



UPDATES AND SPOTLIGHTS ON SOME HEPATOBILIARY PARASITES

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Parasites are common worldwide and are classified by the site of infestation (blood, tissue, intestine).

Most are intestinal, but some have a life cycle primarily involving the biliary tract. This predisposes patients to complications from parasite-induced biliary obstruction. Secondary bacterial infections and cholangiocarcinoma are the most serious complications associated with these parasites. Hence, accurate diagnosis to tailor effective therapy is necessary (Khandelwal *et al*, 2008).



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4 Metacercariae in flesh or skin of fresh water fish are ingested by human host.

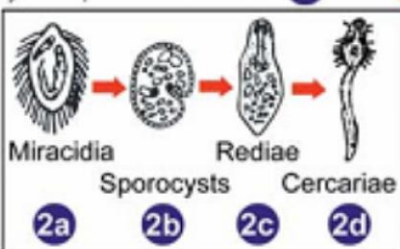


i = Infective Stage

d = Diagnostic Stage

Free-swimming cercariae encyst in the skin or flesh of fresh water fish. 3

Eggs are ingested by the snail. 2



1 Embryonated eggs passed in feces. d

Adults in biliary duct 6

5 Excyst in duodenum



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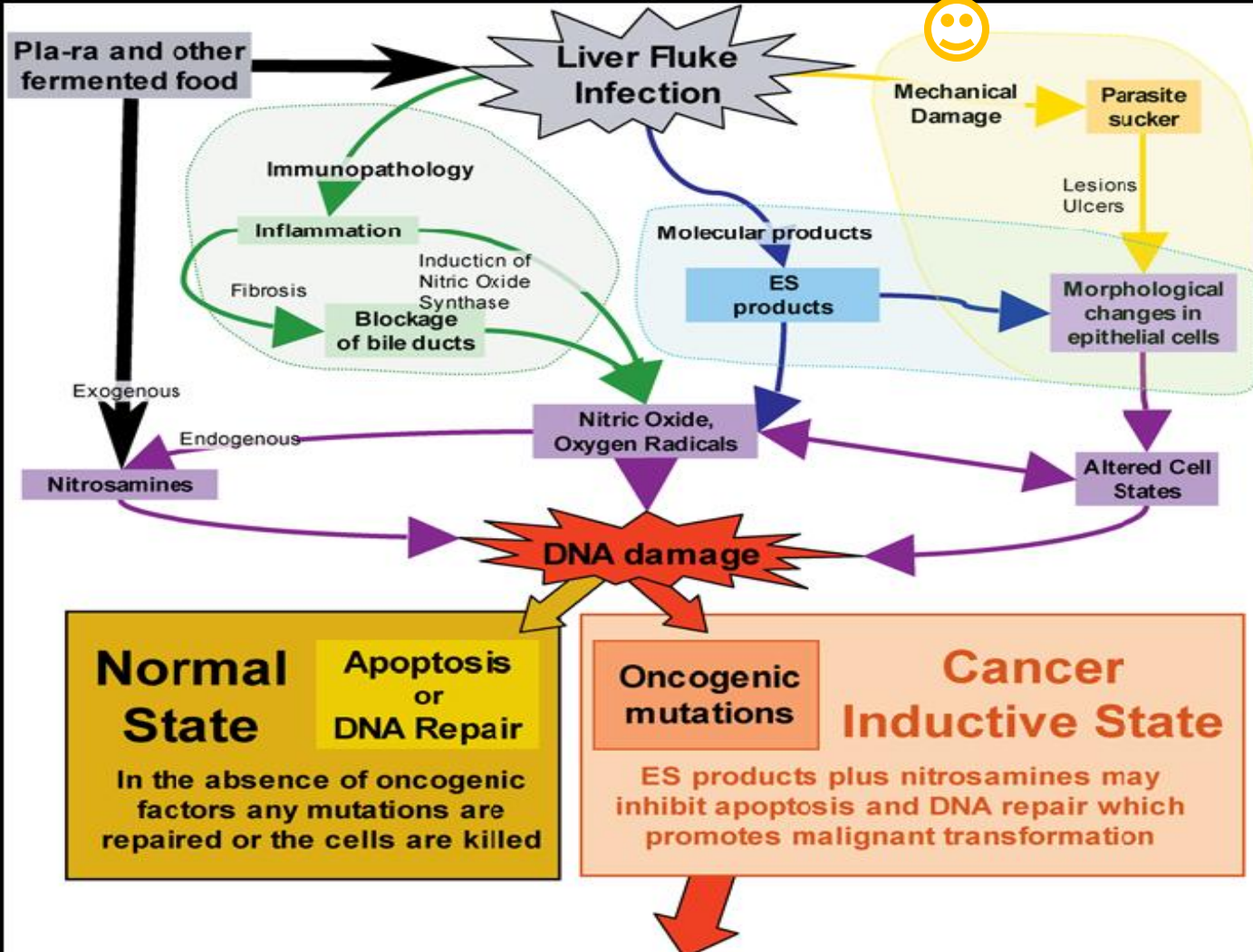
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carcinogen (IARC)

There is no stronger link between a parasite and cancer than that between *O. viverrini* and CCA - indeed WHO data suggest that as many as one-third of the nine million infected people will contract cancer (Parkin, 2006).

