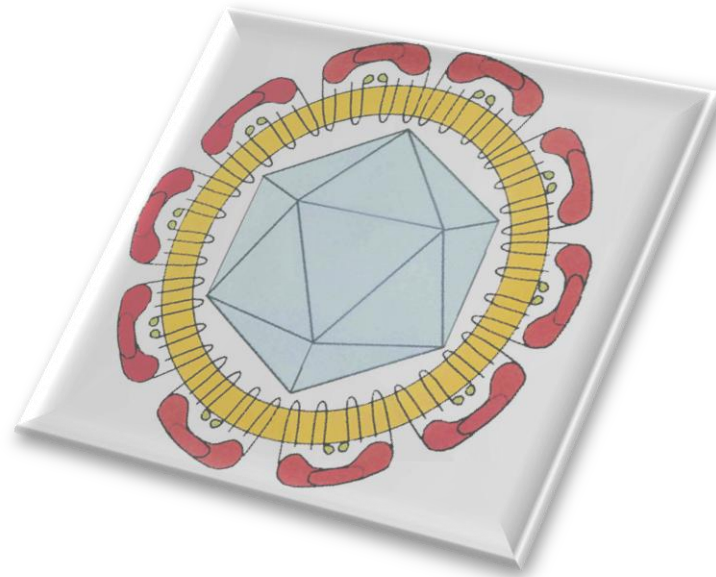
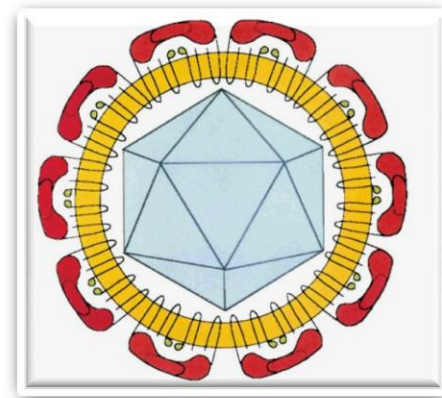


Tick-borne Encephalitis



TICK-BORNE ENCEPHALITIS



- Agente (TBEV), famiglia *Flaviviridae*
- Malattia dell'uomo che colpisce il sistema nervoso centrale (meningite, encefalite, meningoencefalite), con sequele neuropsichiatriche permanenti in $\pm 20\%$ dei casi. Talvolta semplice sindrome febbrile
- Trasmessa da zecche (*Ixodes ricinus* principale vettore in Italia), che fungono da vettori e da reservoir, con trasmissione transtadiale e transovarica (quest'ultima di limitata importanza
➔ ruolo secondario delle larve nella trasmissione)

TICK-BORNE ENCEPHALITIS

L'infezione umana avviene tramite morso di zecca; tramite consumo di latte crudo di animali (ovi-caprini, bovini) infetti; in lab.

Non vi è trasmissione interumana (segnalato 1 caso di trasmissione transplacentare)

Ospiti principali: microroditori selvatici, ruminanti selvatici e domestici

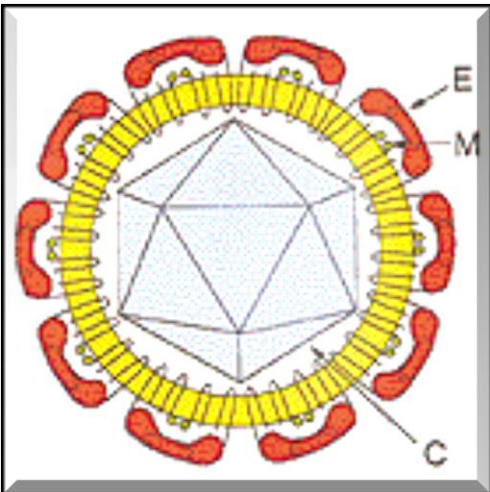
Diffusione: Europa, Asia (3 sottotipi: European, Siberian, Far Eastern)

TICK-BORNE ENCEPHALITIS

10000 casi umani / anno, 3000 in Europa occidentale

Diffusione: Europa, Asia (3 sottotipi: European, Siberian, Far Eastern)

Singola open reading frame (ORF) codificante per 3 proteine strutturali (E, envelope; C, capside; M, membrana) e 7 proteine non strutturali (NS1, NS2A, NS2B, NS3, NS4A, NS4B, NS5)



La glicoproteina E dell'envelope è responsabile della formazione di Ab neutralizzanti e dell'instaurarsi di una risposta immunitaria protettiva. La variabilità aminoacidica intra-sottotipo è bassa (2%), quella tra sottotipi più elevata (3% - 5%) e condiziona un diverso comportamento sia dal punto di vista ecologico (diverso vettore), sia dal punto di vista clinico (TBEv-Sib e TBEv-FE più patogeni)



