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Goal of the lecture:

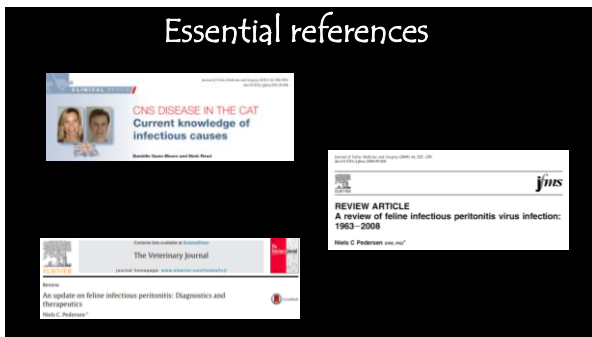
provide an "update" on Feline Infectious Peritonitis (FIP)
focusing on the neurological signs of the disease

INDEX

1. Introduction
2. Etiology and pathogenesis
3. Clinical presentation
4. Diagnosis



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CNS Inflammatory disorder

[pathogenesis of the lesions in the nervous tissue]

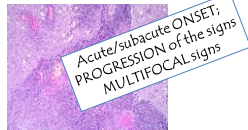
ENCEPHALITIS/ENCEPHALOMYELITIS???

CNS INFLAMMATORY LESION:

- ◊ Leucocytes infiltration in the nervous tissue
- ◊ Changes in the permeability of the blood-brain barrier (BBB)
- ◊ Diffusion through contiguity /blood stream
- ◊ **Multifocal/diffuse lesions**



CLINICAL SIGNS:
Reflect the pathogenesis of the
CNS inflammatory lesions



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CNS disease in the cat: current knowledge of infectious causes.

Gunn-Moore DA, Reed N. J Feline Med Surg. 2011 Nov;13(11):824-36.

"Neurological disease is common in cats – accounting, for example, for approximately 10% of cases in two separate UK-based feline medicine referral clinics. There are many different causes of central nervous system (CNS) disease in cats and about 30–45% of cases are believed to be infectious in origin."

VIRAL

Feline coronavirus (FCoV)
Feline immunodeficiency virus (FIV)
Feline leukaemia virus (FeLV)
Feline panleukopenia virus (FPV)
Rabies virus
Aujeszky's disease virus
Feline herpesvirus-1 (FHV-1)
Borna disease virus (BDV)
Certain arboviruses

FUNGAL

Cryptococcus species
Blastomycetes species
Histoplasma species
Aspergillus species
Dematiaceus fungi

OTHER:

Feline polioencephalomyelitis
Viral non-FIP encephalitides
***non-suppurative meningoencephalitis**
(of unknown cause)
Feline spongiform encephalopathy (FSE)

BACTERIAL and RICKETTSIAL

Pasteurella species S
Laphylococcus species
Other aerobic organisms
Anaerobic organisms
Mycobacteria
Bartonella henselae and related species
Ehrlichia species

PROTOZOAL and PARASITIC

Toxoplasmosis
Cuterebra larval migration
Visceral leishmaniasis (eg. Toxocara)
Sarcocystis species
Dirofilaria immitis

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Main infectious CNS diseases

CNS disease in the cat: current knowledge of infectious causes.
Gunn-Moore DA, Reed N. J Feline Med Surg. 2011 Nov;13(11):824-36.

(92 neurological cases of cats with histopathologic lesions
consistent with a CNS inflammation and/or infection)

Etiology	Number	%
FIP	47	51
Non-FIP "viral" Encephalitides	32	35
Toxoplasmosis	8	9
Bacterial infections	3	3
FIV	1	1
Cryptococcosis	1	1



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2.



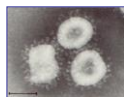
FIP: aetiology and pathogenesis

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FIP



- ♦ Viral disease → Immune-mediated mechanism
- ♦ FATAL disease
- ♦ caused by a feline CORONAVIRUS (FCoV)
- ♦ 2 Biotypes: FECV e FIPV
- ♦ FIPV: effusive ("wet") → not neurologic
"dry" → neurologic
- ♦ Multiorganic syndrome
- ♦ Neurologic multifocal syndrome



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Feline Coronavirus (FCoV)

FECV: enteric biotype, ubiquitous & widely diffuse:
mild, subclinical enteric infection

FIPV: virulent biotype: Immune-mediated disease affecting
individual cats: **Feline Infectious Peritonitis**