This is a striking figure compared to data from other carcinogenic microbes, such as *Helicobacter pylori*, human papilloma virus and the hepatitis viruses, where less than one percent of infected individuals develop infection-related cancers (Herrera *et al.*, 2005).



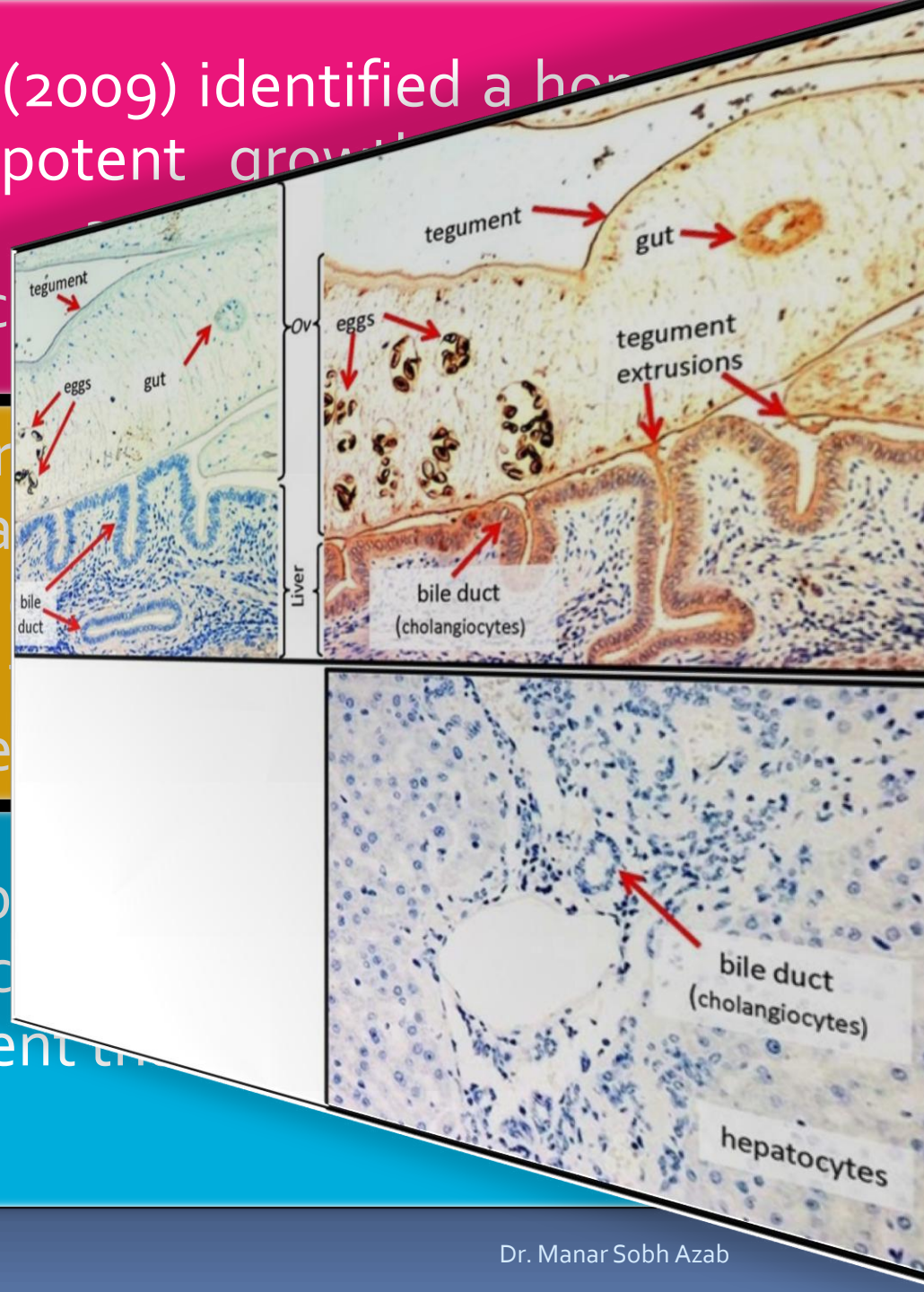
Proposed Mechanisms of *Opisthorchis*-Derived CCA Initiation (Sripa *et al.*, 2007)



Smout *et al.* (2009) identified a homolog of human gastrin, a potent growth factor for proliferation excretory/secretory (ES) products.

Soluble ES products from parasites, a proliferation cell line, and can be blocked.

