in 120 patients (84.5% of cases), disorder in 15 patients (10.56% of cases), hematic in 6 patients (4.22% of cases), gelatinous in 1 patient (0.70% of the cases).

The ascites were clearly rich in protein in 97.18% of the patients (138 patients), in 4 cases (2.81% of the patients) the fluid was not quite rich, but the blood-ascites albumin gradient was <11 , And therefore in favor of an ascites rich in protein

The fluid was lymphocytic in 112 cases (78.87% of the patients).

The search for BK in the LA by direct examination, carried out in all the patients, returned positive in only one case.

The PCR (GeneXpert) technique in ascitic fluid, requested in 57 cases (seen as a recent technique), returned positive only in 2 cases (3.5% of patients)

The ADA assay performed in all cases found a positive (threshold value of 30 IU / L) in 126 patients (88.73% of cases) with an average of 83.22 UIL [30 -600 UIL], a negative (threshold value of 30 IU / L) in 16 cases (11.26% of cases) (Figure 1)

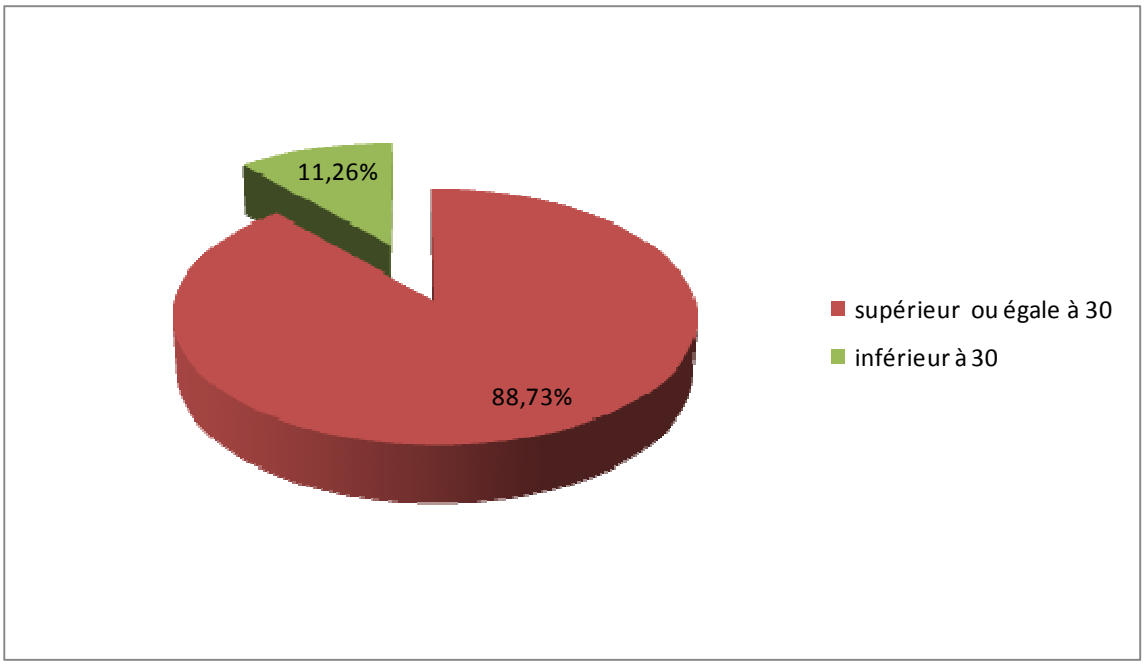

Figure 1: Rate of adenosine deaminase in the ascites fluid

Imaging (abdomino-pelvic ultrasound or abdomino-pelvic CT) was performed in all patients, free ascites were detected in 112 cases (78.88%), and a compartmentalized ascites in 30 cases, ie 21.12% of patients, Peritoneal nodules in 1 case (0.7% of patients), deep lymph nodes in 18 cases (12.67% of the patients), a thickening of the loops in 8 cases (4.22% of the patients) (5.63% of patients), an agglutination of the loops in 8 cases (5.63% of the patients)

A TBK assessment of all patients revealed a positive IDR in 32 patients (22.53% of cases), abnormal chest x-ray in 82 patients (57.74% of cases), positive sputum BK in 4 Cases (2.8% of

patients)

A Quantiferon was performed in 30 cases, positive in 4 cases (13.3% of the patients).