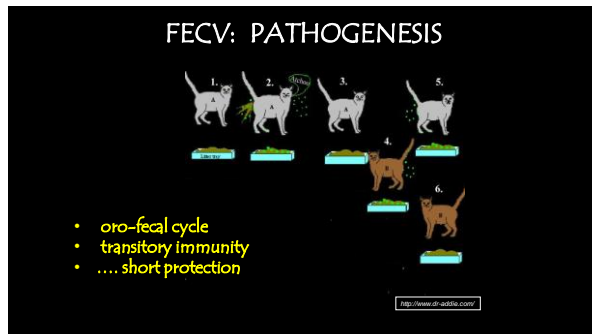
The "killer" FIPV is a variant of the enteric FECV!

MOST ACKNOWLEDGED THEORY:

FIPV originates by **internal mutations** of the viral
genome of the persistently infected host



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FCEV infected cats: what happens then?

1. **Majority of cats: SIS Model** → the cat eliminates the FECV, *develops short duration antibodies* and, after a while, becomes again vulnerable to the infection
2. **~ 13%:** the cat is clinical healthy but becomes a long-life shedder of the virus
3. **~ 4%:** the cat is **resistant** → no virus elimination and no antibodies development
4. **~ 5-10%:** the cat develops FIP:
endemic forms (++)
epidemic forms (-)




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out of 10 FCEV-infected cats, only ONE develops FIP!!



GENETICS?

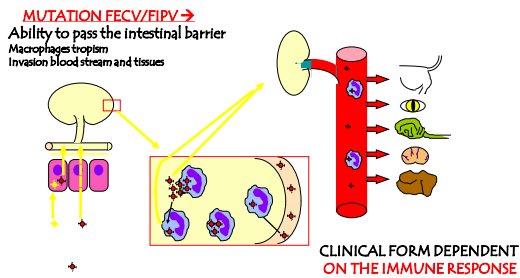
Environmental Predisposing Factors :



- ◊ Overcrowded catteries
- ◊ participation to exhibitions and shows
- ◊ high cats turnover
- ◊ Stress!!

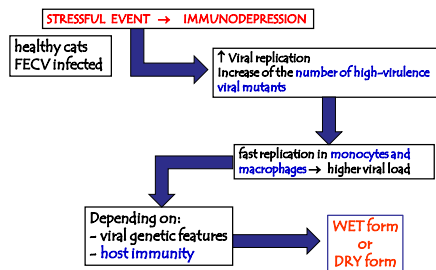
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FIP PATHOGENESIS

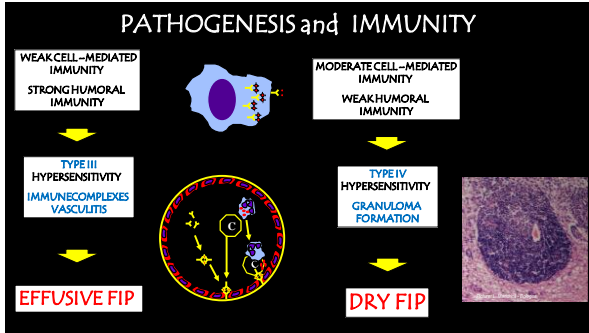


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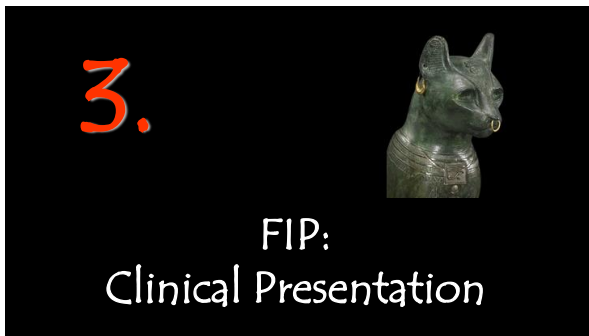
FIP PATHOGENESIS



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CLINICAL PRESENTATION

SIGNALEMENT

AGE: 6 months-5 years; peak after weaning
and between 6-24 months;
other peak between 14-15 years;
AUTUMN and WINTER PERIOD

SEX: NO sex predisposition

BREED: PUREBRED → 'GENETIC SENSITIVITY' or *MODUS VIVENDI?*

environmental factors: →
CATTERIES and STRESSORS



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CLINICAL PRESENTATION

ANAMNESTIC "prerequisites"