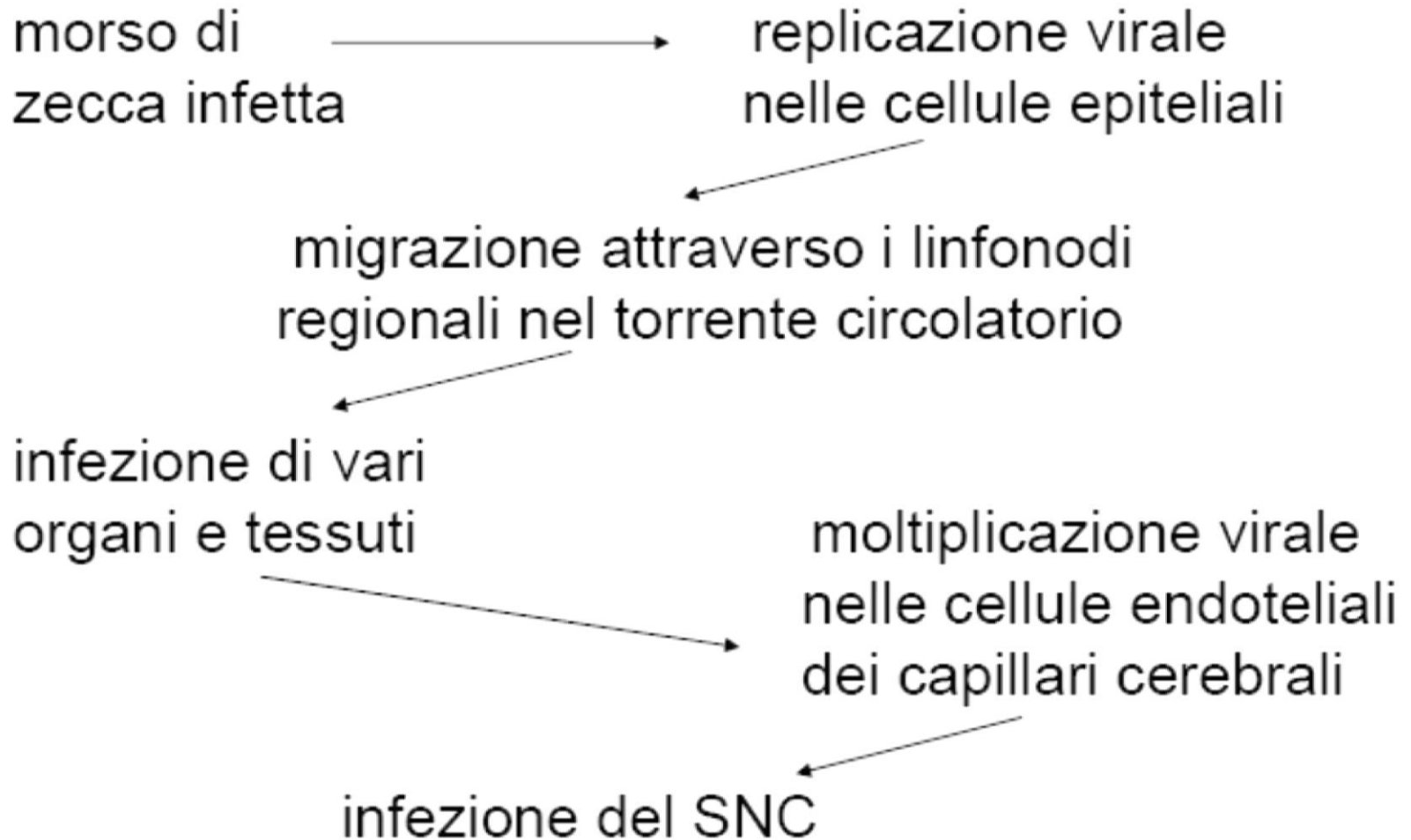
TICK-BORNE ENCEPHALITIS

- **Tempo di incubazione 7 – 14 gg.**
- **Andamento bifasico: prima fase febbrile (2 – 4 gg) in concomitanza viremia, segue dopo \pm 8 gg nel 20-30% dei casi una seconda fase con coinvolgimento del SNC. Letalità \pm 1%**
- **Profilassi: protezione dal morso di zecca; vaccinazione (Ticovac/Ticovac Junior, vaccino spento, 3 dosi) per persone esposte a rischio**
- **Diagnosi diretta: PCR; indiretta: HI, ELISA (cross-rettività con *Flavivirus*)**

Vaccine	Schedule	Rapid Schedule	Length of protection	Age range
TicoVac (Baxter) 0.5ml	3 doses on days 0, between 1 and 3 months later and then between 5 and 12 months after the second dose	2nd dose can be given 2 weeks after the 1st dose	*First booster no more than 3 years after 3rd dose. After this, boosters may be given at 3 - 5 year intervals if at risk	Persons at least 16 years of age
TicoVac (Baxter) 0.25ml Junior	3 doses on days 0, between 1 and 3 months later and then between 5 and 12 months after the second dose	2nd dose can be given 2 weeks after the 1st dose	First booster no more than 3 years after 3rd dose. After this, boosters may be given at 3 - 5 year intervals if at risk	Children above 1 year of age and below 16 years of age

***In those aged > 60 years, booster intervals should not exceed three years**

TICK-BORNE ENCEPHALITIS: PATOGENESI

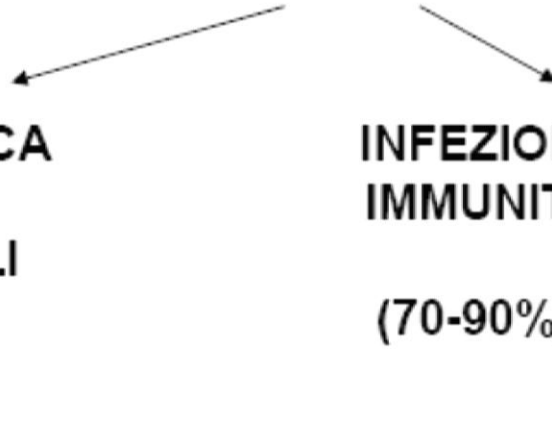


MORSO DI ZECCA INFETTA

**FASE PRODROMICA
SINTOMI
SIMILINFLUENZALI
(10-30%)**

**INFEZIONE ASINTOMATICA CON
IMMUNITA'
(70-90%)**

MANIFESTAZIONI CLINICHE



MANIFESTAZIONI CLINICHE

```
graph TD; A[MANIFESTAZIONI CLINICHE] --> B[MENINGITE (43-55%)]; A --> C[ENCEFALITE (40-50%)]; A --> D[MENINGOENCEFALITE O MENINGOENCEFALORADICOLITE (10-15%)];
```

MENINGITE
(43-55%)

ENCEFALITE
(40-50%)

**MENINGOENCEFALITE O
MENINGOENCEFALORADICOLITE**
(10-15%)

TBE - EPIDEMIOLOGIA

- zecche *vettori e reservoir* di TBEV (*Ixodes ricinus* vettore di TBEv-Eu, *I. persulcatus* vettore di TBEv-Sib e FE)
- rimangono infette tutta la vita
- trasmettono alla progenie
- piccoli roditori ospiti principali di TBEV
- tasso di infezione medio delle zecche 0.1% con punte max 1%
- La distribuzione della TBE in Europa è associata alla dinamica stagionale della zecca e alle particolari caratteristiche della superficie del terreno in termini di vegetazione e temperatura

TBE - EPIDEMIOLOGIA

Alcuni fattori condizionanti la trasmissione della TBE:

- densità di popolazione delle zecche e dei loro ospiti**
- presenza di nuovi ospiti suscettibili**
- % di ospiti immuni**
- caratteristiche del biotopo**
- temperatura**
- cambiamenti sociali**

TBE - EPIDEMIOLOGIA

Trasmissione del virus dal vertebrato alla zecca

- trasmissione possibile solo durante la fase viremica e a certi titoli virali
- per la maggior parte degli ospiti animali TBEV è apatogeno (talvolta encefalite nel cane)
- gli ospiti infetti sviluppano anticorpi e restano immuni per la vita

Trasmissione del virus dal vertebrato alla zecca

- ospiti con viremia di una certa durata e con titoli virali elevati
- un numero sufficiente di nuovi ospiti suscettibili

- ospiti di grosse dimensioni per il mantenimento di un elevato numero di zecche

Vertebrate hosts of *Ixodes ricinus* which may transmit the virus – Wild animals



Ticks can become airborne: they bite birds and bats.



Many ground-dwelling animals attract ticks: various species of mice and lizards.



Hosts below and above ground could be: mole, weasel, marten, badger, porcupine, squirrel.



Predators and prey alike attract ticks: insectivores like hedgehog or shrew, but also fox and hare.



Ticks also feed on larger mammals: wild boar, mouflon, roe deer and red deer.