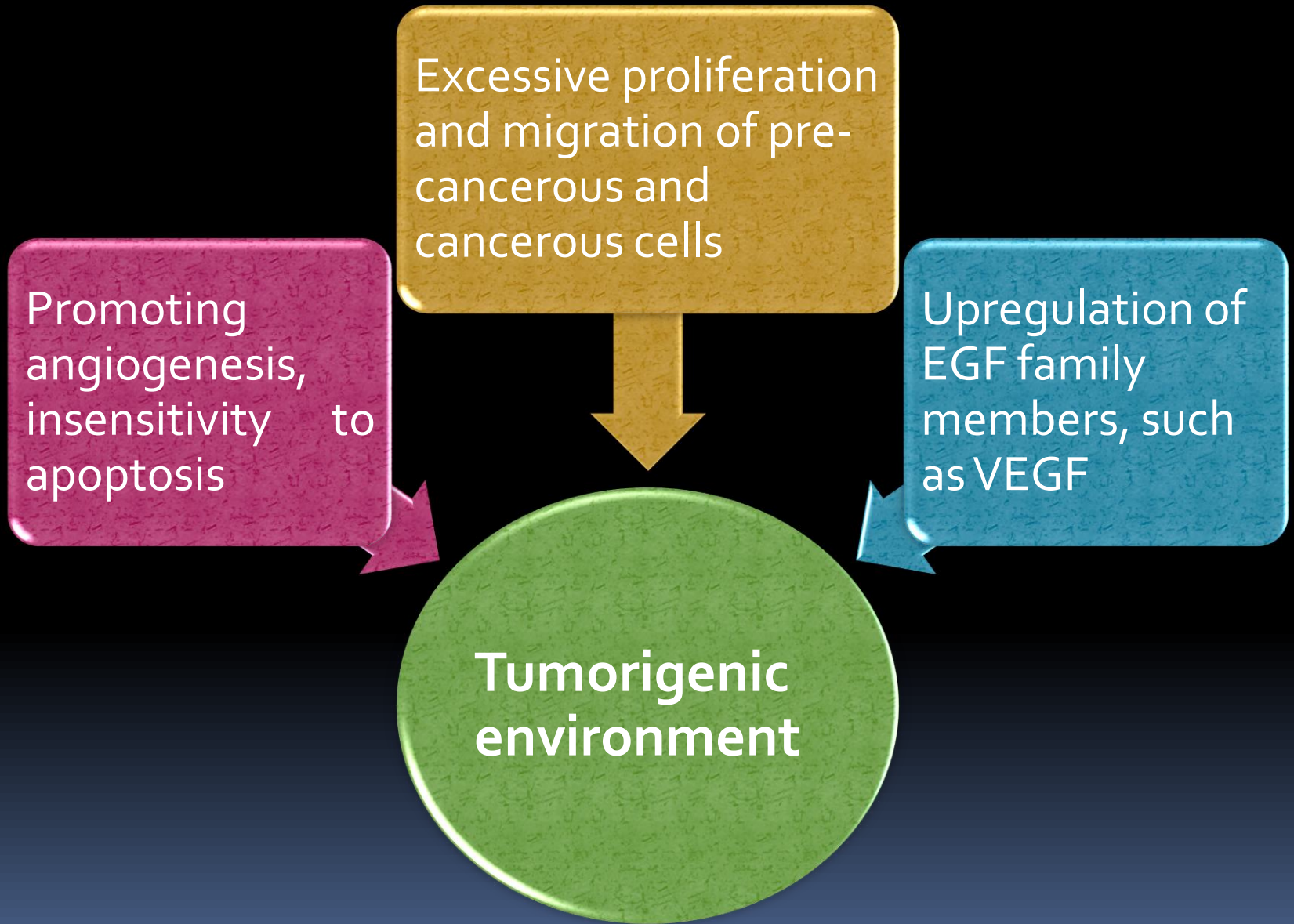
This data implies a mitogenic factor in an environment (2009).



human gastrin, a potent growth factor for proliferation excretory/secretory (ES) products.

Schistosoma viverrini cause liver cancer (CCA) products.

major factor in the development of liver cancer (2009).



