Nefrita endemica, de la rar la mai des

Spitalul Clinic Judetean de Urgenta “Pius Branzeu” Timisoara

Clinica de Nefrologie

DR.MARC LUCIANA

DR.CHISAVU LAZAR

MAI 2017

- H.E. 49 ani , Otelu Rosu,CS
- Antecedente H-C: neaga
- Antecedente personale: varice MI drept operate, colon iritabil
- Vanzator de posete de lux

OCTOMBRIE 2019

- D.V. 30ani Timisoara,TM
- Antecedente H-C& P: neaga
- Medic – Centru de recuperare Dezna
- Casa de vacanta – Poiana Marului

DEBUT

- **CLINIC**
  - **12-17.05 – Pneumopatie interstitiala (febra, frison, tuse seaca)→ internare la Spitalul Municipal Caransebes**

- **CLINIC**
  - **24-26.10.2019 Sindrom febril (39C) – 3 zile la domiciliu → Paracetamol**
  - **27-31.10.2019 internare Clinica de Boli Infectioase**

0.7mg/dl **Creatinina serica = in limitele normale** **1,1mg/dl**

TRATAMENT: reechilibrare HE si AB

Cefort 2x1g/zi

- Dupa 5 zile de terapie
  Creatinina serica = 5.4 mg/dl
  Uree serica = 70mg/dl

- Dupa 4 zile de terapie
  Creatinina serica= 5.1mg/dl
  Uree serica = 69mg/dl

CLINICA DE NEFROLOGIE

BIOLOGIC

17.05. leucocite= 8980/dl
trombocite= 112000/dl
proteina C reactiva= 15mg/l
creatinina serica=5.4mg/dl
uree= 96mg/dl
sumar de urina – L -1-2/camp, H-absente,proteine neg
proteinurie/24h= 1.1g/24h
AgHBs,Ac antiHCV, Ac antiHIV –neg

ECO: RD=12.5cm, IP=2.5cm, fara staza fara calculi; RS=14.7cm IP=2.5cm fara staza fara calculi.

BIOLOGIC

31.10 leucocite = 12.000/dl
trombocite = 132000/dl
proteina C reactiva = 46mg/l
creatinina serica = 5.1mg/dl
uree= 69mg/dl
sumar de urina – L -1-2/camp, H-absente, protein neg
proteinuria/24h = 1.267g/24h
AgHBS, Ac antiHCV,Ac anti HIV- neg

ECO: RD=11cm, IP=2,5cm, fara staza, gravela calcara 2mm caliceal superior ; RS=12,5cm IP=2cm fara staza , fara calculi.

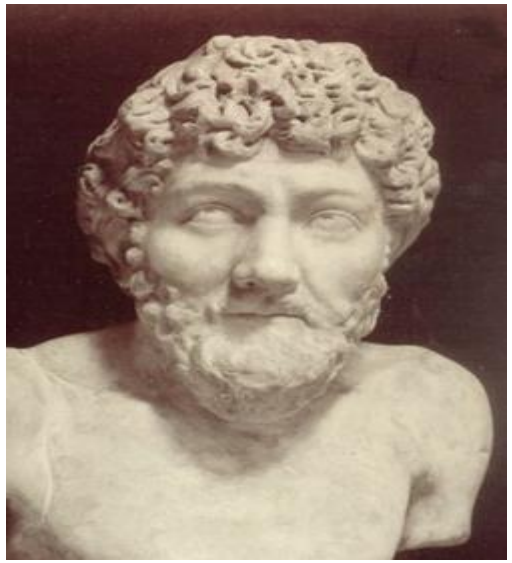
Ce reprezinta cele 2 cazuri pt voi in situatia data?