The findings for other concomitant TBK sites revealed pulmonary localization in 46 patients (32.39%), intestinal in 8 patients (5.6% of cases), lymph node in 14 patients (9, 85% of cases)

The diagnosis of peritoneal TBK It was retained on a cluster of arguments: Clinical, Radiological and Biological: (Figure 2)

- In 1 case he was detained before the isolation of BK in the LA.
- In 126 cases, it was retained before the positivity of the ADA rate.
- In 15 cases, it was retained after recourse to peritoneal biopsies (ADA and GeneXpert being negative).

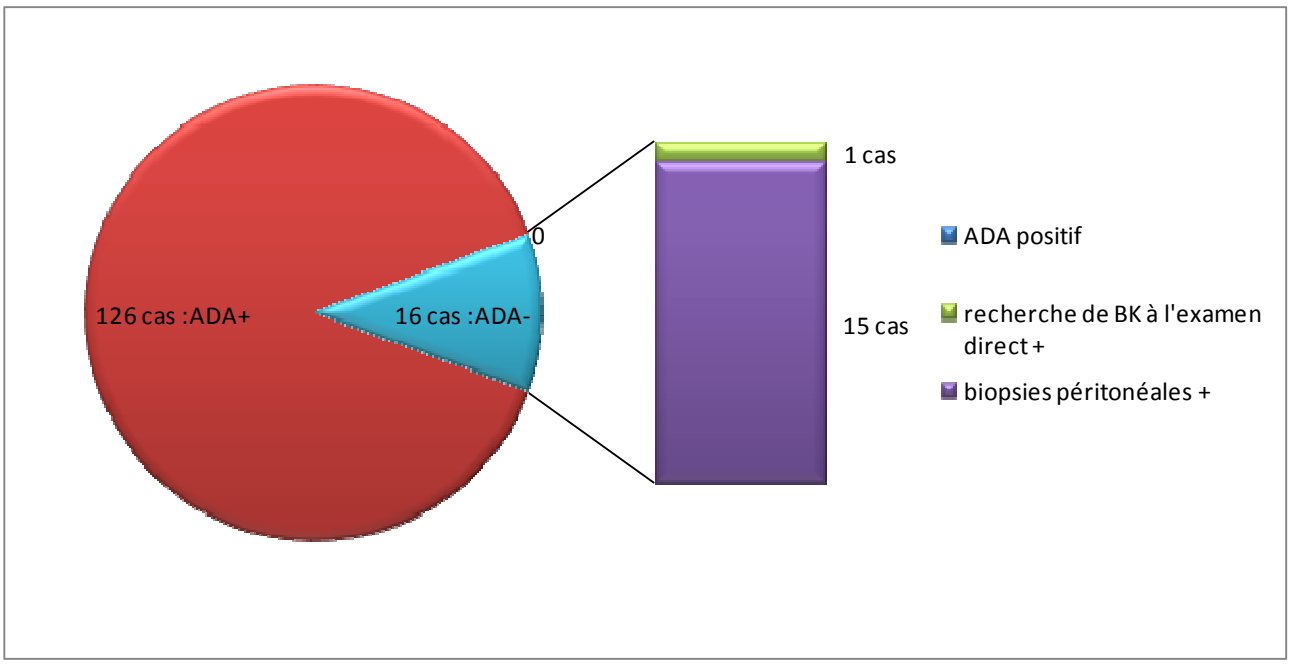

Figure 2: Diagnostic elements of the TBK

In the 126 patients with a positive ADA (88.73% of the cases), the diagnosis of peritoneal TBK was retained.