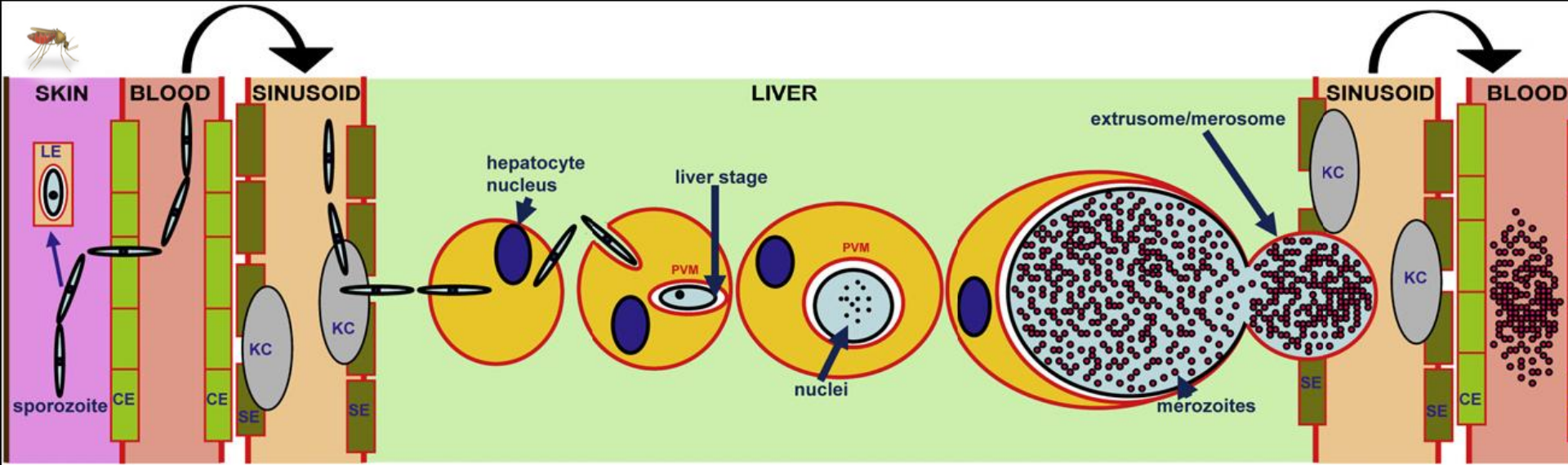
MALARIA

Malaria is a major global health problem, found most acutely in Sub-Saharan Africa and in some parts of Asia and South America.

Each year there are about 600 million new clinical cases and at least one million individuals, mostly children, die from malaria infections.

Various attempts at eradicating this disease have so far been unsuccessful, and in fact within the last 10 to 15 years the burden of malaria has been increasing.

These realities have compounded the urgency of finding novel treatment strategies that will be less vulnerable to the development of parasite resistance (Rodrigues *et al.*, 2008).



SKIN TRAVERSAL

PARASITE:

- CSP
- TRAP
- SPECT1
- SPECT2
- TLP
- PL
- CelTOS

HOST:

NF-kappaB

LIVER SINUSOID & HEPATOCYTE TRAVERSAL

PARASITE:

- CSP
- TRAP
- SPECT1
- SPECT2
- CelTOS

HOST:

HGF
MET
HSPGs
NF-kappaB

HEPATOCYTE INVASION

PARASITE:

- CSP
- TRAP
- P36
- P52/P36p
- AC α
- AMA1?
- TRSP?

HOST:

HGF
MET
HSPGs
CD81
NF-kappaB
SR-BI

LIVER STAGE DEVELOPMENT

PARASITE:

- UIS3
- UIS4
- SAP1/SLARP

HOST:

HO-1
L-FABP
NF-kappaB
HGF
MET
SR-B1

LATE LIVER STAGE DEVELOPMENT & MEROZOITE EGRESS

PARASITE:

?

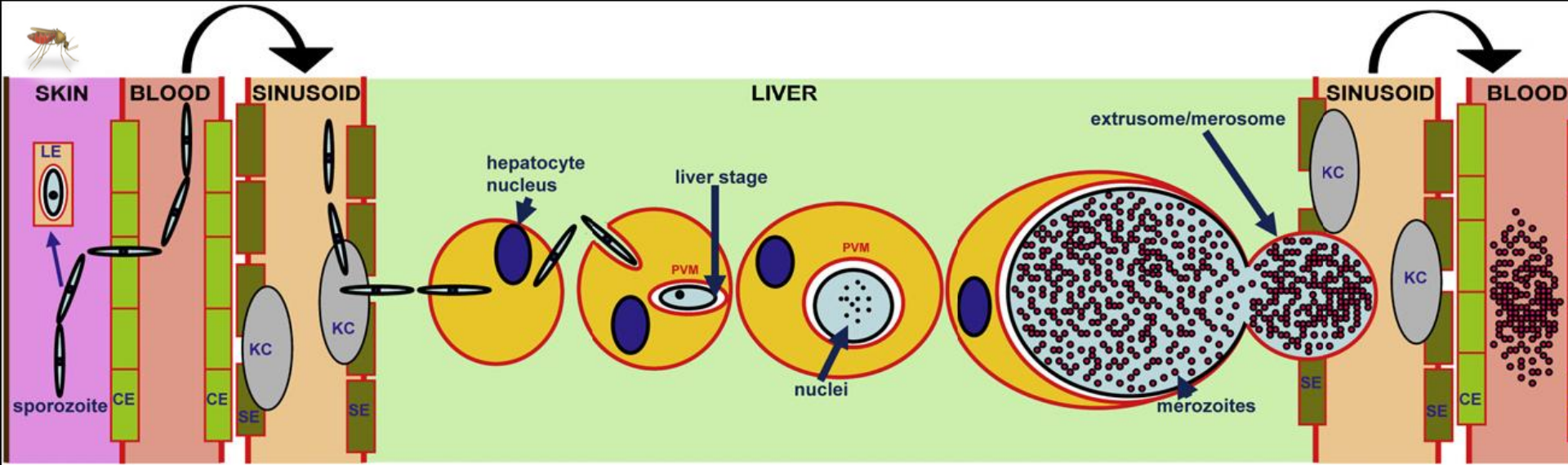
HOST:

?

The Sporozoite Journey to the Hepatocyte and Subsequent Liver Stage Development: Parasite/Host Interactions (Vaughan *et al.*, 2008).

Several works confirmed the links between liver infection and lipoprotein pathways (Shakibaei and ...). However, from these reports, it was not ... involved in the

By using several types of inhibitors including RNA interference (RNAi) both in vitro in cultured human cells and in vivo in a mouse model of infection, Rodrigues *et al.* (2008) have identified a major lipoprotein receptor, class B, type I scavenger receptor (SR-BI), as a functionally important host factor for both sporozoite invasion and EEF development.