A) SEPSIS

B) LEZIUNE ACUTA DE RINICHI

C) BOALA CRONICA DE RINICHI

METODA INVINGE GENIUL



ESOP

LA FONTAINE

LEZIUNE ACUTA DE RINICHI AKIN 3

ETIOLOGIE

PRERENALA

NU deshidratare
hipovolemie
cauze de sepsis
sangereaza
LAR **se instaleaza treptat** , in timp, sub supraveghere medicala si terapie in ambele cazuri

RENALA INTRINSECA

POSTRENALA

ECO – rinichi fara staza

LAR DE CAUZA RENALA INTRINSECA - ETIOLOGIE

LEZIUNI DE VASE MARI

ARTERE
- Tromboza
- Embolie
- Anevism disecant
- Takayasu
- Traumatism e

VENE RENALE
- Tromboza (NM)
- Compresiune

- **Lombalgie usoara**
- **Fara elemente clinice /biologice**

LEZIUNI DE VASE MICI

GN/VASCULITE
- ANCA , Ac anti MBG –neg
- Crioglobuline –neg
- LUPUS – absenta criterii SLICC
  - AAN-neg
  - profil ANA –neg
- HUS – nu exista elem clinice sau imunologice (panel bacterii enteropatogene -Neg)

FARA SINDROM NEFRTITIC

NECROZA TUBULARA ACUTA

TOXICA / ISCHEMICA

TOXICE ENDOGENE
- HB
- MIOGLOBIN
- AC.URI

ISCHEMIE SEVERA

XICE EXOGENE
- dicamente-**aminoglicozide**, AINS, chimioterapice
- Otravuri: venin de sarpe, ciuperci
- Etilenglicol, toluene, benzen
- Substanta de contrast

NEFRITE TI ACUTE

- INFECTIOASE
- AUTOIMUNE
- POSTMEDICAMENTOASE
- ETIOLOGIE NEPRECIZATA

NEFRITE TUBULOINTERSTITIALE ACUTE

POSTMEDICAMENTOASE

Cel mai frecvent
BETALACTAMINE (peniciline, cefalosporine)
dar si quinolone, AINS, diuretice, rifampicina

CLINIC: dureri artic, febra, rash
BIOLOGIC: leucociturie sterila, eozinofilie, eozionfilurie .

Clinic - febra
Biologic – fara elemente
DAR
Administarea de Cefort in ambele cazuri !!!!!!

AUTOIMUNE

Lupus eritematos sistemic

CLINIC: criterii SLICC
BIOLOGIC: AAN + , profil ANA+ , C3 scazut

NU exista criterii clinice
Biologic: **profil ANA neg**, **AAN neg**

INFECTIOASE

BACTERIENE: PNA, Leptospiroza, Legioneloza, Scarlatina
VIRALE: citomegalvirus, hantavirus, mononucleoza, febra muntilor Stancosi

CLINIC: **PNA** = dureri lombare, febra ,PDU,
leptospiroza = febra, dureri musculare
BIOLOGIC: **PNA**= leucociturie, bacteriurie, urocutura poz, probe inflamatorii crescute,LAR
leptospiroza = leucocitoza marcata cu neutrofilie, probe infl crescute, LAR, hepatocitoliza

NU exista criterii clinice/biologice de PNA , mononucleoza sau scarlatina

- **Ac antiLeptospira –Neg**
- **Ac anti Borrelia –Neg**
- **IgM CMV –neg**
- **IgM Epstein Bar-neg**
- **Corpocultura-neg**