- The GeneXpert was requested in only 41 cases among the said patients only (seen that it is a recent technique), of which only 2 cases returned positive
- The search for BK in the LA by direct examination was requested in all patients and negative income at home
- There was no recourse to peritoneal biopsies

In the 16 patients with ADA negative:

- The GeneXpert was asked at home and it came back negative
- The search for BK in the LA was requested in all the patients and positive income in only one case which allowed us to retain the diagnosis

- The use of peritoneal biopsy was carried out in the other 15 patients and positive income in them, which allowed us to retain the diagnosis. (Table 1)

Table 1 : Summary of Diagnostic Elements of Peritoneal Tuberculosis

Array of arguments		Case	Percentage
Isolation of BK		1	0.70%
ADA positive (126 cases)	GeneXpert +	2	4.87%
	GeneXpert -	39	95.12 %
	GeneXpert not done	85	59,85 %
ADA negative and GeneXpert negative (16 cases)	Positive peritoneal biopsies	15	100 %
(NB: biopsies done in 15 cases)	Negative peritoneal biopsies	0	0%

The evolution under TTT anti bacillary :

• was good with regression of ascites in 140 patients; Including 4 patients with hepatic cytolysis, who justified the discontinuation of treatment with progressive reintroduction which took place without incident

• 2 deaths before starting anti-bacillary treatment

DISCUSSION

Peritoneal tuberculosis constitutes a major public health problem in Morocco and is the second most important extrapulmonary location of tuberculosis after lymph node localization [4] and the first most frequent abdominal localization [5].

It is a predominantly female condition [1, 2,4], our series finds the same data as the literature with a female frequency of 71,83%. It is especially the prerogative of the young subject between 35 and 45 years [2,4], in our series, the average age was 44,3 years.

Its diagnosis represents a real challenge for the clinician, on the one hand because of the great polymorphism and the non-specificity of its clinical manifestations, and on the other hand to the limits of its diagnostic means [2], thus peritoneal biopsy by Laparoscopy or laparotomy remains the most reliable means of diagnosis even though it is burdened with a non-negligible morbidity and mortality.

Its clinical manifestations are very variable, and can not on its own confirm the diagnosis [5]. A

meta-analysis based on 35 studies, performed by Sanai et al, found abdominal pain in 64.5% of cases, fever in 59%, weight loss in 61%, diarrhea in 21, 4% of cases, and constipation in 11% of patients with peritoneal tuberculosis [2]. In Morocco, in a series of 300 cases of peritoneal tuberculosis, febrile ascites was the most frequent reason for consultation 58% [6]. The data in our series are similar to those in the literature with abdominal pain in 64.78% of cases, febrile syndrome in 53.52%, AEG in 91.54% of cases, Diarrhea in 7.04% of cases. Pulmonary pleuro signs (cough, dyspnea) are sometimes associated with other signs [7,8]. They were found in 18.3% of cases in our series.

Radiological examinations are of little interest in the absence of any other localization. [9] In our series they revealed peritoneal thickening or infiltration in 4.22% of patients, peritoneal nodules in 0.7% of patients, lymphadenopathy Profiles in 12.67% of patients, a thickening of the loops in 5.63% of the patients, an agglutination of the loops in 5.63% of the patients

Like clinical and radiological signs, biology is not specific. The ascites fluid is usually citrin yellow, rarely sero-haematic or turbid, exudative in nature, with a protein content of more than 30 g / l and a predominantly lymphocyte cytological formula.

Many authors confirm these data [2, 4, 7, 8, 10]. However, on the one hand, a liquid rich in polymorphonuclear neutrophils (PNN) can not eliminate the diagnosis of TP, indeed, and for reasons not yet well understood, patients with underlying renal insufficiency can have a d NNP-rich ascites [2,11]. On the other hand, lymphocyte predominance can also be encountered in case of ascites on portal hypertension following antibiotic therapy for ascitic fluid infection [2].

In our study the fluid was lymphocytic in 78.87% of patients.

As for the biochemical study of the ascites fluid, a protide level in the ascites fluid> 25 g / l is found in 100% of cases of peritoneal tuberculosis [2]. However, the sensitivity of this test decreases (42-72%) in the case of peritoneal tuberculosis complicating decompensated cirrhosis [2, 12]. This rate> 25 g / l is also found in 100% of cases of ascites of renal origin, in 22% of cases of cirrhosis, in 100% of cardiac ascites and 95% of carcinomas Peritoneal [2], it is a test therefore that although sensitive, lack of specificity. The results of our study confirm these data, the ascites was exudative in 97.18% of the cases (138 patients).