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PARASITE:

?

HOST:

?

The Sporozoite Journey to the Hepatocyte and Subsequent Liver Stage Development: Parasite/Host Interactions (Vaughan *et al.*, 2008).

Practice Points

Characterization of the role of host factors that influence *Plasmodium* liver infection is a must, as these may contribute to the design of rational interventional strategies for the development of novel prophylactic or therapeutic drug targets (Rodrigues *et al.*, 2008).

Targeting host components offers major advantages over targeting the parasite itself, including the inherently lower vulnerability of such drugs, used either alone or in combination therapies, to the development of resistance by the parasite (Cunha-Rodrigues *et al.*, 2006).

Practice Points

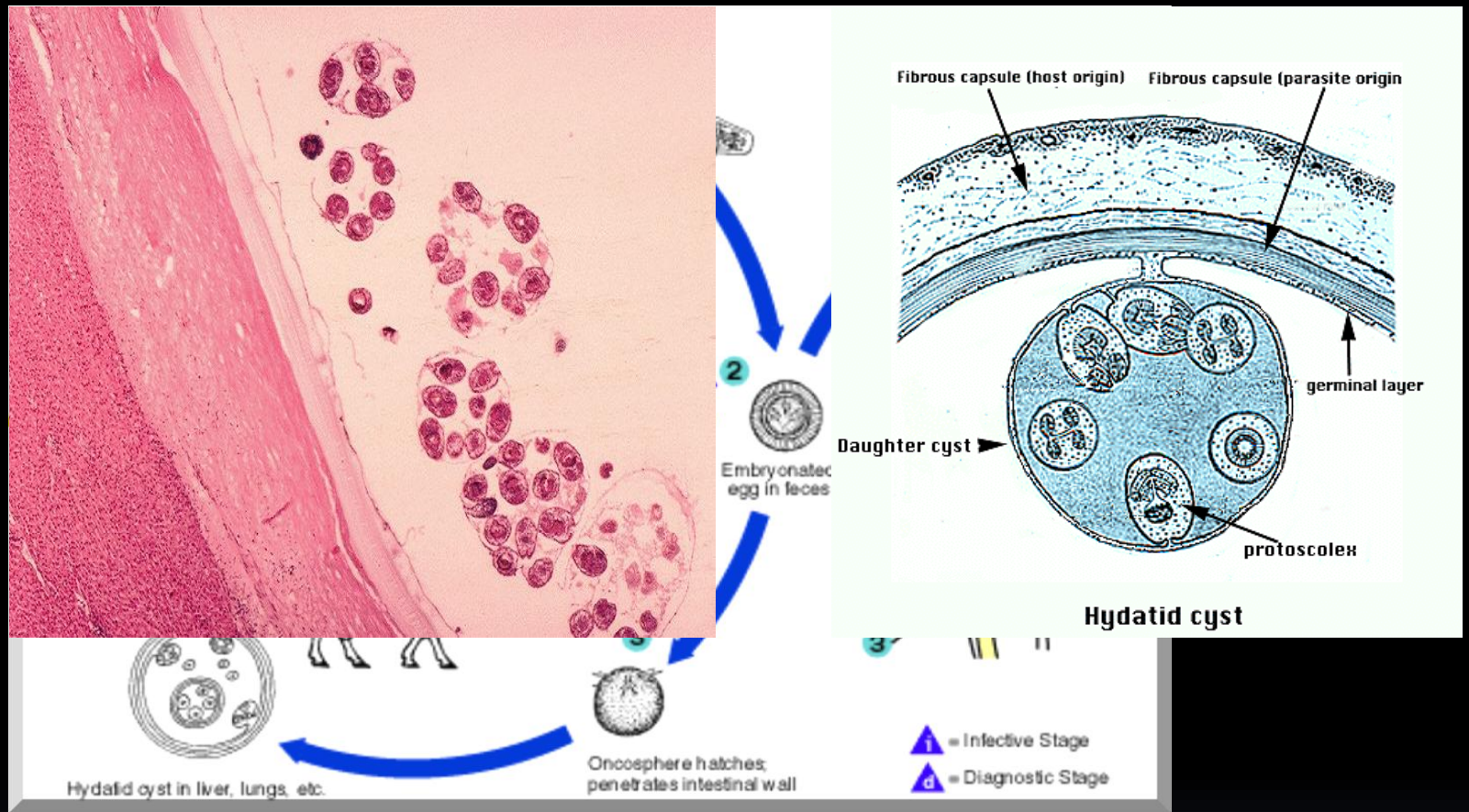
As a second key advantage, the host factor approach also offers significantly higher potential for accelerated drug discovery and development through synergies with ongoing output from other disease pipelines. This potential emerges particularly well in the present case of SR-BI, which has recently been proposed to function as a receptor for several pathogens, including hepatitis C virus (HCV) (Scarselli *et al.*, 2002), mycobacteria (Philips *et al.*, 2005), and bacteria (Vishnyakova *et al.*, 2006).

Interestingly, it has been proposed that HCV requires functional cooperation between the host's SR-BI and tetraspanin CD81, the latter having also been implicated in *Plasmodium* sporozoite invasion (Silvie *et al.*, 2003, 2007). By further exploring the parallels between these infection pathways, one can now hope for increasing synergies between all of these fields for years to come.