MAI 2017

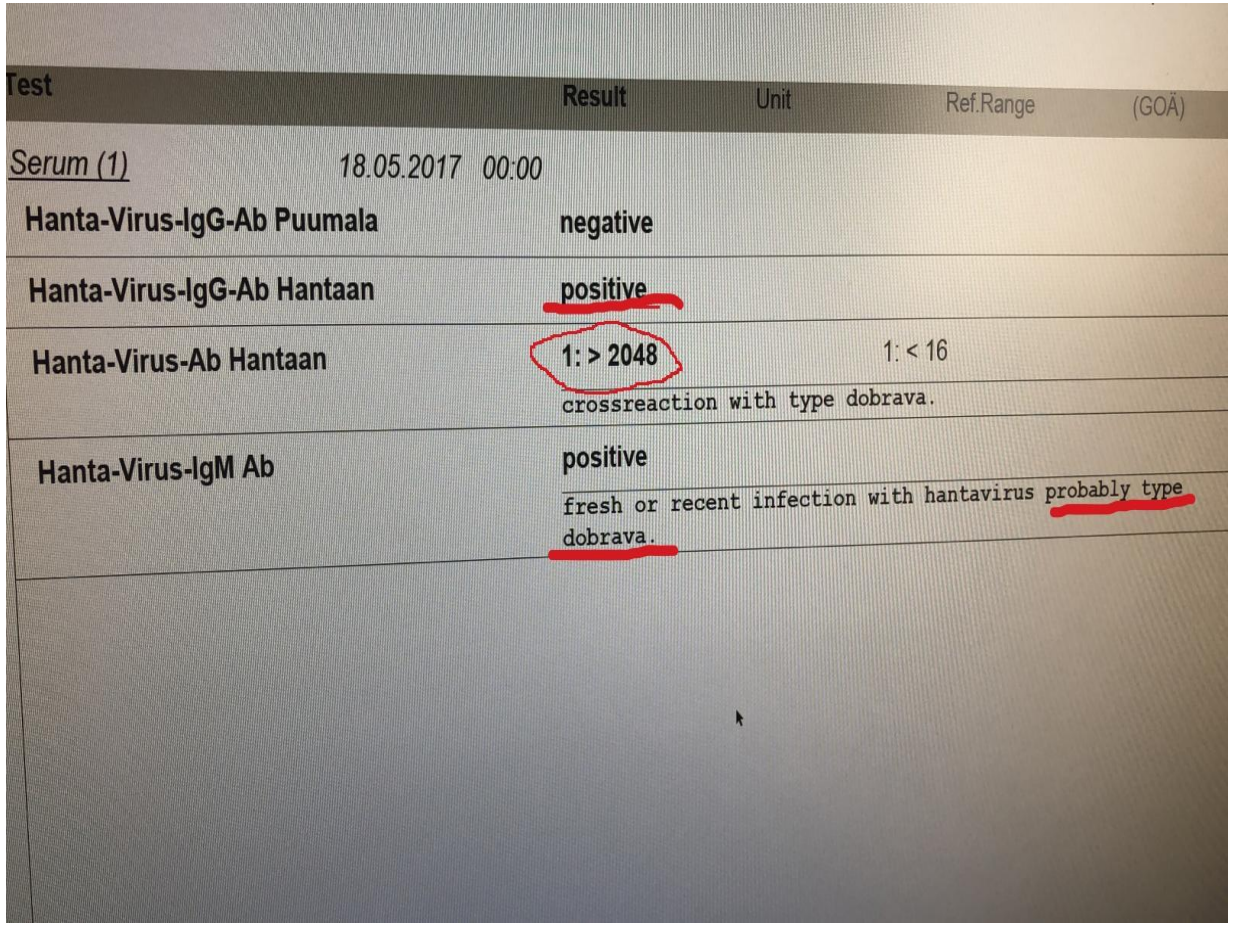
Sindrom febril
+
Manifestare pulmonara de aspect nespecific
+
LAR

SINDROM PNEUMO-RENAL ACUT
FEBRA HEMORAGICA ??????

1. EBOLA
2. FEBRA HEMORAGICA MARBURG
3. HANTAVIROZA

DOZARE ANTICORPI ANTI HANTA

(HEIDELBERG -GERMANIA)



Test	Result	Unit	Ref.Range	(GOÄ)
Serum (1)	*18.05.2017 00:00*			
Hanta-Virus-IgG-Ab Puumala	negative			
Hanta-Virus-IgG-Ab Hantaan	positive			
Hanta-Virus-Ab Hantaan	1: > 2048		1: < 16	
	crossreaction with type dobrava.			
Hanta-Virus-IgM Ab	positive			
	fresh or recent infection with hantavirus probably type dobrava.			

LABORLIMBACH HEIDELBERG

DAkkS

BIOCLINICA

B-dul Cetatii Nr 53b
RO-300358Timisoara, Romania

Laboratory-Report 566153241

Entry / Output 05.11.2019 / 07.11.2019 16:13
Customer
Patient
Patient-Code:
Born
Gender male

Dear Colleague(s)
thank you for your order. Hereby we advise you the following findings:

Analysis	Result	Unit	Ref.Range	GOÄ
1 Serum from 01.11.2019				
Legionella Ab IgM	57	U/ml	< 120	
Hanta-Virus-IgG-Ab Puumala	negative			
Hanta-Virus-IgG-Ab Hantaan	positive			
	examined serotype: Hantaan, Puumala, Dobrava, Seoul, Sin Nombre			
Hanta-Virus-Ab Hantaan	1: 512		1: < 16	
Hanta-Virus-IgM Ab	positive			
	examined serotype: Puumala, Hantaan, Dobrava, Seoul, Sin Nombre			
	Fresh or recent infection with hantavirus type dobrava or hantaan.			