The serum-ascites albumin gradient has a more cost-effective diagnostic efficacy than the protide level in the ascites fluid [2,17]. A rate <11 g / l is found in 100% of cases of peritoneal tuberculosis, however, its specificity is low. In fact, its interest is mainly to differentiate the secondary ascites to an HTP of the other causes of ascites. This makes it possible to limit investigations that are sometimes invasive only to the cases of ascites of unexplained origin. [2, 13]. In our study the use of the blood-ascites albumin gradient was done in 2.81% of cases, in all these patients the rate was <11.

Other parameters in the biochemical study of the ascites fluid have proved their effectiveness with sensitivities and specificity which can reach 100%, in particular the dosage of adenosine deaminase (ADA). This is a ubiquitous enzyme that catalyzes the deamination of adenosine to inosine and that of deoxyadenosine to deoxyinosine with release of ammonia into the medium. This enzyme is widely found in T lymphocytes, monocytes and macrophages activated during a cell-mediated immunity process, which would explain the increase in activity during tuberculous pathologies.

The activity of ADA results from the action of two isoenzymes ADA-1 and ADA-2 which have different pHi and affinities relative to their substrates, adenosine and deoxyadenosine. The presence of ADA-1 in biological fluids is mainly due to cellular necrosis, whereas ADA-2 is released by

monocytes and macrophages stimulated by an infectious agent. [14, 15] The importance of the determination of these isoenzymes in a tuberculosis process, and in particular ADA-2 which is more specific, is still open to discussion.

ADA activity is most often measured by the Giusti method which uses adenosine as substrate and ammonium sulfate as the standard. One unit of ADA enzyme corresponds to the release of 1 $_{u}$mol of ammonia / L / min at 37 ° C quantified by the chemical reaction of Berthelot (hypochlorite, phenol, nitroprusside) [16]. This simple, fast and inexpensive technique can be easily implemented.

Several studies evaluating the diagnostic utility of ADA activity measurement in peritoneal tuberculosis have been published [17].

In the Burgess study of 178 fluid pairs of ascites / sera representing different etiologies of peritoneal effusion: chronic liver disease, cirrhosis, heart failure, malignancy, tuberculosis, transudate and nephrotic syndrome. The diagnosis of tuberculosis was positive in 18 patients with a mean Ada activity of 61.6 U / L (17.5-115 U / L), this activity was significantly increased compared to other diagnostic groups <0, 05). The choice of the threshold value of 30 U / L corresponded to a sensitivity of 94% and a specificity of the order of 92% [15].

In South Africa In 92 patients, including 30 patients with peritoneal tuberculosis, 21 with malignant ascites and 41 patients with cirrhosis, Sathar et al. Have evaluated the activity of ADA in LA. The ADA results showed significantly higher activity in the group of patients with tuberculosis with an average value of 101.84 U / L vs 19.35 U / L in the malignant ascites group and 13.49 U / L in that group With cirrhosis (p = 0.0001). The threshold value of 30 U / L was associated with a sensitivity and specificity of 93% and 96% respectively [19].

This leads to conclude in place of the measurement of ADA activity in the ascites fluid in the diagnosis of peritoneal tuberculosis. For an average threshold value of 30 U / L correspond a significant sensitivity and specificity.

The utility of the peritoneal ADA assay depends more on economic and epidemiological criteria than on its sensitivity or specificity: in endemic areas where invasive techniques such as laparoscopy are not available or costly, ADA is useful; The ADA will be useful if, positive, it confirms a clinical suspicion of TBK in an inoperable patient [20].

In our study, in our patients, non-invasive examinations and positive ADA rates resulted in the diagnosis of TBK in 88.73% of patients without recourse to peritoneal biopsies with an average ADA activity of 83.22 IU / L.

They did not allow the diagnosis to be made in 11.26% of patients, in this group (apart from the case of the patient with a positive BK test) a laparoscopy was performed .

CONCLUSION

The determination of the activity of adenosine deaminase constitutes a rapid, early, less invasive diagnostic means of easy and inexpensive implementation with excellent sensitivity and specificity for the diagnosis of peritoneal tuberculosis.

It may be an alternative to laparoscopy, the use of which is limited and unavailable in high-endemic countries.

REFERENCES

[1] Robaday S, Belizna C, Kerleau JM, Héron F, Cailleux N, Lecomte et al. La tuberculose péritonéale: une entité toujours présente A propos de 4 observations. Rev Med interne **2005**; 26 : 738-743.