Ruolo delle diverse specie animali nell'epidemiologia della TBE



viremia 2-8 giorni con alti titoli, ospiti più probabili trasmettitori alle zecche



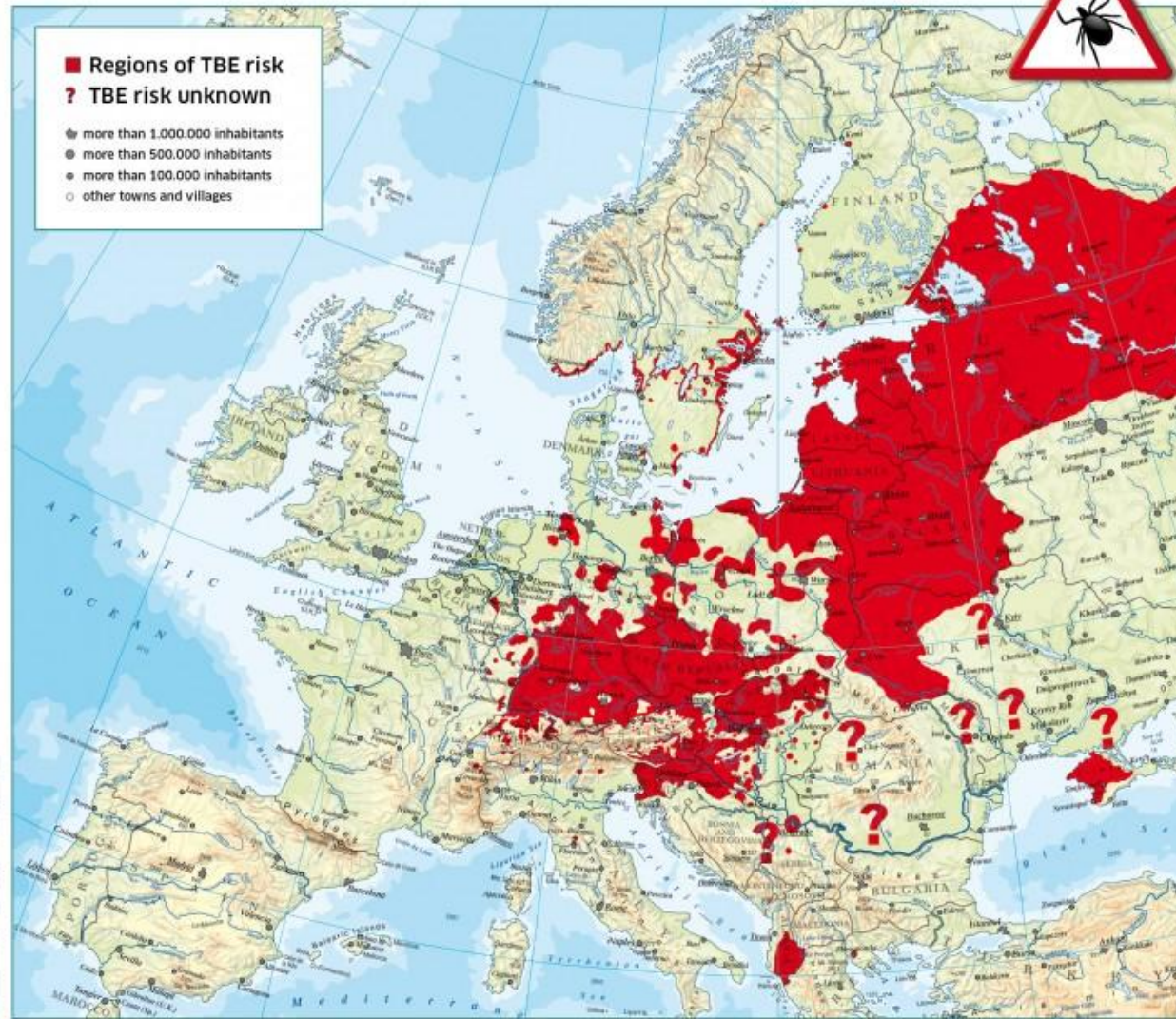
viremia breve ma in grado di "nutrire" molte zecche



nessun ruolo come reservoir ma in grado di mantenere le popolazioni immature

TBE*/FSME in Europe 2011

* Tick-Borne Encephalitis/Frühsummer-Meningoencephalitis



The extent of epidemiological assessment of TBE cases varies between countries. The data presented here may therefore not be entirely complete, and it cannot be excluded that TBE viral infection - with subsequent development of the disease - will occur in new areas. This map is based on documented cases of TBE virus infection as reported by WHO and national health institutions. Last updated: December 2011. Baxter AG, Industriestraße 67, 1221 Vienna, Austria

The map is a service by Baxter.

BS-VA-436 December 2011

Number of reported cases of TBE from various European countries and Russia:

Country	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Austria ^m	89	128	84	102	178	109	128	99	62	41	60	54	60	82	54	100	84	45	86	79
Croatia	23	60	27	76	87	59	57	25	24	26	18	27	30	36	38	28	20	12	20	0
Czech R. ^m	193	356	338	629	613	744	571	415	422	490	719	411	647	606	500	642	1,029	542	630	816
Denmark									1	4	3	1	1	4	8	4	0	2	1	1
Estonia ^m	37	68	163	166	177	175	177	404	387	185	272	215	90	237	182	164	171	140	90	179
Finland	9		14	25	16	23	10	19	17	12	41	33	38	16	31	17	18	20	23	26
France	2	1	2	5	4	6	1	1	2	5	0	0	2	6	7	0	6	6	10	0
Germany ^m		44	142	118	306	226	114	211	148	115	133	253	226	278	274	431	546	238	285	314
Hungary ^m	222	288	206	329	258	234	224	99	84	51	45	76	80	114	59	90	115	170	53	55
Italy			2	2	8	6	8	8	11	5	15	19	6	14	23	22	14	4	34	32
Latvia ^m	122	227	287	791	1,366	1,341	716	874	1,029	350	544	303	153	365	251	142	170	171	181	328
Lithuania ^m	9	14	17	198	284	426	309	645	548	171	419	298	168	763	425	242	462	234	220	617
Norway ^m									1	1	2	1	2	1	3	0	5	12	9	8
Poland ^m	8	4	8	249	181	267	257	201	209	101	170	205	126	339	262	174	316	233	202	335
Russia ^m	5,486	5,225	6,301	7,893	5,596	5,982	9,548	6,539	6,987	9,955	5,931	6,339	5,150	4,770	4,235	4,551	3,510	3,098	2,817	3,721
Slovak R ^m	14	24	16	51	60	89	101	76	54	57	92	76	62	74	70	28	91	46	77	71
Slovenia ^m	235	245	210	194	762	260	406	274	136	150	190	260	262	275	204	297	445	196	246	307
Sweden ^m	54	75	83	51	116	68	44	76	64	53	133	128	105	105	160	130	163	190	224	211
Switzerland ^m	26	37	66	44	97	60	62	123	68	112	91	107	53	116	138	206	259	113	127	118

