# Infection Control in Healthcare Personnel: Epidemiology and Control of Selected Infections Transmitted Among Healthcare Personnel and Patients Parvovirus B19 Supplement

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# A. Background

This document contains supplementary information to the Parvovirus B19 section of the Infection Control in Healthcare Personnel: Epidemiology and Control of Selected Infections Transmitted Among Healthcare Personnel and Patients. The *Guideline for infection control in health care personnel, 1998* (1998 Guideline) did not provide a recommendation for healthcare personnel infected with parvovirus B19. This integrated assessment of two systematic reviews was conducted to address this gap and determine the risk period of transmission among symptomatic adults infected with parvovirus B19. These systematic reviews examined the duration of viral shedding and symptoms and identified the serial interval for transmission pairs. Indirect evidence from children was not included.

## B. Recommendation and Evidence to Decision Framework

#### 1998 Recommendation<sup>1</sup>

- 1. Text:
  - a. Because of the serious nature of the consequences for the fetus, female personnel of childbearing age need to be counseled regarding the risk of transmission of B19 and appropriate infection control precautions.
  - b. Work restrictions are not necessary for personnel exposed to B19.
- 2. Recommendation:
  - a. Ensure that pregnant personnel are aware of the risks associated with parvovirus infection and of infection control procedures to prevent transmission when working with high-risk patient groups. *Category IB*
  - b. Do not routinely exclude pregnant personnel from caring for patients with B19. Category IB

#### Recommendation Update: Good Practice Statements<sup>2</sup>

- 1. For asymptomatic healthcare personnel who have an exposure to parvovirus B19:
  - Work restrictions are not necessary.
  - Wear source control through the 14th day after last exposure.
- 2. For healthcare personnel known or suspected to have the early symptoms (i.e., prodrome) of parvovirus B19 infection:
  - Exclude from work until:
    - At least 5 days have passed from symptom onset, AND
    - They are fever free for at least 24 hours without the use of antipyretics, AND
    - Symptoms are improving
  - Wear source control upon return to work until resolution of their respiratory symptoms.

For recommendations about healthcare personnel who are pregnant or intending to become pregnant, please see the **Pregnant HCP** section.

Table 1. GRADE Evidence to Decision Framework: Parvovirus B19

	Health system and public health recommendations
Benefits & harms	<ul> <li>The evidence suggests</li> <li>viral shedding occurs for five days and resolves with or before the resolution of fever, which ended by day 14 for participants who were seronegative at inoculation and developed infection;<sup>3</sup> and</li> <li>the longest estimated contagious period is 26 days starting with the longest estimated serial interval of 32 days<sup>4</sup> and subtracting the shortest incubation period of six days<sup>5</sup>. However, this does not align with previous studies<sup>6-8</sup> reporting serial intervals of 7 to 11 days.</li> </ul>
Certainty of the evidence	There is moderate certainty in the evidence for the duration of viral shedding and fever, <sup>3</sup> and there is very low certainty in the estimated serial interval <sup>4,9,10</sup> and incubation period <sup>5,10</sup> .
Outcome importance	Healthcare systems and facilities may place a high value on preventing transmission in healthcare settings given the recent increase in parvovirus B19 activity in the US. <sup>11</sup>
Balance	The balance of the evidence supports reliance on the duration of fever as a conservative proxy for infectiousness in formerly healthy, formerly seronegative adults with symptomatic parvovirus B19 infection.
Resource use	No cost-effective analysis was conducted. However, these recommendations provide guidance where none previously existed and offer opportunities for healthcare facilities and systems to balance potential cost savings from prevention of healthcare-associated parvovirus B19 infections among patients and HCP, with the human resource considerations necessary to ensure adequate staffing ratios.
Population- & setting- specific differences	Data was insufficient to support population-specific sub-analyses, however these recommendations support maintenance of appropriate staffing levels, ensuring sufficient care for patients across different settings, populations, and needs.
Acceptability	No assessment of knowledge, attitudes, and practices was performed. However, the Workgroup discussed acceptability and determined this recommendation is likely acceptable given the short duration of work restriction.
Feasibility	No implementation assessment was conducted. However, the Workgroup discussed feasibility and assumed this recommendation to be feasible given the shorter duration of work restriction.
Intentional vagueness	Source control devices are not specified to allow for provider preference in selection. Exposure to parvovirus B19 and prodromal symptoms are defined in the supporting narrative.