- ◊ CONTACT with other cats (till 18 months earlier)
- ◊ STRESSFUL EVENT

ASPECIFIC SIGNS

- ◊ "malaise"; more or less prolonged
- ◊ FEVER; antibiotic-resistant
- ◊ progressive WEIGHT LOSS

SPECIFIC SIGNS

"EFFUSIVE" FORM

"DRY" FORM

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EFFUSIVE FORM

- ◊ ABDOMINAL EFFUSION
- ◊ pleural effusion
- ◊ pericardial effusion

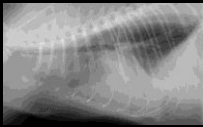


Table 1. Variability in clinical signs of effusive (wet) FIP

Clinical signs referable to involvement of the:	% of affected cats
Peritoneal cavity	98.0
Peritoneal and pleural cavity	22.0
Pleural cavity	11.0
Peritoneal cavity and eyes	2.8
Peritoneal cavity and CNS	1.9
Peritoneal and pleural cavity, CNS	0.9
Peritoneal and pleural cavity, eyes	0.9
Pleural cavity, CNS and eyes	0.9
Peritoneal cavity, CNS, eyes	0.9

Pedersen, JFIM, 2009

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EFFUSIVE FORM

Cat MC by
NRN 692



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EFFUSIVE FORM

Course: 2-5 weeks

- ◊ High Fever, sometimes intermittent
- ◊ Anorexia and weight loss
- ◊ Ascitis (75%) and/or pleural or pericardial effusion (25%)
- ◊ vague gastroenteric signs → jaundice
- ◊ late stage: multi-organ spontaneous hemorrhages (DIC)



EFFUSION:

- ◊ yellowish, sticky
- ◊ marked protein concentration (>35g/l)
- ◊ macrophages and neutrophils
- ◊ < 5 x 10⁶ nucleated cells/exudate ↔
- ◊ Bacterial infections: much more WBCs
- ◊ sterile



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DRY FORM

SIGNS:

non neurological

ABDOMEN:

- ◊ bumpy kidneys
- ◊ enlarged mesenteric lymph nodes
- ◊ jaundice

EYE:

- ◊ retinal hemorrhages
- ◊ uveitis

neurological

- ◊ ataxia 2/4 limbs
- ◊ tetra/paraparesis
- ◊ seizures
- ◊ nystagmus and tremors
- ◊ cranial nerves deficits
- ◊ behavioural abnormalities
- ◊ obtundation → stupor

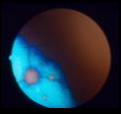
Clinical signs observed in cats with dry FIP	% of affected cats
Jaundice	100
Ascites	100
Enlarged spleen	100
Enlarged kidneys	100
Enlarged mesenteric lymph nodes	100
Enlarged and pale liver	100
Enlarged and pale spleen	100
Enlarged and pale kidneys	100
Enlarged and pale lymph nodes	100
Enlarged and pale thymus	100
Enlarged and pale pancreas	100
Enlarged and pale intestines	100

Pedersen, JFMS, 2009

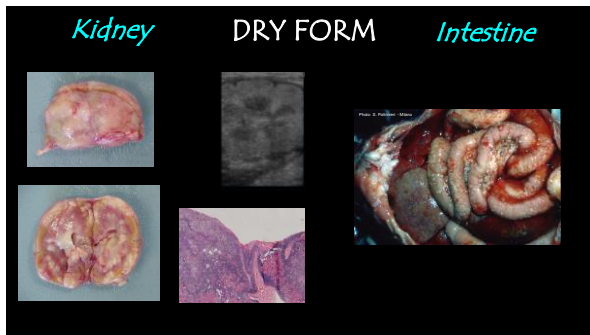
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DRY FORM:

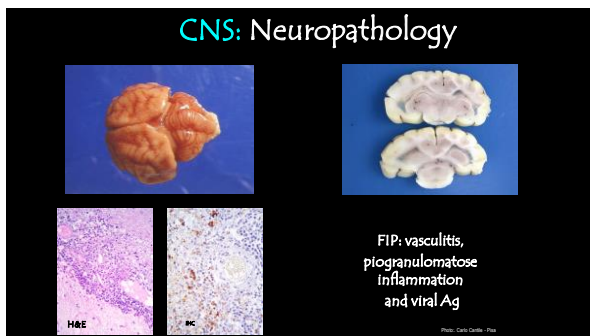
eye



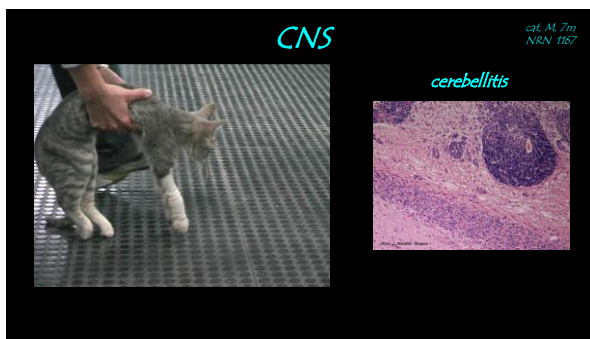
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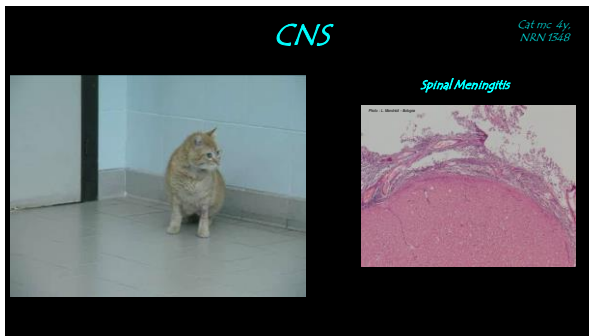
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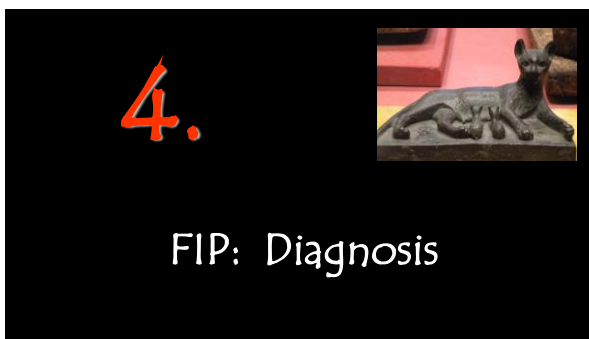
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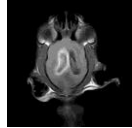


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Diagnostic work-up

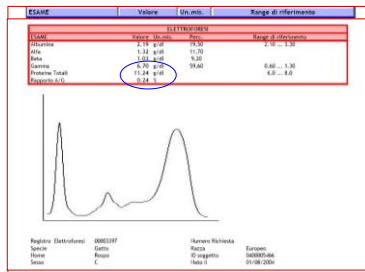
1. Neurologic examination
2. Ophthalmologic examination
3. CBC and hematobiochemical profile
4. Serology
5. Cerebrospinal fluid examination
6. PCR
7. Magnetic Resonance Imaging
8. Neuropathology

**MULTIFACTORIAL
DIAGNOSIS!!!**



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DIAGNOSIS: proteins and electrophoresis



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DIAGNOSIS: serology and PCR

- Most of FIP cases have high Antibodies titers
- Seldom in wet form : negative results
- dry form: high antibodies titers – usually >1280

**Ab titers does not distinguish
between FECV and FIPV!!!**

**PCR from adequate substrate
(CSF, exudates, blood, tissues)**



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DIAGNOSIS: Cerebrospinal fluid

- ◇ Difficult to obtain!!
- ◇ Turbidity
- ◇ Marked mixed pleocytosis
- ◇ Marked protein increase
- ◇ Pandy test markedly positive



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DIAGNOSIS: Cerebrospinal fluid

Quotazioni Studio (Biologia) 6 Venerdì 22/12/2006 Rifer. 01000210011 - 0100000001077

Sette di gestione: Cerebrospinali

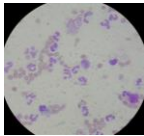
ESAME	VALORE	Un. Mis.	Range di Riferimento
Proteina totale	110.0	mg/dL	0 - 30
Albumine	110.0	mg/dL	7 - 28
Conto cellulare	11.0	/L	0 - 8
Polimorfonucleari	88.0	%	
Mononucleari	12.0	%	
Aspetto	torbido		
Altri	Reattivo		
Turbidità	Prezioso		

Registro Logico: 01000214

Nome: Carlo ID soggetto: 0100014014
Cognome: Carlo Data: 01/01/2001
Sesso: M Stato: 01/01/2001