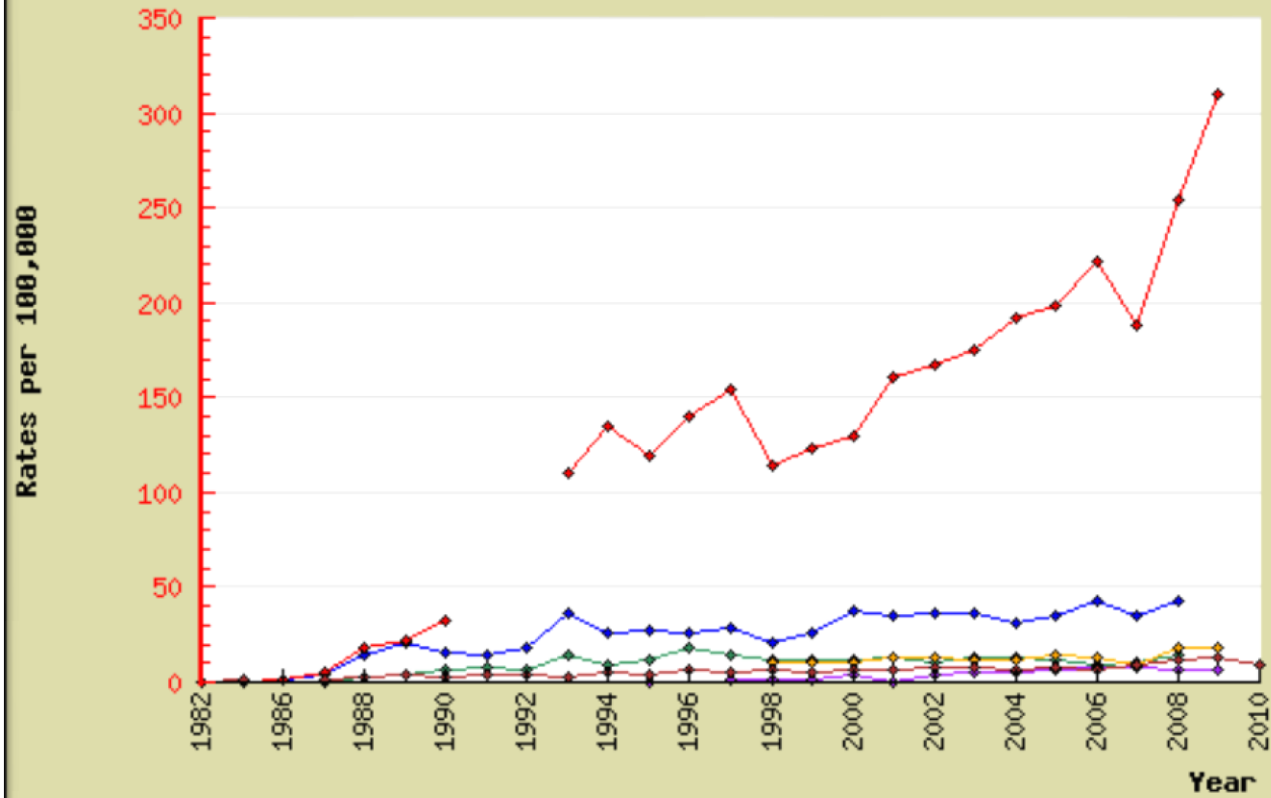
Number of reported TBE cases 1990-2007, Stas J.

Tick borne encephalitis in Europe and beyond – the epidemiological situations as of 2007. Euro Surveill 2008; 13

Number of reported TBE cases 2008 and 2009: Personal communication, Prof. J. Stas

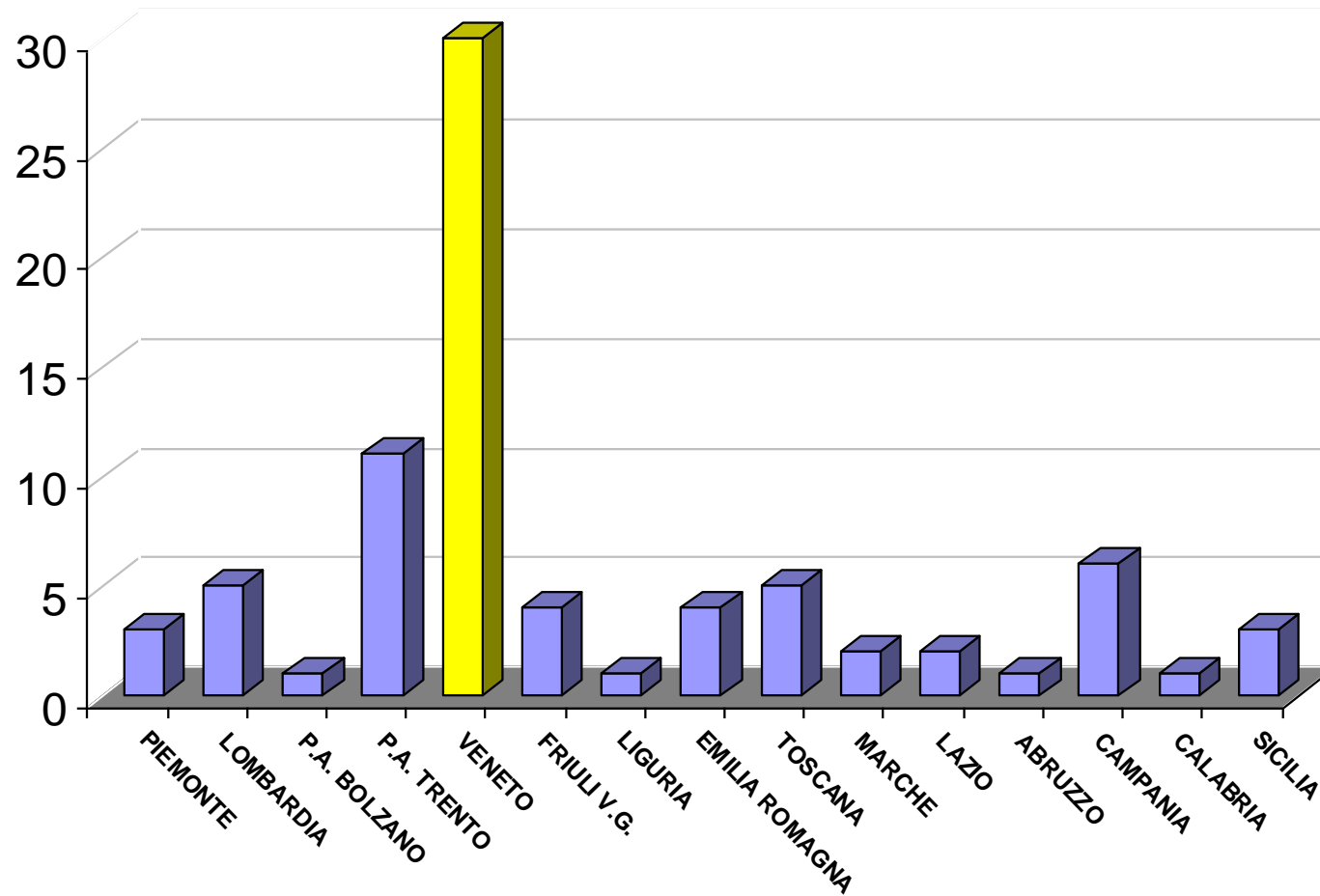
^mmandatory reporting, *preliminary data

Disease Comparisons - GIDEON



- ◆ Czech Republic. Lyme disease, cases (Rates per 100,000)
- ◆ Slovenia. Lyme disease, cases (Rates per 100,000)
- ◆ Slovakia. Lyme disease, cases (Rates per 100,000)
- ◆ Hungary. Lyme disease, cases (Rates per 100,000)
- ◆ Germany. Lyme disease, cases (Rates per 100,000)
- ◆ United States. Lyme disease, cases (Rates per 100,000)

CASI UMANI DI TBE IN ITALIA (2000 – 2003)



CASI UMANI DI TBE IN VENETO (1994 – 2005)

anno	casi non residenti notificati ULSS n.1	casi residenti notificati ULSS n.1	casi totali notificati ULSS n.1	casi totali notificati Regione Veneto
1994	1	4	5	5
1995	-	4	4	4
1996	2	5	7	7
1997	1	5	6	6
1998	1	8	9	10
1999	1	2	3	4
2000	2	7	9	8
2001	1	13	14	19
2002	2	6	8	9
2003	1	3	4	6
2004	1	10	11	19
2005	2	5	7	13