FORME CLINICE

FEBRA HEMORAGICA CU SINDROM RENAL(FHSR)

- Clinic: febra inalta, durere lombara abdominala, hemoragii,petesii, CID,tulburari digestive : greata, varsaturi, diaree
- Biologic : trombocitopenie
  retentie azotata marcata
  sumar de urina “alb”
  proteinurie nefritica
- Tratament: simptomatic(echilibrare HE si AB)
  etiologic – **NU EXISTA**
- Mortalitatea **5-15%**

FORMA FRUSTA

AFECTARE RENALA

SINDROM PULMONAR HANTAVIRAL

- **Clinic: initial**- simptome nespecifice de pneumopatie acuta(febra, firson, mialgii, tuse seaca)
  Dupa aprox 5 zile: brusc acuta, colaps CV, evolutie rapida pre EPA
- Biologic:trombocitopenie
  retentie azotata marcata
  sumar de urina “alb”
  proteinurie nefritica
- Tratament- symptomatic
- Mortalitate **40%**

EVOLUTIE

FAVORABILA

VANZATORUL DE POSETE

- **Normalizarea creatininei serice**
- **Normalizarea aspectului Rx**
- **Fara sechele pulmonare**

MEDICUL

- **Normalizarea creatininei serice**
- **Fara sechele**

Hantavirusurile

- Genul Hanta face parte din **familia Bunyaviridae**, o familie de peste 300 de virusuri care **infecteaza animale, oameni, plante si artropode**;

- Se impart in virusuri asociate cu **Lumea Veche** si cu **Lumea Noua**, in functie de regiunea geografica, vectorul animal si tipul de manifestare umana a infectiei, respectiv **febra hemoragica cu sindrom renal** (HFRS) sau **Nefropatia endemica** si **sindrom pulmonar hantaviral** (HPS).

TABLE 1. Geographic distribution of and disease associated with Old World and New World strains of hantavirus

Group and subfamily	Virus isolate or strain	Abbreviation[a]	Geographic distribution	Rodent host	Associated disease
Old World					
Murinae	Hantaan virus	HTNV	China, South Korea, Russia	*Apodemus agrarius*	HFRS
	Dobrava-Belgrade virus	DOBV	Balkans	*Apodemus flavicollis*	HFRS
	Seoul virus	SEOV	Worldwide	*Rattus*	HFRS
	Saaremaa virus	SAAV	Europe	*Apodemus agrarius*	HFRS
	Amur virus	AMRV	Far East Russia	*Apodemus peninsulae*	HFRS
	Soochong virus	—	South Korea	*Apodemus peninsulae*	Unknown
Arvicolinae	Puumala virus	PUUV	Europe, Asia, and Americas	*Clethrionomys glareolus*	HFRS/NE
	Khabarovsk virus	KHAV	Far East Russia	*Microtus fortis*	Unknown
	Muju virus	MUJV	South Korea	*Myodes regulus*	Unknown
	Prospect Hill virus	PHV	Maryland	*Microtus pennsylvanicus*	Unknown
	Tula virus	TULV	Russia/Europe	*Microtus arvalis*	Unknown
	Isla Vista virus	ISLAV	North America	*Microtus californicus*	Unknown
	Topografov virus	TOPV	Siberia	*Lemmus sibericus*	Unknown

