

ROSS RIVER VIRUS



“The Entry of Charles VIII into Florence”, oil on wood panel, 1518, Francesco Granacci, Galleria degli Uffizi, Florence.

In March 1494, King Charles VIII of France was having the time of his life. Together with his playboy cousin Louis, the Duke of Orleans, he was attending the magnificent jousting tournaments in the city of Lyon, where he had recently moved his court. Charles was so overcome by the spectacular martial arts on display, that he decided to undertake a great enterprise - the invasion of Italy! Or so Jean St Gelais, a friend and confidant of

the Duke's recorded. In truth however King Charles had already given a great deal of thought to the invasion. In 1483, on the death his father King Louis XI, Charles inherited a strong France and a weak claim to the Kingdom of Naples. The tenuous basis of this claim lay over two centuries in the past, when Pope Clement IV in 1265, granted the kingdom of Naples to Charles of Anjou, the brother of King Louis IX. Very soon however disputes broke out with the King of Aragon in Spain, who also claimed the Kingdom of Naples for himself via a complex series of royal inheritances. Eventually in 1442, the Spanish threw the French out of Naples. The French House of Valois, however, never relinquished their claim to the Kingdom of Naples, and never forgot it. Charles VIII decided that the time had come to win back his rightful inheritance. His cousin Louis promised his whole hearted support to the enterprise, mostly due to the fact that his own family had a weak claim to Milan, which he hoped he may be able to claim, as an offshoot to Charles's invasion of Italy

For the enterprise Charles gathered a formidable army, consisting of 9000 heavily armored knights 20,000 French infantry, and 6,000 Swiss Pikemen, considered to be some of the fiercest soldiers of the day. In addition to this impressive array, Charles's army boasted the largest artillery train that Europe had ever seen, over 70 large cannon. The French army moved into Italy in August 1494, in what became known as the "First Italian War" - a series of wars that would last until 1559, that saw most of Western Europe drawn into a conflict essentially between France and Spain over their "rights" to the Kingdom of Naples. Italy was not a united nation in the Sixteenth century, rather, a bewildering collection of city-states of perpetually changing alliances and allegiances. This state of disunity was no match for the French Army with its mighty cannon, and one by one, the city-states, Pisa, Genoa, Florence, fell to Charles virtually without opposition. In Milan, the Duke of Sforza, allied himself to Charles, and let him through to Rome unopposed. Charles left his cousin Louis, in the region of Milan to protect his supply lines in order to move on to Rome, leaving strict instructions to keep open his lines of supply...which Louis cheerfully ignored by attacking Milan to make good his own claim on that city as soon as Charles had left. This was despite Milan declaring for King Charles!

Pope Alexander VI, being Spanish, sympathized with Naples and King Ferdinand of Aragon, but he dared not oppose Charles's all conquering army, and so grudgingly granted him passage through Papal lands to Naples. Charles triumphantly entered Naples on March 28, 1495, and declared himself its new King. The rest of Europe, now seriously alarmed at the ease with which Charles had essentially conquered most of the Italian peninsular, now sought to deal with Ferdinand in an anti-French alliance that would restore the balance of power in Europe. Ferdinand masterfully gathered an impressive anti-French alliance consisting of Pope Alexander VI, the German "Holy Roman Emperor", the powerful Venetian Republic and not least the Duke of Milan, who now abandoned Charles, on account of being attacked by the Duke of Orleans. All of a sudden Charles found himself in an a very precarious situation, trapped in the south of Italy with half of Europe now allied against him! Furious at his cousin Louis, who was not doing well against the Duke of Milan and in serious trouble himself, Charles decided to make his escape from Naples, but left half his army in occupation of it. After coming to Louis' rescue, on 6th July 1495 Charles won an impressive victory over the army of the league against him in the north of Italy at the battle of Fornovo, which allowed him to

escape back to France, where he plotted his next invasion and revenge. This never came however. On 7th of April 1498 as he was walking with the Queen through a dark passageway in the Chateau of Amboise, he hit his head on a low lying lintel, and about two hours later lost consciousness and died, possibly from an extradural hematoma. As he was without living issue, his cousin Louis, gained the throne as King Louis XII. Soon after Charles had left Naples Ferdinand had expelled the French and reclaimed the Kingdom for the House of Aragon. Charles' efforts had all seemed to come to nothing.

Today the "First Italian War" is a long forgotten conflict over a long forgotten dispute. But Charles VIII did leave two quite unexpected legacies to posterity. The first was to the cultural history of France. Whilst in Italy Charles had become immensely taken with the great works of the Italian Renaissance, especially in Medici Florence. He brought back to France a love of the new learning and new Art, and gave great patronage to Italian Artists and Architects especially in his renovation works at the Chateau of Amboise where he employed Pacello da Mercogliano, Domenico da Cortona and Fra Giocondo to convert the Gothic building into the brilliant style of the Italian Renaissance. Charles in large part brought the Renaissance to France. Francis I would build on what Charles had begun, becoming a patron to no less than Leonardo da Vinci who would die at the Chateau of Amboise where he would be laid to rest.