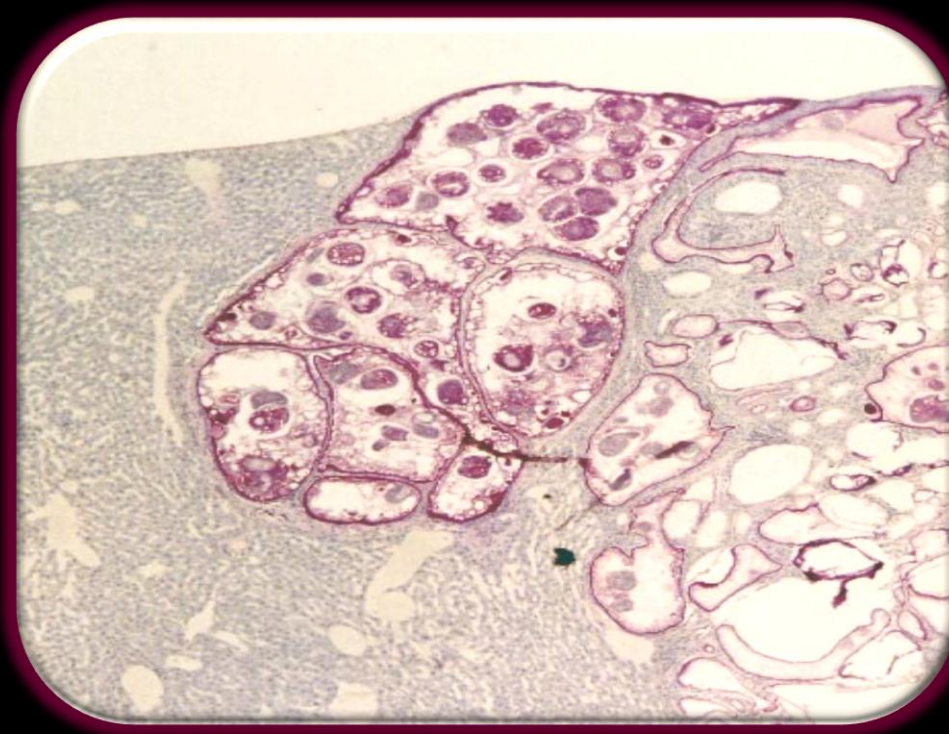
HYDATID DISEASE



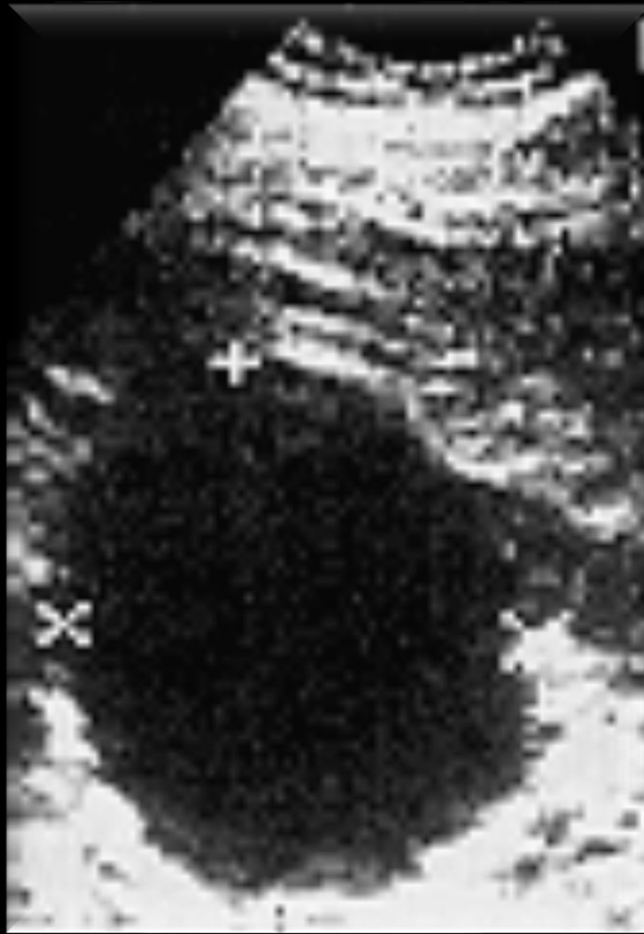
Hydatid disease is caused by larvae of the sheep-dog tapeworm *Echinococcus* and there are estimated to be 2-3 million cases worldwide (Craig *et al.*, 2007). Echinococcosis is classified under the category of invasive cestode (tapeworm) infections.