New World					
Sigmodontinae	Sin Nombre virus	SNV	North America	*Peromyscus maniculatus*	HPS
	Monongahela virus	MGLV	North America	*Peromyscus leucopus*	HPS
	New York virus	NYV	North America	*Peromyscus leucopus*	HPS
	Black Creek Canal virus	BCCV	North America	*Sigmodon hispidus*	HPS
	Bayou virus	BAYV	North America	*Oryzomys palustris*	HPS
	Limestone Canyon virus	—	North America	*Peromyscus boylii*	Unknown
	Playa de Oro virus	—	Mexico	*Oryzomys couesi*	Unknown
	Catacamas virus	—	Honduras	*Oryzomys couesi*	Unknown
	Choclo virus	—	Panama	*Oligoryzomys fulvescens*	HPS
	Calabazo virus	—	Panama	*Zygodontomys brevicauda*	Unknown
	Rio Segundo virus	RIOSV	Cost Rica	*Reithrodontomys mexicanus*	Unknown
	Cano Delgadito virus	CADV	Venezuela	*Sigmodon alstoni*	Unknown
	Andes virus	ANDV	Argentina, Chile	*Oligoryzomys longicaudatus*	HPS
	Bermejo virus	BMJV	Argentina	*Oligoryzomys chocoensis*	HPS
	Pergamino virus	PRGV	Argentina	*Akodon azarae*	Unknown
	Lechiguanas virus	LECV	Argentina	*Oligoryzomys flavescens*	HPS
	Maciel virus	MCLV	Argentina	*Bolomys obscurus*	HPS
	Oran virus	ORNV	Argentina	*Oligoryzomys longicaudatus*	HPS
	Laguna Negra virus	LANV	Paraguay, Bolivia, Argentina	*Calomys laucha*	HPS
	Alto Paraguay virus	—	Paraguayan Chaco	*Holochilus chacoensis*	Unknown
	Ape Aime virus	—	Eastern Paraguay	*Akodon montensis*	Unknown
	Itapúa virus	—	Eastern Paraguay	*Oligoryzomys nigripes*	Unknown
	Rio Mamore virus	—	Bolivia, Peru	*Oligoryzomys microtis*	Unknown
	Araraquara virus	—	Brazil	*Bolomys lasiurus*	HPS
	Juquitiba virus	—	Brazil	*Oligoryzomys nigripes*	HPS
	Jaborá virus	—	Brazil, Paraguay	*Akodon montensis*	

APODEMUS AGRARIUS (Hantaan)

APODEMUS FLAVICOLLIS (Dobrava)

CLETHIRIONOMYS GLAREOLUS (Pumaala)

Ecologie

- Riscul de infectie se coreleaza cu numarul rozatoarelor din acea zona;
- Are evolutie ciclica;
- In Europa temperata, varful incidentei Hantavirozelor este maxim in “anii catarg”- anii cu productie mare de nuci.
- Infectia se transmite orizontal.

- Contactul cu excremente, urina sau saliva rozatoarelor;
- Prin aerosoli;
- Virusul supravietuieste intre 14 si 40 de zile in mediul extern;
- Risc crescut la: agricultori, padurari, taietori de lemne, fermieri, constructori, plimbari in padure, etc…

Epidemiologie

- Peste 35.000 de cazuri de infectie cu H. Puumala raportate in Europa pana in 2006 (95% dupa 1990);
- 24.000 de cazuri in Finlanda
- Peste 1000 de cazuri in nordul Suediei, Germania (Baden, Bavaria), Norvegia, Franta si Belgia (zona endemica Ardennes)
- In Balcani, numeroase epidemii in 1995- razboaiele Iugoslave (354 cazuri), in 2002 si 2005;

- In Romania, in anul 2015, s-au raportat 19 cazuri suspecte de Hantavirus, dintre care s-au confirmat 6, toate in regiunea Moldovei, cate 1 caz in Vrancea si Neamt si 4 cazuri in Iasi.

- Varful de incidenta se afla primavara, in august (vacante) si noiembrie-decembrie - cea mai mare densitate de rozatoare;

- Raport barbati:femei 2:1;

- In Romania in 2015, toti cei 6 au fost barbati si au provenit din mediul rural.