Charles's second legacy to posterity was somewhat more infamous than his contribution to the cultural history of the West. Whilst in Naples a mysterious disease broke out among his troops. This provided the first well documented European cases of syphilis. The Neapolitans called it the "French Disease" assuming that it had come from them. Outraged at such a shameful accusation, the French responded in kind by naming it the "Neapolitan Disease"; perhaps not without some justification, as some modern research suggests that in fact syphilis could have been a New World Disease, brought back to Europe by the first Spanish Conquistadors who had sailed with Columbus in 1492!

Syphilis was an early example of so-called toponymy (from the Greek words topos "place" and onoma "name"). Place names are important to every culture because they contain a wealth of historical, cultural and linguistic information and also serve to label events and incidents associated with them. Diseases and pathogens not uncommonly carry the names of places associated with their discovery. The positive aspect to toponymy is that it can add a unique and interesting story that provides a glimpse into discovery, history and culture. The negative aspect, of course is that locals prefer not to have their region named after a disease! The first written records of an outbreak of syphilis in Europe occurred in 1494 in Naples during a French military invasion of that city. The people of Naples claimed that it was spread by French troops and so they called it the "French disease", to which the French took great offense, and responded by calling syphilis the "Neapolitan disease".

In Australia - for better or worse - there are a number of toponymous names for diseases, among them the so-called "Ross River" disease.

ROSS RIVER VIRUS

Introduction

Ross River Virus is an arbovirus, i.e. a virus which is transmitted via the bite of an arthropod, in this case a mosquito.

Ross River Virus is an **alphavirus**.

Ross River Virus is the **most common** and **most widespread** arboviral disease in Australia.

Major outbreaks have been recorded in all parts of Australia, primarily from January to May each year.

Ross River Virus is also endemic throughout Papua New Guinea, Indonesia and the Solomon Islands. It has also been recorded in other Pacific islands such as Fiji.⁵

All the infective alphaviruses essentially cause a similar disease pattern in humans, and are principally characterized by:

1. Fever
2. Joint involvement
3. Rash.

Epidemics are usually related to environmental conditions that encourage mosquito breeding such as warm weather with heavy rainfall, floods, and high tides that inundate salt marshes or coastal wetlands.

Ross River Virus is usually a benign self-limiting illness, and most patients recover fully within a few weeks, although some patients may experience a protracted or intermittent course of up to 6 months.

There is no current vaccine available and no *specific* treatment.

Terminology:

The study of place names is called **toponymy** (from the Greek words topos “place” and onoma “name”).

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Ross River as well as **Hendra, Bairnsdale, Murray Valley** and **Barmah Forest** are all examples of Australian places that have had diseases named after them.

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In 1918 the Influenza pandemic was commonly referred to as the “Spanish flu”, a great source of irritation to the Spanish, particularly as the exact origins of the influenza virus were essentially unknown, though the troops of World War I, a conflict in which Spain was neutral, were probably responsible for its rapid dissemination across the globe

History

The Ross River Virus was first isolated in 1959 from **Aedes vigilax** mosquitoes collected near **Ross River** in **Townsville**, Queensland, Australia.

The cause role of Ross River Virus disease was confirmed in 1971 by isolation of the virus from the blood of an Indigenous child with the disease.

Note that some Aedes species of mosquitoes have recently been renamed **Ochlerotatus spp.**

Epidemiology

Ross River Virus is the **most common** and **most widespread** arboviral disease in Australia around inland waterways and coastal regions.

It is considered endemic throughout most parts of Victoria, particularly around inland waterways and coastal regions, and until recently had not been reported in **metropolitan Melbourne**, though some cases have now been recorded in Melbourne’s extreme south.

Major outbreaks have been recorded in all parts of Australia, primarily from January to May each year. Epidemics are usually related to environmental conditions that encourage mosquito breeding such as warm weather with heavy rainfall, floods, and high tides that inundate salt marshes or coastal wetlands.

Ross River Virus is also endemic throughout Papua New Guinea, Indonesia and the Solomon Islands. It has also been recorded in other Pacific islands such as Fiji.

Clinical features of infection are rare before puberty, after which the disease has a similar pattern at all ages.

Pathology

Organism

Arboviruses are viruses that are spread by the bite of arthropods, particularly mosquitoes.

They are divided into:

1. Alphaviruses:

There are four infective alphaviruses including:

- **Ross River**
- Barmah Forest
- Sindbis
- Chikungunya virus.

2. Flaviviruses.

- Murray Valley encephalitis virus
- Dengue virus

The alphaviruses are a group of small enveloped single-strand positive-sense RNA viruses.

Reservoir

Ross River Virus is maintained in a primary mosquito - mammal cycle involving **macropods** (particularly the western grey kangaroo), and possibly other **marsupials** and **wild rodents**.

A human - mosquito cycle may occur in explosive outbreaks.