Notifiche Regione Veneto

anno	B.Lyme (695.9)	TBE (063)
2000	83	8
2001	112	18
2002	118	9
2003	108	5
2004	168	19
2005	123	13
totale	712	72

Figure 25. Number of TBE cases (bars) and incidence per 100 000 inhabitants (line) by year, Italy (n=159)

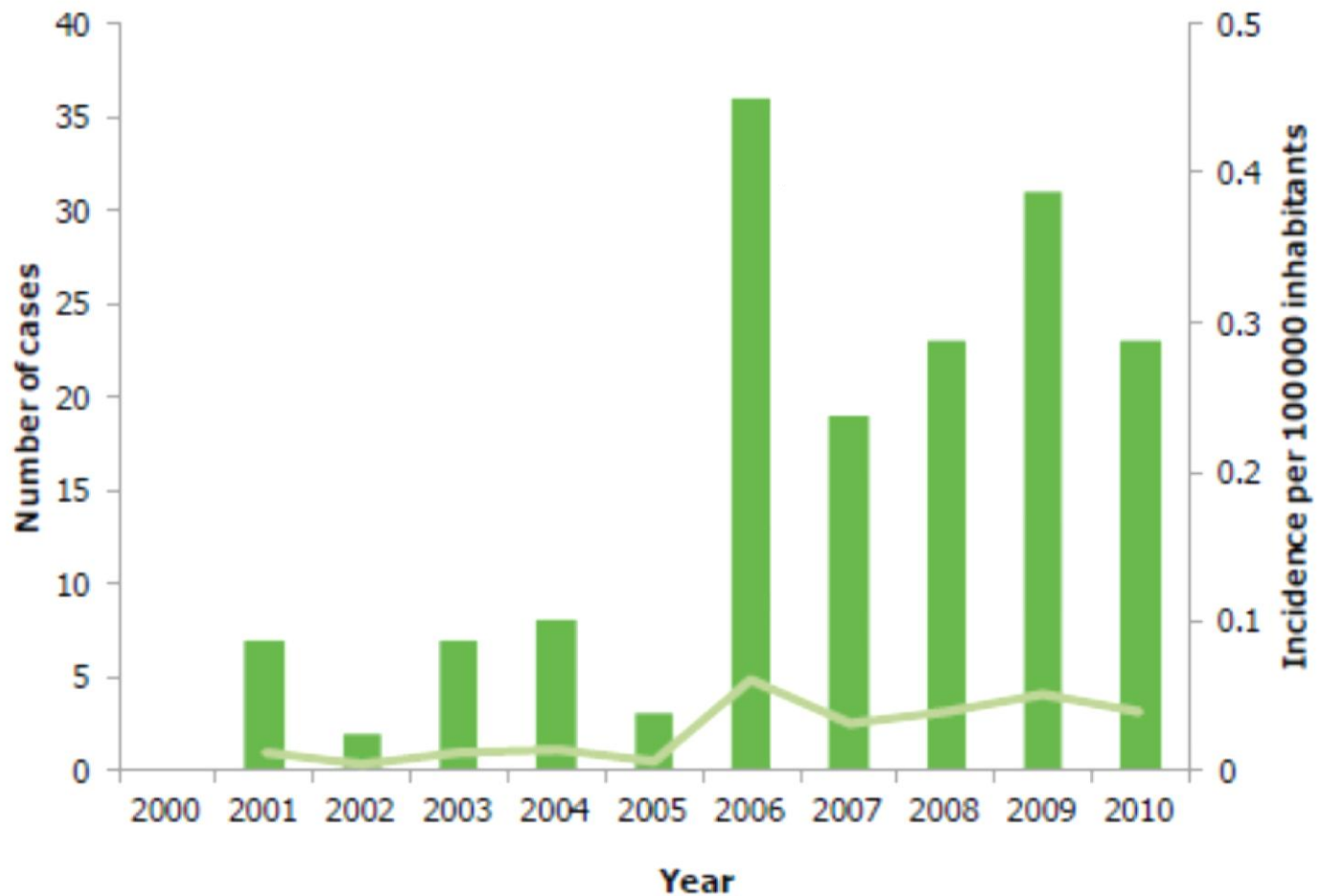


Figure 26. Number of TBE cases by gender and age, Italy (n= 159, data from 2001–2010 pooled)