#### C. Methods

This is a systematic review of the best available evidence on elements of the natural history of parvovirus B19 that will be used to inform strategies to prevent transmission of parvovirus B19 in healthcare settings.

# **C.1.** Key Question Development

Key Questions were adapted for parvovirus B19 from a review evaluating the risk period for transmission of SARS-CoV-2 and seasonal influenza.<sup>12</sup> The Key Questions were developed by occupational health, infectious disease, and systematic review methodology subject matter experts using the PICO framework<sup>13</sup> (Population, Intervention, Comparator, and Outcome). The Key Questions used to guide the literature review are:

- KQ1. Among symptomatic adults infected with parvovirus B19, what is the duration of shedding of replication competent virus/infectious virus measured via viral culture or polymerase chain reaction (PCR)?
- KQ2. Among symptomatic adults infected with parvovirus B19, what is the association between duration of symptoms and duration of shedding of replication competent virus/infectious virus measured via viral culture or polymerase chain reaction (PCR)?
- KQ3. Among symptomatic adults infected with parvovirus B19, what is the risk period for transmission to an uninfected individual based on time since onset of symptoms in or exposure to source patients?

#### C.2. Literature Search

A CDC informationist (J.T.) adapted search strategies<sup>12</sup> for parvovirus B19 and performed these searches in MEDLINE, EMBASE, CINAHL, Cochrane Library, and the Public Health Database from the start of each database to either February 10 (KQ2) or April 3, 2025 (KQ1, KQ3). The detailed search strategies are provided in *Tables 6-8*.

#### C.3. Study Selection

Results of the literature searches were uploaded into EndNote 21 (Clarivate Analytics©, Thomson Reuters, New York, NY, USA), duplicate records were removed, and unique titles and abstracts were uploaded to Covidence (Veritas Health Innovation Ltd., Melbourne, VIC, Australia) where a second round of deduplication was conducted. Two reviewers (D.O.S., D.T., C.S., J.B., E.C.S., M.M, M.D., M.W.) independently screened all titles and abstracts and removed irrelevant references. Relevant full texts were screened independently by two reviewers (D.O.S., D.T., C.S., J.B., E.C.S., M.M, M.D., M.W.) and disagreements were resolved by consensus. All studies were screened according to the pre-identified exclusion criteria below, and results of the study selection process are provided in *Figures 1-3*.

Criteria for excluding studies from the literature review include:

- 1. No full text available;
- 2. Laboratory or animal studies (i.e., no examination of live humans);
- 3. Not available in English;
- 4. No primary data;
- 5. No population of interest (i.e., primary cases who were children < 17 years of age);
- 6. Insufficient methodologic reporting (i.e., meeting abstract or poster);
- 7. No intervention of interest (i.e., no parvovirus exposure); or
- 8. No outcomes of interest.