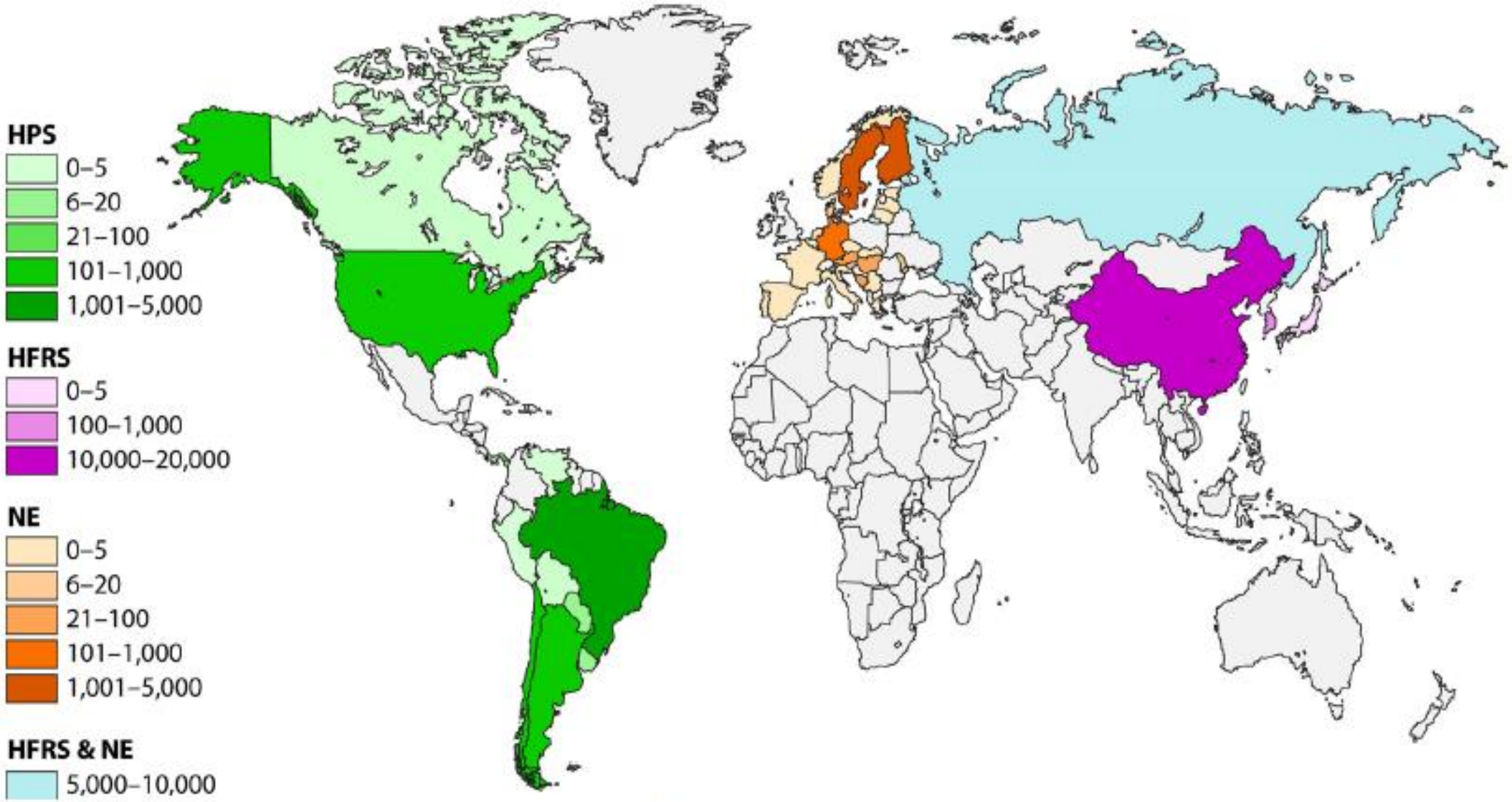