Cystic echinococcosis, which is caused by *E. granulosus* and has a worldwide distribution with a predominance in sheep-raising areas

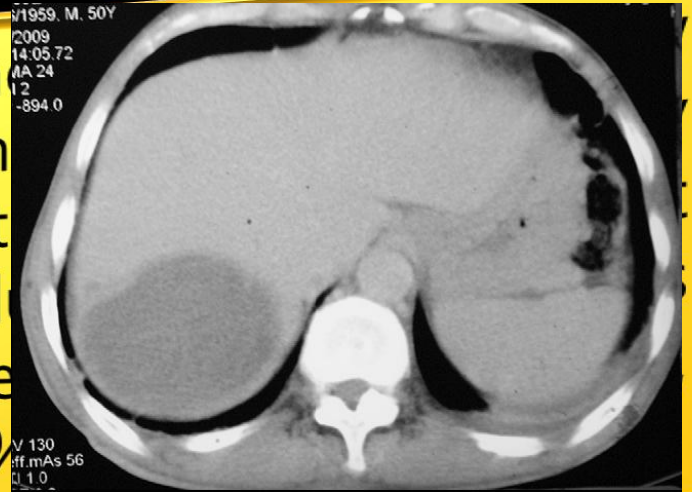


Alveolar echinococcosis which is rare and potentially fatal. *E. multilocularis* is restricted to the northern hemisphere (King *et al.*, 2000)

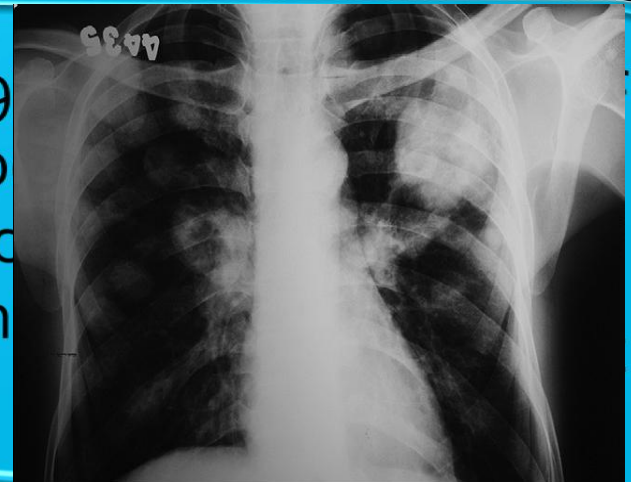


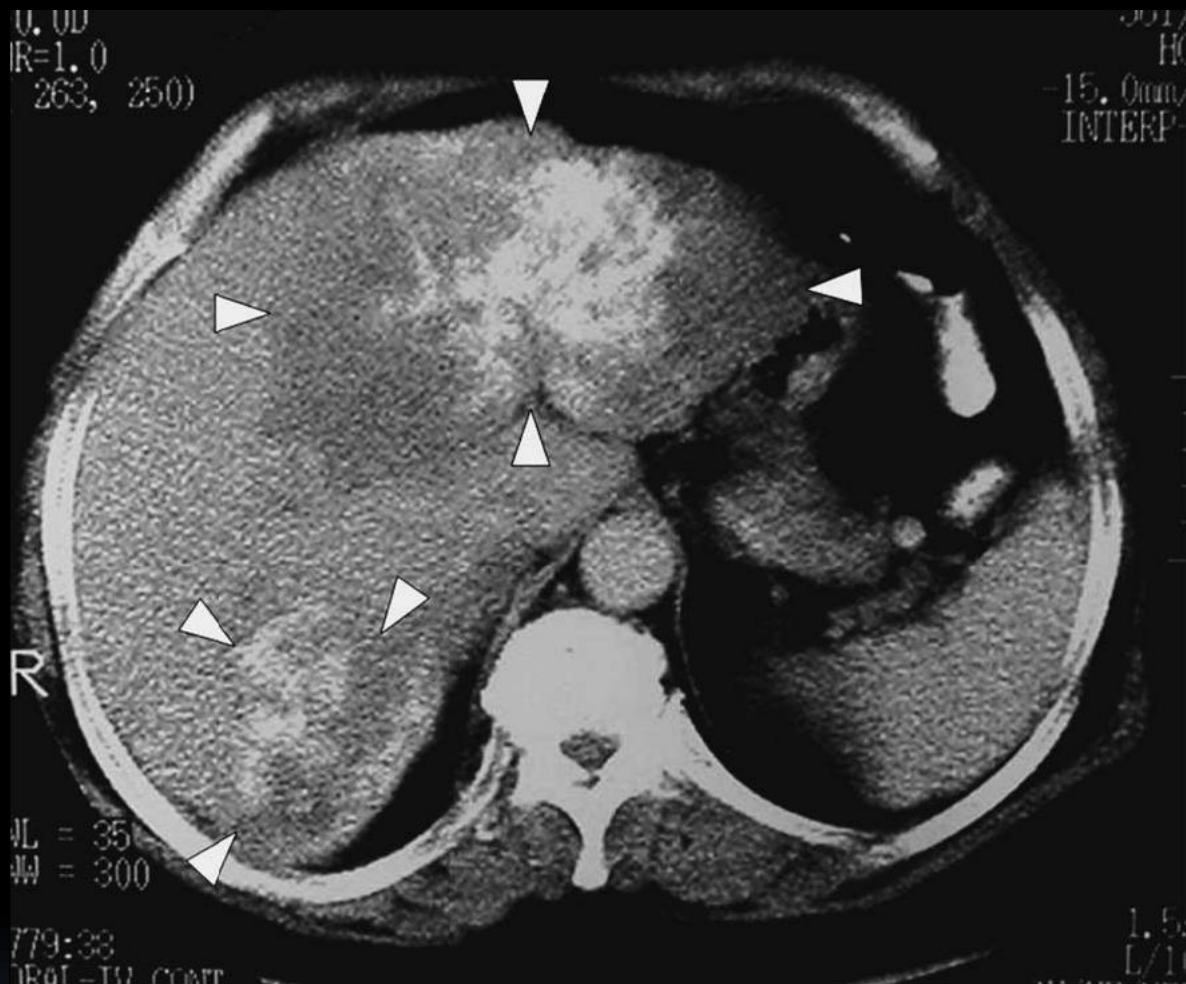
Classification proposed by the WHO Informal Working Group on Echinococcosis (WHO, 2003)

