



Australian Paediatric Surveillance Unit
STUDY INFORMATION SHEET
Juvenile onset
Recurrent Respiratory Papillomatosis (JoRRP)

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BACKGROUND

Juvenile onset Recurrent Respiratory Papillomatosis (JoRRP) is a condition in which benign papillomata develop and recur in the larynx. JoRRP usually develops in infancy or early childhood (median age=4 years).¹ It is the most common benign neoplasm of the larynx in children.² Common presenting symptoms include: stridor, chronic cough, recurrent pneumonia, failure to thrive, dyspnoea, dysphagia and acute respiratory distress in children with upper respiratory tract infection.² In about one third of children with JoRRP the disease spreads into the trachea and bronchi, with the risk of respiratory obstruction.³ Malignancy is a rare but recognised development in RRP.

JoRRP is caused by human papillomavirus (HPV) infection. HPV 6 and HPV 11 are considered the most common causative genotypes.⁴ Perinatal transmission from mothers with genital condylomata is thought to be the main method of transmission. Recent evidence also suggests ascending infection through premature rupture of membranes at birth or through handling a neonate by an infected person. A meta-analysis of prospective studies found that mothers whose cervical swabs were HPV-positive on PCR were 5 times more likely to give birth to an HPV-positive infant than were HPV-negative mothers, and that vaginal delivery was twice as likely to result in HPV transmission as was caesarean section.⁵ However, the mechanisms of infection have not been fully documented and JoRRP is rare in neonates born to HPV-positive mothers⁶, and neonates born vaginally to HPV-negative mothers may be HPV-positive.^{5,7}

Treatment is primarily by surgical debulking of papillomata to reduce airway obstruction. Multiple surgeries are common: on average, 4 surgical procedures in the first year after diagnosis.⁸ Debulking is usually performed by micro-debrider, carbon dioxide laser, cold steel excision, or, more recently, by office-based laser surgery (in adults). Adjuvant treatment using antivirals (cidofovir, ribavirin) or monoclonal antibodies (bevacizumab) is sometimes used.

The introduction of HPV vaccination in Australia in 2007 raised the possibility of prevention of RRP. The two HPV vaccines, Cervarix® and Gardasil®, confer protection against HPV 16 and 18 which are responsible for about 70% of cervical cancer worldwide.⁹ Gardasil® also offers protection against HPV 6 and 11, which cause genital condylomata and JoRRP. Gardasil® was used in the national program in a three dose schedule between 2007-2017 and was initially provided to females aged 12-26 years, until the end of 2009, to girls aged 12-13 between 2007-2012 and to both boys and girls aged 12-13 from 2013-2017. From 2018 the extended spectrum nine-valent HPV vaccine Gardasil9, which covers an additional 5 oncogenic HPV types, was introduced as a two dose schedule for those aged 14 and under at date of first dose.¹⁰

The APSU study is the first prospective study of RRP worldwide. It will provide an estimate of incidence and data on mode of delivery, maternal history and HPV vaccination status, lesion HPV types, ethnicity, age of onset of diagnosis and duration and nature of treatment. These data are likely to support further research into the biological, maternal and obstetric aspects of RRP. Cases in which HPV typing has been conducted can provide data on the virological characteristics of the disease, from which the impact of HPV vaccination on RRP can be followed. Over the first 5 years of surveillance, the study documented a declining incidence of the disease following the HPV vaccination program, a world first.¹¹

STUDY OBJECTIVES

1. To estimate the Australian incidence of RRP in children aged < 15 years
2. To describe:
 - a) Symptoms, clinical presentation and treatment of RRP in Australia
 - b) Characteristics of maternal and delivery history
 - c) Child and maternal HPV vaccination history
 - d) Viral types isolated in biopsy samples
 - e) The distribution of RRP and HPV genotypes according to antenatal maternal HPV vaccination status, and child vaccination status
 - f) Current methods of treatment of JoRRP in Australia

CASE DEFINITION

Please report any infant or child under the age of 15 years diagnosed with Juvenile onset Recurrent Respiratory Papillomatosis (JoRRP) involving the larynx confirmed by endoscopy of the larynx AND by histology.

Probable case: as above but without histological confirmation

Any case reported with no laryngeal involvement will be reviewed, and where accepted as non-laryngeal RRP, will be reported separately.

FOLLOW-UP OF REPORTED CASES

A 2-page questionnaire requesting further details will be forwarded to clinicians who report a case of Juvenile onset Recurrent Respiratory Papillomatosis (JoRRP) together with details on accessing HPV typing (also available on the APSU website – please see www.apsu.org.au)

Data collected for the study will be stored at Kids Research (SCHN), The Children's Hospital at Westmead, in paper and electronic format for a minimum of 15 years after date of publication or termination of the study.

PRINCIPAL INVESTIGATOR

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FURTHER INFORMATION

For further information related to this study or assistance completing the Case Report Form, please contact the APSU by either:

- email: SCHN-APSU@health.nsw.gov.au or
- phone: (02) 9845 3005

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