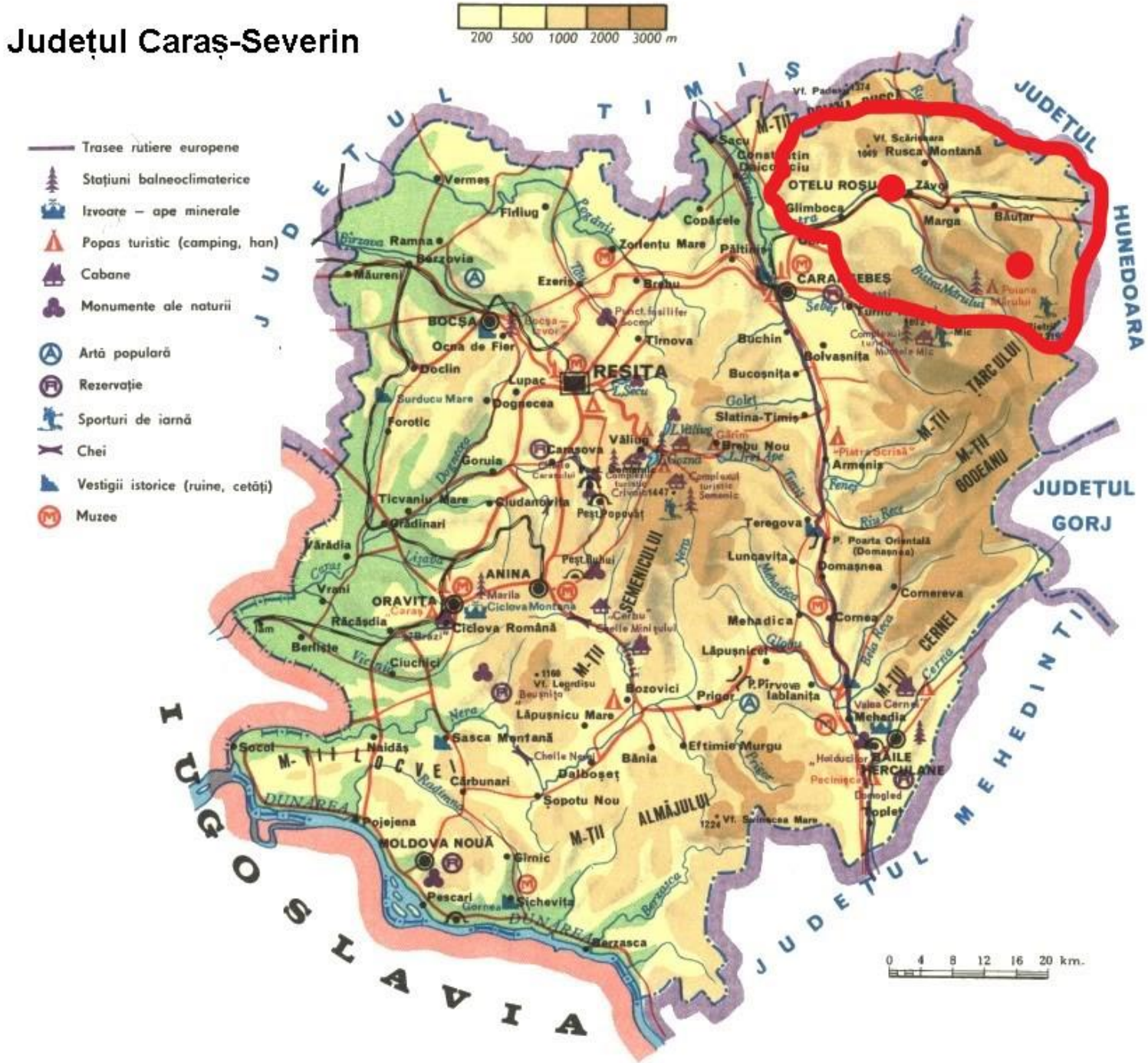