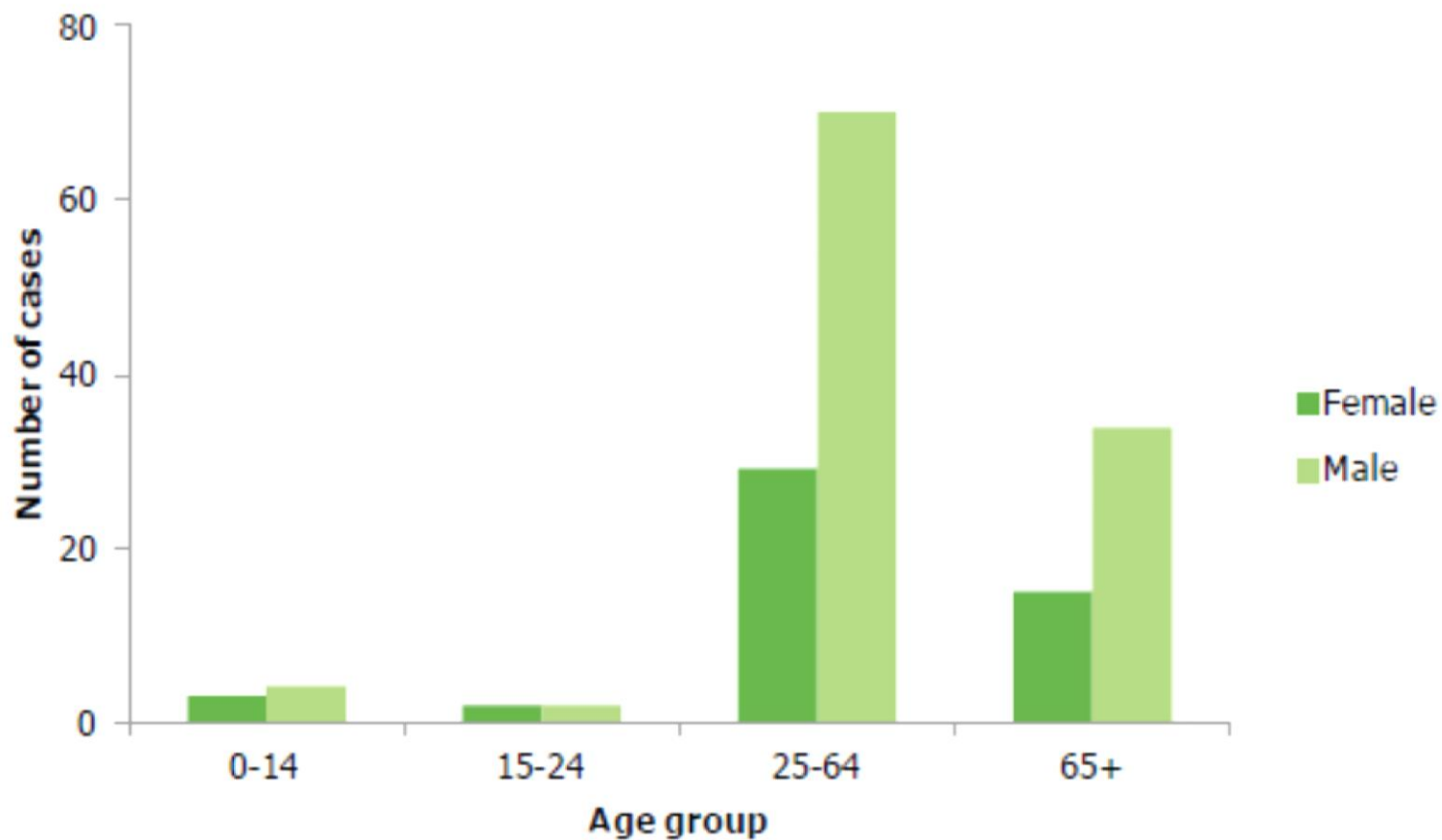
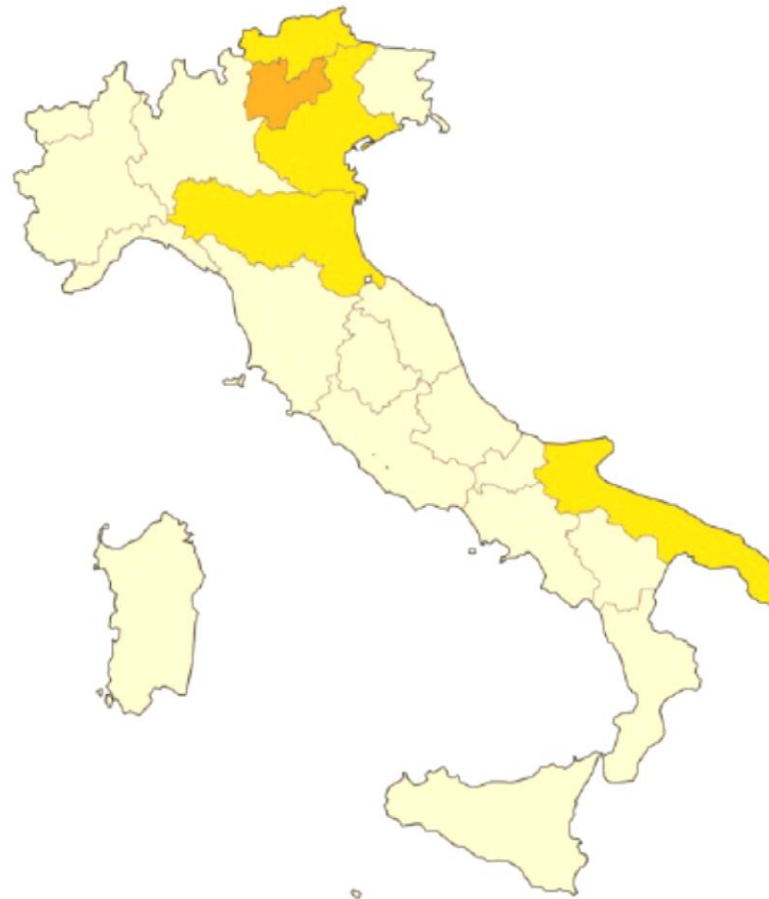
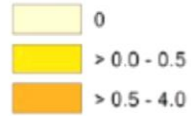


Figure 27. TBE average annual incidence rate per 100 000 inhabitants by NUTS2, Italy (n=159, period 2001–2010)

TBE incidence

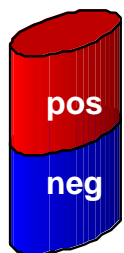


SPECIE	ESAMINATI	POSITIVI (Ab TBE)
CAPRIOLO	53	16 (30%)
CAMOSCIO	22	2 (9%)
CERVO	21	2 (9%)
TOTALE	96	20 (21%)

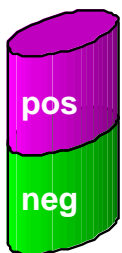
**Risultati di una indagine (2006 – 2007)
condotta nella provincia di BL**