In patients with cystic echinococcosis, single organ involvement and a large cyst. The liver is the most common site of formation, followed by the lungs and other sites (usually the heart, brain and bone) in 10%.

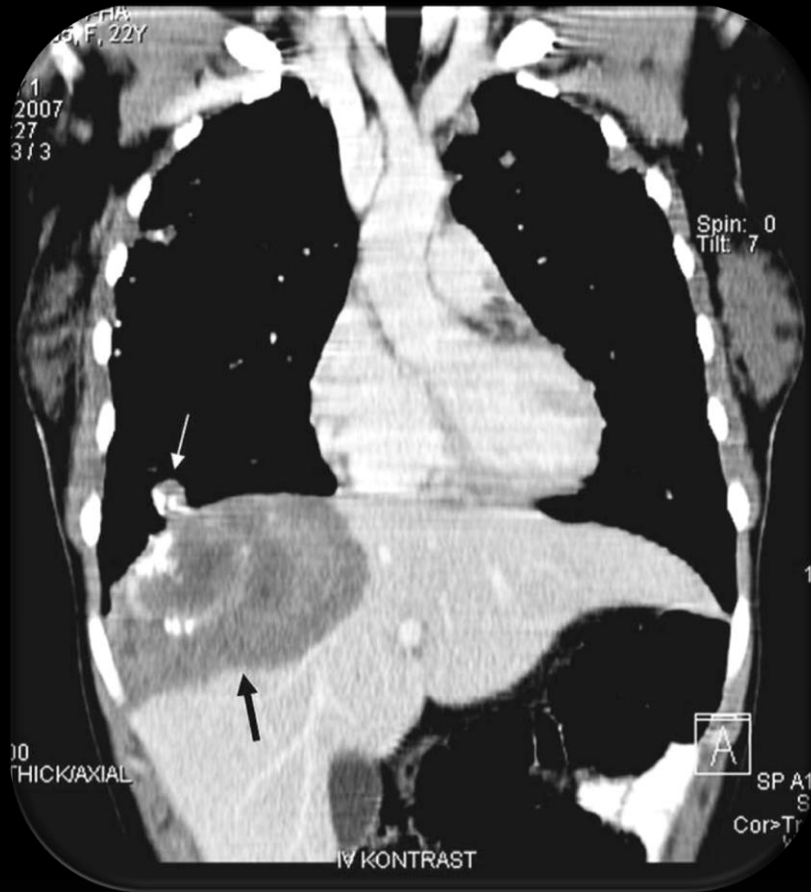


However Havlucu *et al.* (2009) reported multiple innumerable cystic echinococcal lesions in the liver. The multiple *lesions* of cystic echinococcosis in chest X-ray graphy can imitate the malignancy of lung.





Abdominal CT examination reveals two solid lesions (arrowheads) in the right and left lobe of the liver. The lesions have irregular and ill-defined borders secondary to the infiltrative nature of the lesions. Also these have massive calcifications especially in the left lobe. The lesion located in the left lobe infiltrated the left branch of portal vein (Ermis *et al.*, 2007).



Thoracoabdominal CT revealing a large hepatic lesion (black arrow) with internal calcifications and adjacent metastatic calcified subpleural lesion (white arrow) (Ozkok *et al.*, 2008).

Concluding Remarks

CONCLUDING REMARKS

Hydatid cyst is a wide spread disease endemic in rural areas in most parts of the world, particularly the Mediterranean and Middle Eastern countries. Living or having lived in a rural area where animal husbandry is common is still an important risk factor for this disease, but new population migration patterns and improvements in transportation over the past 40 years have caused a change in the profile of this previously unusual disease.

Concluding Remarks

Cystic lesions lend themselves to radiological and ultrasound investigation. Indeed some hydatid disease is found incidentally while investigating other disease. In conclusion, imaging characteristics and/or serological findings may provide the correct diagnosis of hydatid disease at various locations in the human body, but it should be kept in mind that complicated hydatid cysts can cause unusual USG, CT and/or MRI findings, in addition to typical ones (Turgut *et al.*, 2007).

Concluding Remarks

Physicians need to remain aware of its clinical features, diagnosis, treatment and management (Khanfar, 2004). In developed countries where pyogenic liver abscess is more common than hydatid, the diagnosis of the pyogenic abscess is usually confirmed by ultrasound-guided drainage - but hydatid should be considered beforehand in those from high-prevalence areas because of the risk of anaphylaxis when hydatid cysts leak (Cosgrove and Doherty, 2010).



THANK YOU