FIG. 3. Geographical representation of approximate hantaviral disease incidence by country per year. (Courtesy of Douglas Goodin, Kansas State University; reproduced with permission.)

Județul Caraș-Severin



Evolutia clinica

- Perioada de incubatia: 3 saptamani (6-42 zile)
- Infectie generalizata, cu spectru clinic care variaza de la forme subclinice-forme letale;
- Clasic, febra hemoragica cu sindrom renal (nefropatia endemica) are 5 etape: febra, hipotensiune, oligurie, poliurie si de recuperare.
- Rata de deces: 0,1% Puumala, 12-15% Dobrava (din cazurile spitalizate), 15% Hantaan;

TABLE 2. Occurrence of different signs, symptoms, and laboratory findings for patients with serologically confirmed HFRS and HPS

Finding[a]	Occurrence (%) in patients with[b]:				
	HTNV	SEOV	PUUV	SNV	ARAV
Fever	100	100	99–100	100	100
Dyspnea					87
Tachycardia					81
Shock					33
Headache	86–87	89	85–100	71	47
Abdominal pain	85–92	68	64–67	24	NA
Backache	91–95	85	82	29	NA
Nausea	82–91	61	78–83	71	25
Dizziness	50	52	12–25	41	NA
Petechiae	32–94	48	12	0	NA
Minor bleeding	37	7–20	11	NA	9
Internal hemorrhages	34	13	NA	NA	NA
Cough	31	14	60	71	54
Hypotension	80	17	1–2	50	56
Myopia	57	NA	12–31	NA	NA
Arthralgia	NA	NA	0–15	29	NA
Oliguria	60–67	37	54–70		
Polyuria	92–95	63	97–100	40	NA
Leukocytosis	91	69	23–57	95–100	67
Thrombocytopenia	78	83	52–75	100	93
Hematocrit					70
Proteinuria	100	94	94–100	40	NA
Hematuria	85	73	58–85	57	NA
S-creatine	97	83	Yes	No	51
Mortality	5–10	<1	0	40	54

Puumala

- Debut abrupt cu febra, cefalee, dureri abdominale, uneori diaree sau varsaturi;
- Uneori sunt prezente fenomene cerebrale cu ameteli, somnolenta.
- Miopia instalata brusc este semn patognomic de nefropatie endemica - 30% din cazuri.
- Cazurile severe- hipotensiune sau soc.
- Semne de afectare renala care apar din ziua 3-4 manifestate prin: oligurie, anurie, crestere de creatinina, proteinurie, necesitatea hemodializei (5%).

- In a 2-a saptamana de boala apare poliuria;

- Pot aparea infiltrate pulmonare, aritmii, petesii, iar la copii glomerulonefrita mezangio-capilara;

- Tipice pentru Puumala sunt:
  - Proteinuria
  - Cresterea proteinei C reactive
  - Trombocitopenia
  - Leziune acuta de rinichi

  Dupa un episod de nefropatie epidemica, creste riscul prezentei proteinuriei tubulare si a hipertensiunii arteriale la 6 ani.

Hantaan

- Tablou clinic asemanator cu cel din infectia cu subtipul Dobrava
- Mult mai des:
  - Soc cardiogen
  - Hemoragii severe
  - Diselectrolitemii
  - Leziune acuta de rinichi
  - Edem pulmonar
  - Petesii
  - Hipotensiune urmata de hipertensiune arteriala

Dobrava

- Tabloul clinic se aseamana cu cel din infectia cu subtipul Puumala, insa este mai sever;
- Complicatii hemoragice, chiar soc hemoragic (28%);
- Oligurie (47%);
- Ascita si pleurezie;
- Sechele neurologice severe.

Diagnosticul paraclinic

- Prezenta anticorpilor IgG si IgM impotriva proteinei N sunt detectabili inca de la aparitia simptomelor.
- Metoda ELISA inventata de CDC detecteaza anticorpii in 4-6 ore.
- Genomul hantaviral poate fi detectat prin metoda RT-PCR in 12-24 de ore.
- **Bioclinica- anticorpi IgG anti Puumala, IgG anti Hantaan, anticorpi IgM anti Hanta- 247lei (rezultat in maxim 10 zile lucratoare)**

Tratament

- La ora actuala nu exista vaccinuri, antivirale sau imunoterapii pentru tratamentul infectiilor cu Hanta aprobate de FDA;

- Ribavirina, administrata in prima saptamana de simptomatologie, la pacientii cu febra hemoragica si sindrom renal, scade mortalitatea de 7 ori, scade rata de aparitie a leziunii acute de rinichi dar nu are efect asupa sindromului pulmonar hantaviral.

- Tratamentul suportiv este esential:
  - Oxigenare adecvata
  - Control tensional
  - Intubare si ventilatie mecanica
  - Tratamentul aritmiilor
  - Evitarea hiperhidratarii
  - Initierea hemodializei

Preventia

- Controlul numarului de rozatoare – stimularea pradatorilor naturali;

- Deratizarea locuintelor;

- Evitarea contactului cu rozatoarele si cu exrementele, saliva sau urina acestora.

Va multumim!