**MONITORAGGIO
TBE IN FVG: risultati
preliminari della
siero-sorveglianza in
animali domestici e
selvatici.**

Legenda



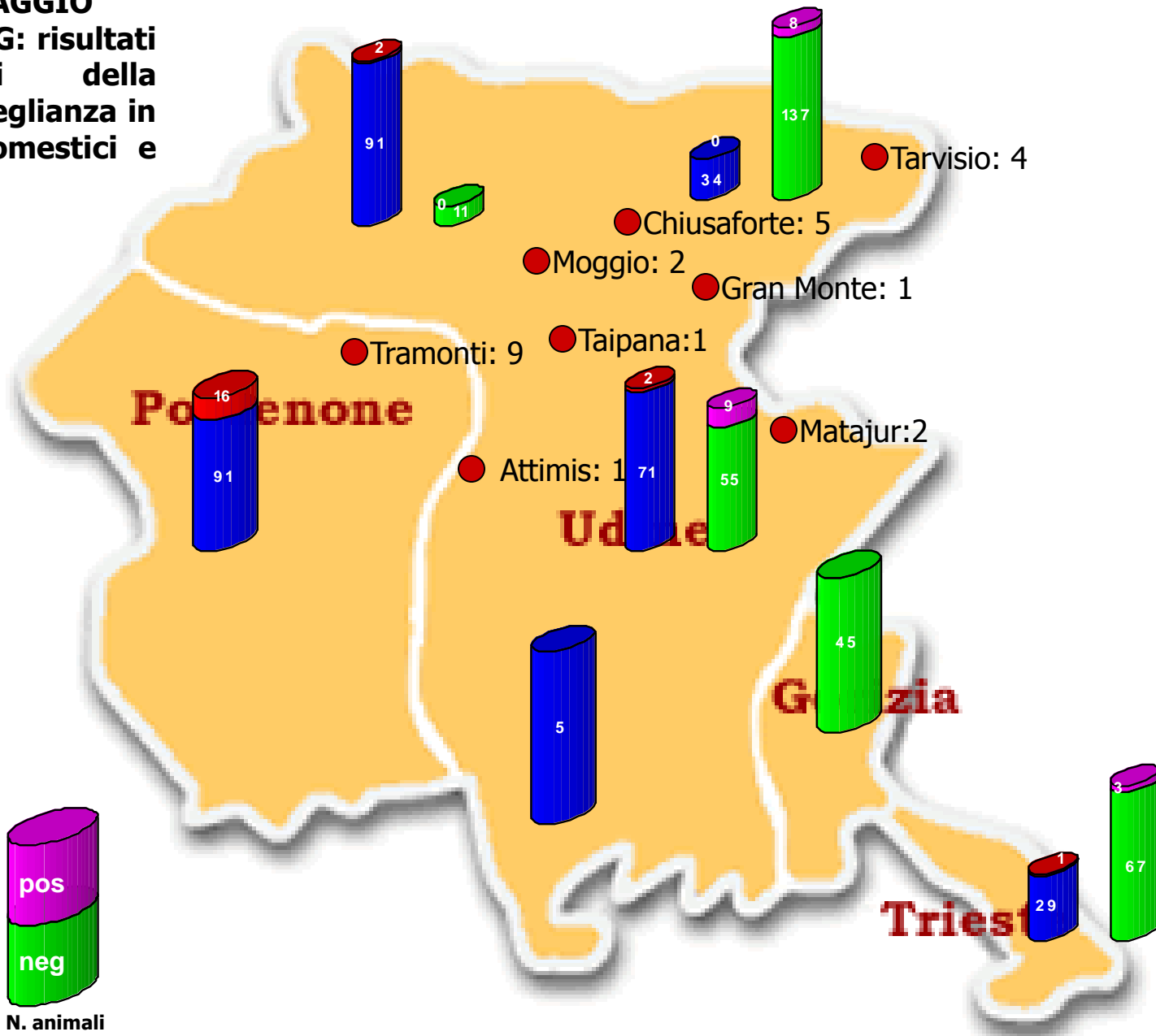
N. animali
ovi-caprini



N. animali
selvatici

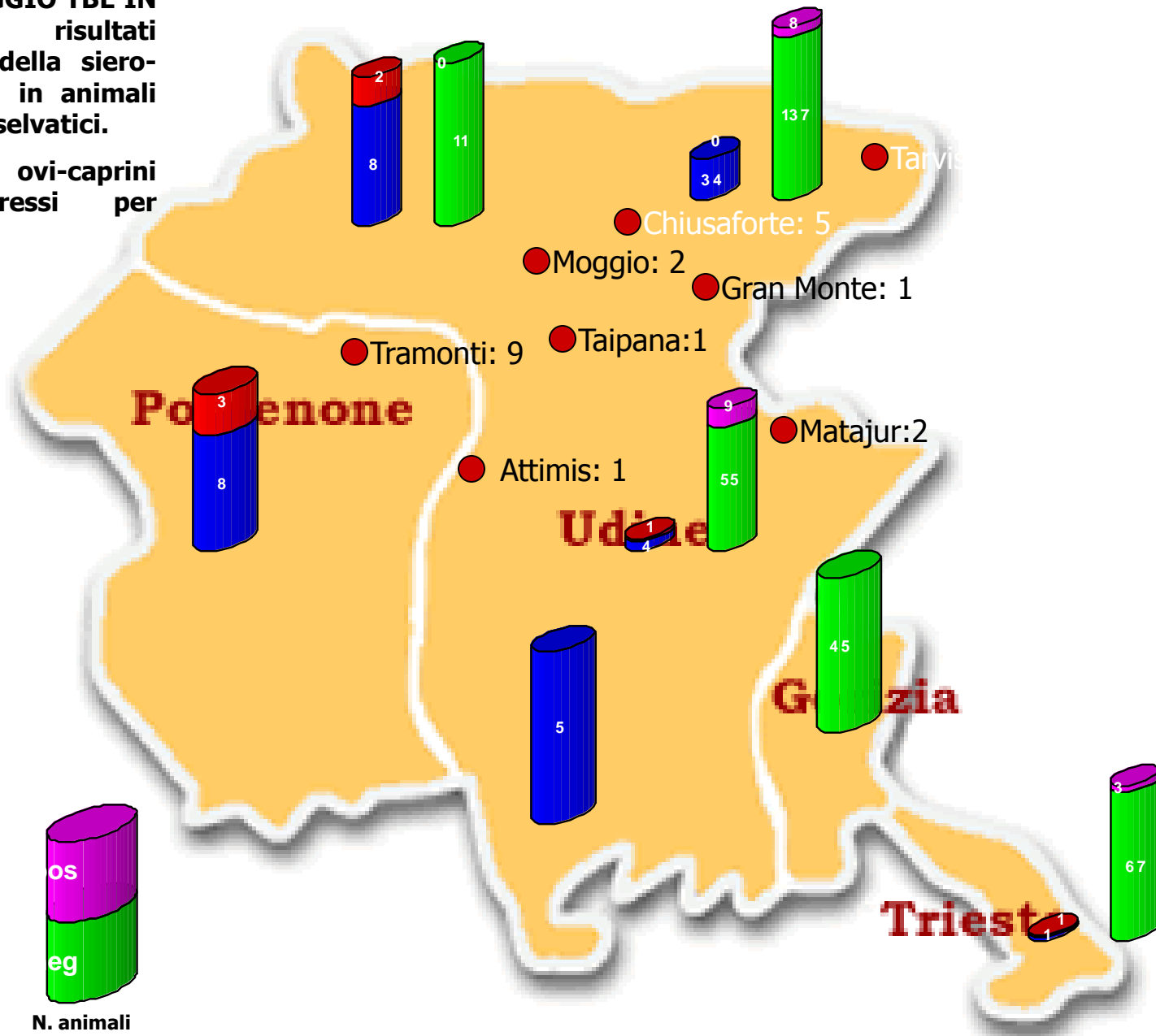


Località, numero casi clinici uomo (fonte uniuud – clin.med luglio 2006)

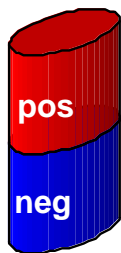


MONITORAGGIO TBE IN FVG: risultati preliminari della sierosorveglianza in animali domestici e selvatici.

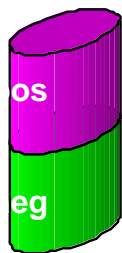
I dati degli ovi-caprini sono espressi per allevamento