Stazione Radiologica

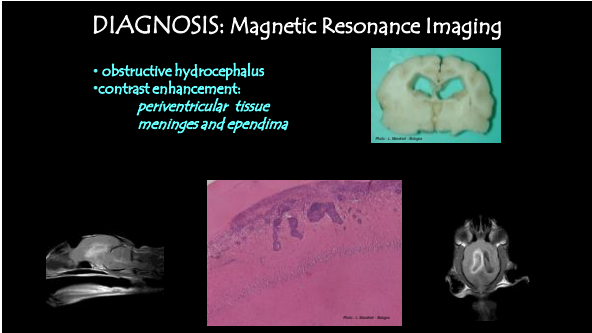
F. no. 10 Responsabile del Laboratorio



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DIAGNOSIS: Magnetic Resonance Imaging

- obstructive hydrocephalus
- contrast enhancement:
periventricular tissue
meninges and ependima



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TREATMENT????



"no treatment has proven effective in curing FIP"

"Currently, **there is no effective treatment for FIP** and mortality is extremely high.

However, the fact that a rare cat appears to make a spontaneous recovery with good supportive care is enough of an impetus to lead owners to try a number of alternative therapies that are touted mainly on the Internet.

Many of these therapies are expensive and come with a high emotional burden. It is important that all such treatments be adequately tested on an adequate number of cats with confirmed disease and in a randomized, placebo controlled and double blinded manner.

The most promising therapies will probably involve drugs that specifically target viral proteins important in viral replication."

(Pedersen, Vet J. 2014)

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A case...just to summarize!



"PACO", cat Mc, 5y, NRN 3324

- since four months, **insidious onset and slow progression of:**
 - mild *gait problems*
 - *tendency to hide and avoid contacts*
- **Recurrent hyperthermia**
- **Weight loss**
- **Normal hematobiochemical exams**
- **Unsuccessful antibiotic treatment**
- In the last month:
 - *aggressive behaviour when touched (pain?)*
 - *crouched gait and weakness*
- **Constant hyperthermia** (from 39° to more than 40°C)
- Therapy with meloxicam
- FeLV/FIV negative



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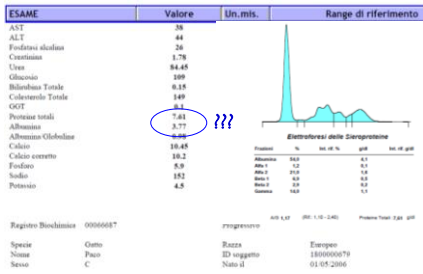
"PACO", Cat Mc, 5y, NRN 3324

.... Neuro exam...



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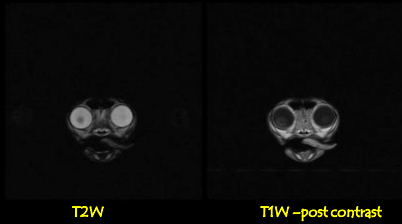
"PACO", Cat Mc, 5y, NRN 3324



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"PACO", Cat Mc, 5y, NRN 3324

Magnetic Resonance Imaging



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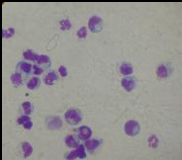
"PACO", Cat Mc, 5y, NRN 3324

Cerebrospinal fluid examination

ESAME	VALORE	Un. mis.	Range di Riferimento
Proteine totali		mg/dl	0 - 30
Albumina		mg/dl	0 - 25
Urea		U/L	0 - 17
Glicemia		mg/dl	0 - 10
Conto cellulare	108		0 - 5

Formula leucocitaria: 10% Polinucleari (granulociti neutrofili), 80% Mononucleari (20% Linfo, 60% Monociti) (cellule citotossiche non presenti)

Colorazione: papanicolaou



N° Accettazione 000000147
Data di arrivo 11/05/2011
Specie Gatto
Razza Europeo
Sesso C
Cod. gata, 1800000479

Campione analizzato: Liquor
Analisi eseguita: Real Time PCR Coronavirus B (POSITIVO)

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"PACO", Cat Mc, 5y, NRN3324

.... 3 days later...



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FIP:



**Take
home message*

- ◊ Cat: infectious disease **more frequent** ↔ dog
- ◊ **Multifocal, progressive signs**
- ◊ **FIP: most represented disease**
- ◊ FIP: viral mutation and immune-dependent pathogenesis
- ◊ FIP: "wet" and "dry" forms
- ◊ FIP: variable **neurologic** and **extra-neurologic signs**
- ◊ FIP – Multifactorial Diagnosis: **electrophoresis, CSF exam, PCR, MRI**
- ◊ FIP: no proven effective treatment

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... questions???



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