Horses can act as amplifier hosts, and appear to develop joint and nervous system disease after infection with Ross River Virus.

Fruit bats might act as vertebrate hosts in some areas.

Vertical transmission in desiccation-resistant eggs of *Ochlerotatus* spp. mosquitoes may be a mechanism to enable the virus to persist in the environment for long periods. This could explain the rapid appearance of cases of Ross River Virus disease after heavy rains.

Transmission

Ross River Virus is transmitted by the **bite of infected mosquitoes**.

In Australian inland areas the principal vector is:

- **Culex annulirostris**

In coastal regions the principal vector is:

- **Ochlerotatus vigilax** in New South Wales
- **Ochlerotatus camptorhynchus** in the southern parts of Victoria and Tasmania

These vectors are well established in Australia.

Incubation Period

- The incubation period is generally around **3 - 11 days**, though it may be up to 21 days in some cases.

Period of communicability

- There is no evidence of direct transmission of Ross River Virus from person to person.
- There is a case report of a blood transfusion derived infection in a patient.³

Susceptibility & resistance

- Infection with the Ross River Virus will confer subsequent life-long immunity.

Clinical Features

Infection is subclinical in up to 60 % of cases.

All the infective alphaviruses essentially cause a similar disease pattern in humans, and are principally characterized by, fever, joint involvement and rash.

Ross River Virus is usually a benign self-limiting illness, and most patients recover fully within a few weeks, although some patients may experience a protracted or intermittent course of up to 6 months.

Clinical features of Ross River Virus can include:

1. Fever
2. Non-specific constitutional symptoms:

- Lethargy
- Malaise
- Anorexia
- Headache
- Myalgias

3. Joint involvement:

- Rheumatic symptoms are present in most patients.
- These consist of arthritis or arthralgia, primarily affecting the:
 - ♥ Wrists
 - ♥ Knees
 - ♥ Ankles
 - ♥ Small joints of the extremities.

- Prolonged symptoms occur relatively commonly:

Earlier studies however may have overestimated the prevalence and duration of symptoms in Ross River Virus disease. Progressive resolution over **3 - 6 months** appears usual. ²

4. Rash:

- A rash can occur up to **2 weeks before or after other symptoms**.
- It can be absent in about one third of cases.
- The rash is variable in:
 - ♥ Distribution
 - ♥ Character
 - ♥ Duration, (but usually around 7 -10 days)
- It may be associated with buccal and palatal enanths (i.e. spots on mucous membranes).

5. Cervical lymphadenopathy is common.
6. Occasionally parasthesiae of the hands and feet.

Investigations

1. Serology:
 - A fourfold or greater rise in titer to Ross River Virus IgG
 - The presence of Ross River Virus IgM
2. PCR testing for Ross River Virus

Management

Prevention

There is no current vaccine available for the Ross River Virus.

The chances of infection can be reduced by avoidance of mosquitoes bites by usual means such as:

- The wearing of long, loose-fitting clothes
- The use effective insect repellents in mosquito-prone areas.
- Avoiding mosquito-prone areas, especially at dusk and dawn when mosquitoes are more active and likely to bite.

Airport vector control in Australia and Papua New Guinea may be necessary to prevent spread from endemic areas to countries where local vectors such as *Aedes polynesiensis* may transmit the disease.

Treatment

There is no specific treatment and this is essentially symptomatic only.

Simple analgesia such as Aspirin, NSAIDs, or paracetamol are usually sufficient to control symptoms.

Notification:

Ross River virus infection is a Group B disease and requires notification within 5 days of diagnosis.

This is a Victorian statutory requirement.

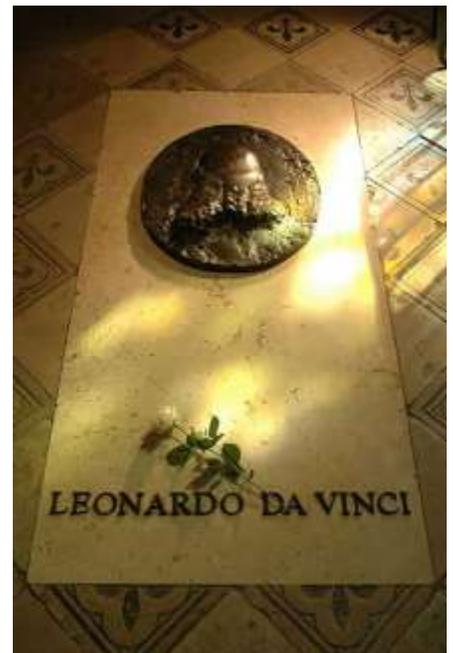
School exclusion:

Exclusion is not required

Appendix 1



Ankle arthropathy in a patient with Ross River disease contracted in Fiji. Note fullness over the lateral malleolus indicating swelling. There is also redness. The patient complained of pain and tenderness around the joint.⁵



The magnificent Chateau of Amboise and the tomb of Leonardo da Vinci

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15 February 2017.