[2] Sanai FM, Bzeizi KI. Systematic review: tuberculous peritonitis presenting features, diagnostic strategies and treatment. Aliment pharmacol Ther **2005**; 22: 685-700.

[3] Riquelme A, Calvo M, Salech F, et al. Value of adenosine deaminase (ADA) in ascitic fluid for the diagnosis of tuberculous peritonitis: a meta-analysis. J Clin Gastroenterol **2006**;40:705—10.

[4] El abkari M, Benajeh DA, Aqodad N, Bennouna S, Oudghiri B, Ibrahimi A. Peritoneal tuberculosis in the Fes university hospital (Morocco): Report of 123 cases. Gastroenterol. Clin Biol **2006**, 30:377-381.

[5] Sotoudehmanesh R, Shirazian N, Asgari AA, Malekzadeh R. Tuberculous peritonitis in an endemic area. Dig Liver Dis **2003**;35:37–40.

[6] Kaya M, Kaplan MA, Isikdogan A, Celik Y. Differentiation of tuberculous peritonitis from peritonitis carcinomatosa without surgical intervention. Saudi J Gastroenterol **2011**;17:312

[7] Khadija,M . La tuberculose péritonéale au CHU Hassan II de Fès : 300 cas- Thèse N°053/**2008**

[8] El Ajmi S, Chatti N, Limam K. La tuberculose péritonéale, aspects actuels à propos de 39 cas observés au centre Tunisien. Médecine du Maghreb **1991**; 27 :11-12.

[9] Dabo , CAT ; Coulibaly, JM ; Kpossou, AR ;et al . Tuberculose péritonéale : quel outil diagnostique ? *Revue Malienne d'Infectiologie et de Microbiologie* **2014***, (3)* Page 34-37

[10] De Escalante yanguela B el al . Ascites by peritoneal tuberculosis. An Med Interna.**2007** May,24(5) :253-254.

[11] Lui SL, Tang S, Li FK, et al. Tuberculosis infection in Chinese patients undergoing continuous ambulatory peritoneal dialysis. Am J Kidney Dis **2001**; 38: 1055–60.

[12] Shakil AO et al . Diagnostic features of tuberculous peritonitis in the absence and presence of chronic liver disease: a case control study. Am J Med. **1996** Feb;100(2):179-85.

[13] Boyer TD. Diagnosis and management of cirrhotic ascites. In: Zakim, D, Boyer, TD, eds. Hepatology: A Textbook of Liver Disease. 4th edn. Philadelphia, USA: W.B. Saunders, **2003**: 631–58.

[14] Gorguner M, Cerci M, Gorguner I. Determination of adenosine deaminase activity and its isoenzymes for diagnosis of pleural effusion. *Respirology* **2000** ; 5 : 321-4.

[15] Conde MB, Marinho SR, Pereira M de F, *et al.* The usefulness serum adenosine deaminase 2 (Ada2) activity in adults for the diagnosis of pulmonary tuberculosis. *Respir Med* **2002** ; 96 : 607-10.

[16] Giusti G. Adenosine deaminase. In : Bergmeyer HU, ed. *Methods of enzymatic analysis*. NewYork : Academic Press, **1974** : 303-7.

[17] Y. El Jahiri, S. Chellak, C. Garcia, F. Ceppa, P. Burnat. L'intérêt du dosage de l'adénosine désaminase dans les liquides biologiques au cours d'une tuberculose. *Ann Biol Clin **2006** ; 64 (2) : 117-24*

[18] Burgess LJ, Swanpoel CG, Taljaard JJ. The use of adenosine deaminase as a diagnostic tool for peritoneal tuberculosis. Tuberculosis (Edinb) **2001** ; 81 : 243-8.

[19] Sathar MA, Simjee AE, Coovalla YM, *et al.* Ascitic fluid gamma interferon concentrations and adenosine deaminase activity in tuberculous peritonitis. *Gut* **1995** ; 36 : 419-21.

[20] Harlan WR , Grimm IS : Tuberculous peritonitis : can ADA keep the laparoscope away ? *Gastroenterology* **1997** ; 113 : 687-9.