Legenda



N. Allevamenti ovi-caprini

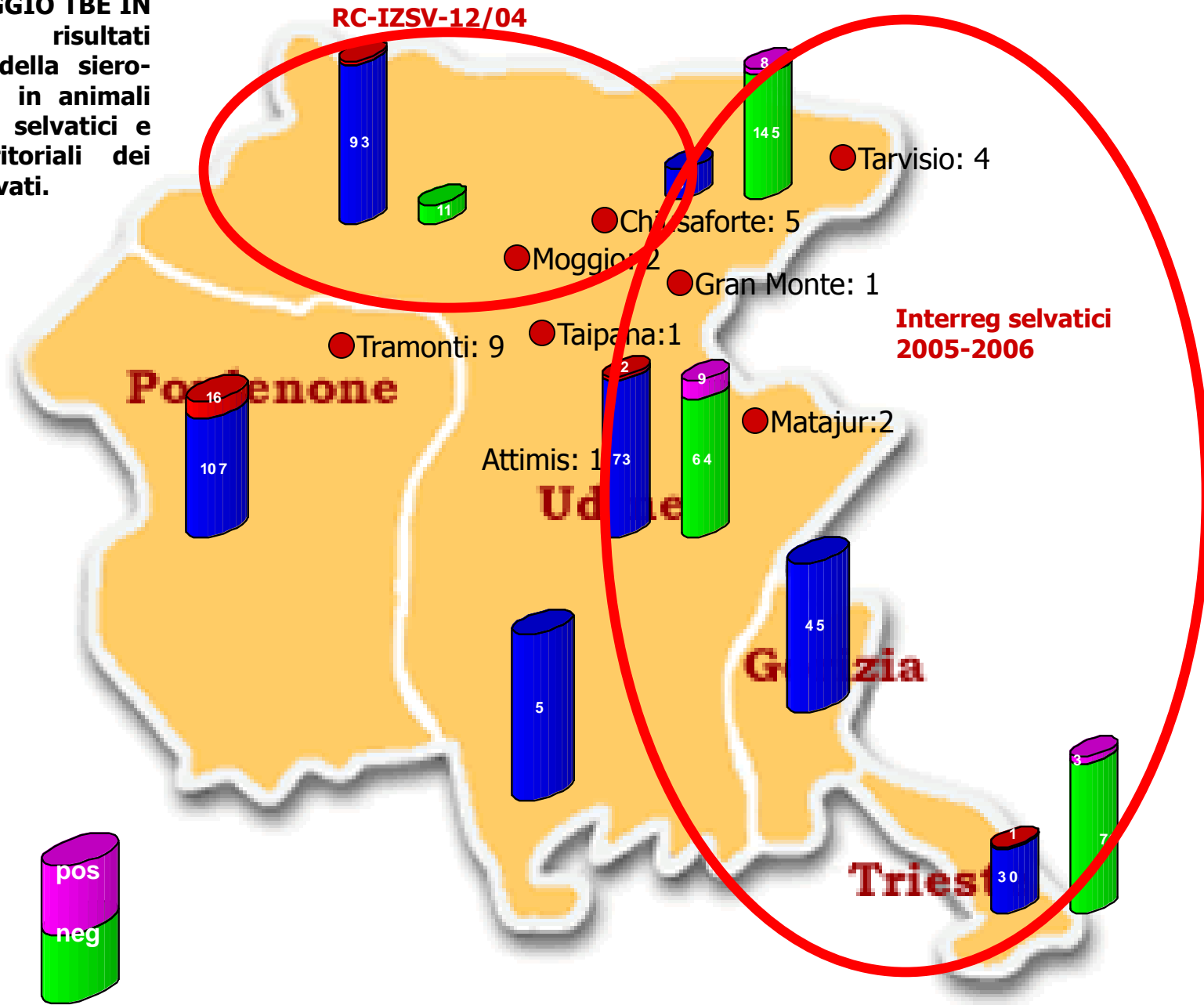


N. animali selvatici

● Località, numero casi clinici uomo (fonte uniuud – clin.med luglio 2006)

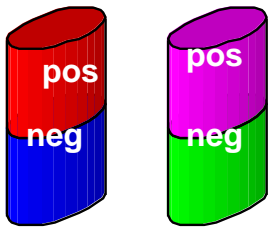
MONITORAGGIO TBE IN FVG: risultati preliminari della sierosorveglianza in animali domestici e selvatici e ambiti territoriali dei progetti attivati.

RC-IZSV-12/04



Interreg selvatici 2005-2006

Legenda



domestico selvatico

N. animali esaminati:

● Località, numero casi clinici uomo (fonte uniuud – clin.med luglio 2006)



Tick-borne diseases

In the days following a tick bite, you should watch out for symptoms of tick-borne diseases to be on the safe side.

In [country], a tick-borne disease to be aware of is Tick-borne Encephalitis which is associated with symptoms like:

- Fever
- Tiredness
- Headache
- Muscle pain
- Nausea

Please contact your doctor if you experience any of these symptoms within 4 weeks after the bite.

The later phase of the disease involves the neurological system with symptoms of meningitis and requires hospitalisation.



Tick-borne diseases in Europe

Tick-borne disease can be found almost all over Europe with some diseases being more prevalent in certain regions.

Before travelling abroad, consult the websites of the national health authorities to enquire about

whether tick-borne diseases are a risk in the region you are travelling to and ask your doctor regarding necessary precautionary measures, especially if you plan to engage in outdoors activities (camping, hiking, hunting, lake or river fishing, etc.) during your visit.

[Name and contact details of health authorities]



Tick-borne encephalitis

Protect yourself against >>



Ticks can pass on serious diseases



© G. Blausen

Ticks are very small and live on the blood of mammals, reptiles and birds. As they feed, they can pick up bacteria or viruses naturally carried by these animals.

Ticks can also bite humans who pass through their living environment, so there is a risk that ticks may transfer infections into your bloodstream. This can cause serious disease.

In Europe, tick-borne diseases to be aware of include: Tick-borne encephalitis, Lyme borreliosis, tick-borne relapsing fever and Crimean-Congo haemorrhagic fever.



© G. Blausen



© G. Blausen

About ticks

Ticks move by walking on the ground and up plants. They latch on to a passing animal or human hosts by using hooks on their legs.



Illustration is only indicative. Sizes can change considerably depending on tick species.

Ticks' life cycles go through four stages: egg, larva, nymph and adult. During the last three stages the tick may bite and can transmit disease.

To the naked eye the larvae look like specks of soot, while nymphs are slightly larger, pinhead or poppy seed size. Adult ticks have eight legs and are the size of small spiders. The adult ticks can also vary in colour, from reddish to dark brown or black. Once fed, a female tick can grow to the size of a pea, as its body fills with blood.



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Risk areas

Ticks are second only to mosquitoes for carrying disease to humans. Due to various factors, there are now more ticks in many parts of [country] and Europe.

In [country], a tick-borne disease to be aware of is Tick-borne encephalitis (TBE) which can occur in areas where infected

ticks that transmit the disease are found. Ticks thrive in shady and humid woodland, clearings with grass, open fields and bushes. They live in both rural and urban locations. Information about which regions are at risk in [country] is available at: [Relevant website]

Preventive measures

Tick-borne diseases can be prevented by avoiding tick bites: use insect repellents and protective clothing, such as long trousers and boots, when venturing into an area where ticks are likely to be present.

In areas where TBE is endemic, vaccines against Tick-borne encephalitis are also recommended. Please be aware that the vaccine against Tick-borne encephalitis

does not protect against any other tick-borne diseases. Ask your doctor for more information.

Early and correct removal of ticks is another important measure. There is a lower risk of infection if a tick is detected and removed quickly. So it is important to check yourself, your children and your pets after having visited places where ticks may be present.

How to detect and remove ticks

After having been outdoors in areas where ticks may live, check your clothes as well as your body for ticks, paying particular attention to the armpits, groin, legs, navel, neck and head. On children, ticks are often found on the head at the hairline. As ticks are very small, they can easily be overlooked.

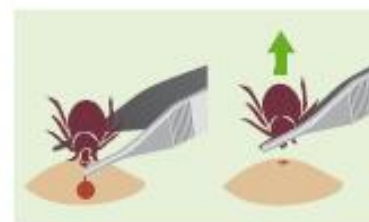
A magnifying glass may be helpful.



A tick bite usually looks like a dark lump with a small scab on the skin which cannot be brushed away. Usually, it does not hurt. Still, the tick should be removed as soon as possible in order to minimise the risk of transfer of bacteria or virus. It is important to remove the whole tick without breaking off the lower body to avoid the head remaining stuck in the wound.

The tick should be removed with tweezers, as close to your skin as possible, pulling carefully and consistently without jerking or twisting.

Be careful not to squeeze the tick's body, and do not apply heat or any substances to the tick, as this may cause it to empty its stomach contents into the wound, which causes bacteria or virus transfer.



Still using the tweezers, wrap the tick in some toilet paper and flush it down the toilet.



Finally, wash your wound with warm water and soap and apply antiseptic, like alcohol or iodine, to the area.

A small part of the tick's mouth may remain in the wound. This is not dangerous and it will disappear after a couple of days along with the wound.

However, if the lesion does not start to resolve after a couple of days, you should see a medical professional as this may indicate an infection (rare).