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The epidemiological aspects of *Entamoeba histolytica* zymodemes

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Accepting that we know the life cycle of *Entamoeba histolytica* in the higher primates, there is then a necessity to endeavour to understand its ability to produce disease.

Primary diagnosis of infection in the host is usually by way of microscopic observation of cysts and/or trophozoites in the stools.

Presence of the parasite does not always parallel clinical presentation. Also treatment regimes initiated to eliminate the organism have in many cases been demonstrated to be unsuccessful.

The presence of the parasite in a host does not always elicit an immunological response. The very strongest possible support for this statement is the published evidence of the lack of clinical amoebiasis in AIDS infected subjects.

These foregoing remarks may appear to be confused or even controversial. However, if it was accepted that there was more than one organism morphologically identifiable as *E. histolytica*, it would then be possible to understand apparent conflicting diagnostic parameters.

It should be remembered that for nearly a century we have known that "Clinical Amoebic Dysentery" is almost invariably accompanied by haematophagus trophozoites in the stools.

By using thin layer starch gel electrophoresis to develop the mobility patterns of -

EC 5319, glucosephosphate isomerase (GPI)

EC 11140, L-malate: NADP⁺ oxidoreductase (oxaloacetate decarboxylating) (ME) EC 2751, phosphoglucomutase (PGM)

EC 2711, hexokinase (HK), SARGEAUNT et al. (1982, 1984, 1987, 1988, etc, etc) have demonstrated a spectrum of profiles for *E. histolytica* and the other intestinal amoebae of man.

Stool containing cysts and/or trophozoites was inoculated into ROBINSON'S medium from which after 48 hr the trophozoites were harvested, lysed and subjected to electrophoresis after which the particular isoenzyme was identified by coupling substrates.

E. histolytica strains are characterized into twenty four different zymodemes (enzyme populations). Of these, ten are known to be associated with clinical amoebiasis, either liver abscess and/or dysentery with haematophagus trophozoites in the stools. Consequently they are regarded as "pathogenic". Twelve strains are associated with asymptomatic infections and are labelled "non-pathogenic". Continuing research using "pathogenic" strains has produced new zymodemes from cloned parents and therefore evidence of genetic exchange in this amoeba.

The definitions for allocating an isolate of *E. histolytica* to a zymodeme are that —

a) The four enzyme systems described must be used.

b) A pathogenic zymodeme should have the absence of an α band in the presence of a β band in PGM.

c) Hexokinase alone does not determine a zymodeme.

The short summary outlined above has now produced sufficient evidence to consider more directly the existence of two "sub species" of *E. histolytica*. Although numerous epidemiological surveys involving thousands of isolates, undertaken in most *E. histolytica* endemic areas of the world corroborate zymodeme characterization of this parasite, just two serve to illustrate most forcibly the precise status of the two organisms.

The epidemiological aspects of *E. histolytica* zymodemes involve many features. The primary consideration is in recognition of a retractable infection in a host. No response to treatment, demonstrated by the continuing presence of the parasite in the stools, indicates in many cases infection with a non-pathogenic *E. histolytica* which can be proven by zymodeme analysis.

A broader aspect is the presence in a population of an increase in the apparent incidence of amoebic infection. Zymodeme characterization will demonstrate the prevalence.

Thirdly, a focus of infection can be easily and quickly identified.

Consideration should also be given to identification of the prevalence of the organism in populations of highly endemic areas, since treatment of subjects in such areas would reasonably only be given to clinical cases.

There is of course no value in treating asymptomatic carriers of non-pathogenic *E. histolytica.* Constant monitoring of the organisms zymodemes in such areas avoids not only overtreatment, but also wastage of large amounts of drugs which for example third world countries cannot afford to buy. This leads to the mention of the most dishonest dumping by pharmaceutical companies of sham drugs, which have led to difficulties in understanding drug regimes.

The problems of treatment of *E. histolytica* infections in subjects receiving steroids can be dramatically answered by knowledge of the amoebic zymodeme. This last point is well illustrated by considering the vast numbers of male homosexuals (20 per cent in London), many of whom have AIDS, and all carrying non-pathogenic *E. histolytica*, some of whom are receiving steroid treatment.

A minor, yet relevant point to make is should nitroimidazoles be given for *E. histolytica* infections in pregnancy. Knowledge of the zymodeme addresses the problem directly.

Knowing the zymodeme profile of any *E. histolytica* infection imported by immigrants can only be regarded as an advantage to the host country.

Summary

All zymodemes of *E. histolytica* can be placed into one of two groups. One group contains all the pathogenic strains and they are synonymous with "Clinical Amoebiasis" (dysentery or liver abscess, etc). The second group contains all the non-pathogenic strains and these are synonymous with "Asymptomatic infections".

TABLE 1	
Zymodeme Distribution of 147 Patients Examined (Durban,	South Africa)

Zymodeme	ł	11	111	V	XI	XIII	XVI	XVIII	Total cases
Amoebic liver cases	_	32	_	_	6	_	_	_	38
Amoebic dysentery		32	_	—	10	—	_	_	42
"Cyst passers"	31	3	26	4	_	1	1	1	67
Totals	31	67	26	4	16	1	1	1	147

TABLE 2 Zymodeme Distribution of *E. histolytica* in Patients Feces After Treatment (Durban, South Africa)

Zymodeme	il	XI
Liver Abcess	3	
Dysentery	3	1

TABLE 3 Zymodeme Distribution in One Family Complex of a Total of 17 Individuals (Takamaka, MAHE, Seychelles)

Sex	Age	Name	No.	<i>E. histolytica</i> zymodeme
M	20	Laval MERITON	S/70	
F	?	Marie MERITON	S/71	H
F	96	Celimen MERITON (ZOUBERT)	S/72	Ш
M	2	* KEIN MERITON	S/76	1
M	7	Clifford MERITON	S/79	111
M	9	Roy MERITON	S/78	IL
F	18	Nadia ALBERT	S/91	III
M	7	Eddison HORTERE	S/82	1
F	24	Marie Alice HORTERE	S/87	1
F	11/2	Nancy ALBERT	S/114	111

* = Tested twice on different specimens and gave same result

In each of the two groups there is a spectrum of zymodeme profiles.

As demonstrated in the latest research these differing profiles are probably related to genetic exchange.

Finally, knowledge of the zymodeme, which is regarded as the very "finger print" of the organism, of any or all *E. histolytica* infections in any population leads to a better understanding of its epidemiological status.



Fig. 1:

Zymodemes of *Entamoeba histolytica* identified using EC 5319 glucose phosphate isomerase (GPI); EC 11140 L-malate: NADP + oxidoreductase (oxaloacetate decarboxylating) (ME); EC 2751 phosphoglucomutase (PGM); and EC 2711 hexokinase (HK).

A zymodeme is a population of amoebae differing from similar populations in the electrophoretic mobility of certain enzyms. The markers for pathogenicity are the absence of the α band together with the presence of the β band in PGM. Advanced bands in HK confirm the PGM results. The only exception is zymodeme XIII which lacks advanced HK bands.

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