Figure 1. Results of the Study Selection Process for KQ1: Duration of Shedding

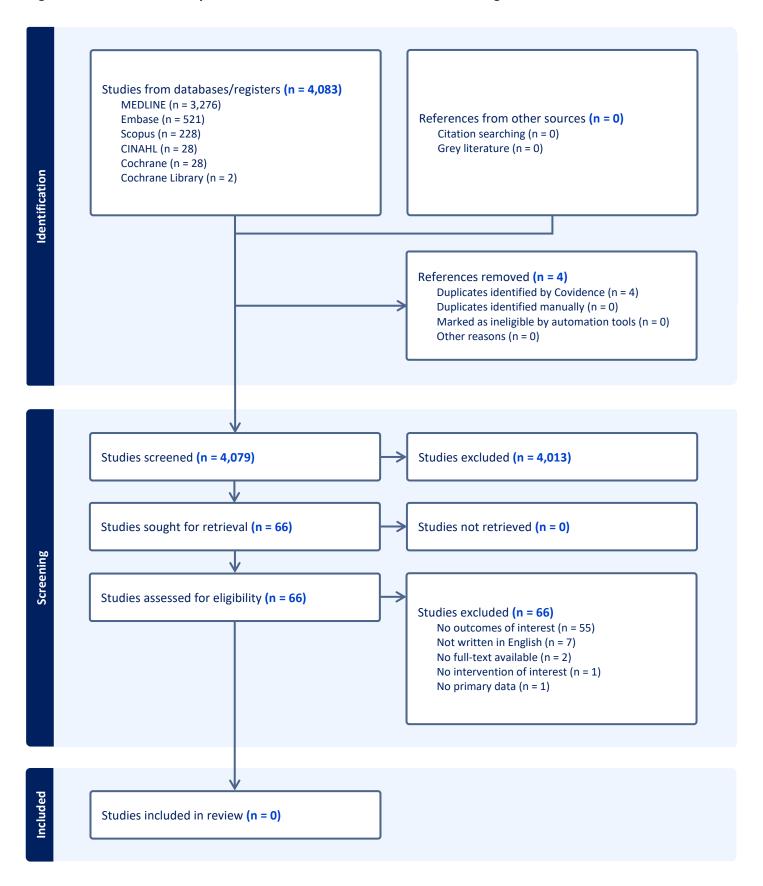


Figure 2. Results of the Study Selection Process for KQ2: Duration of Shedding and Symptoms

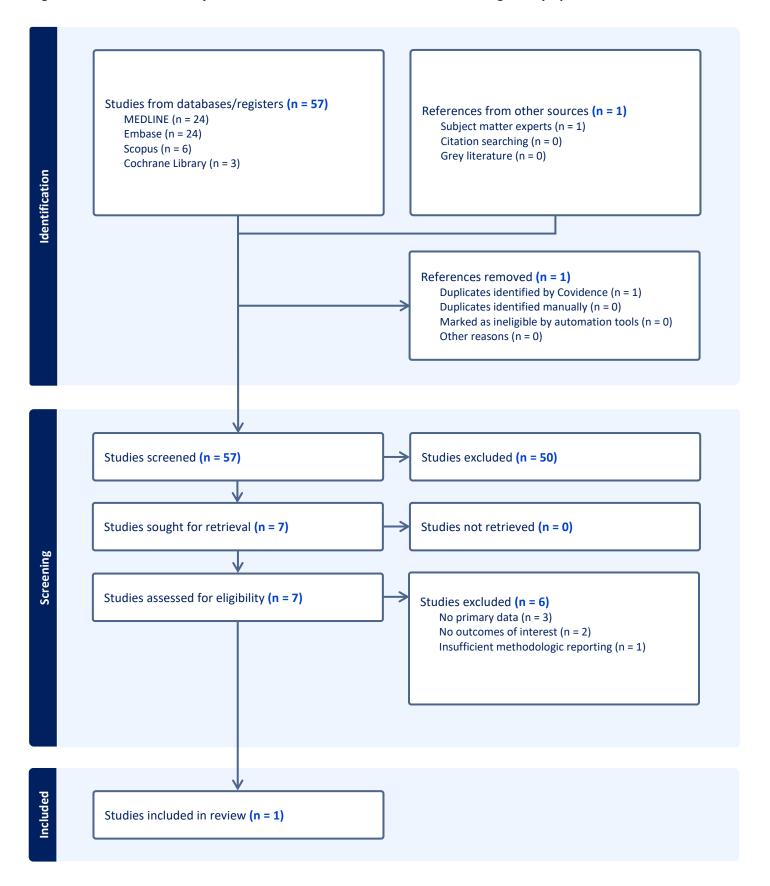
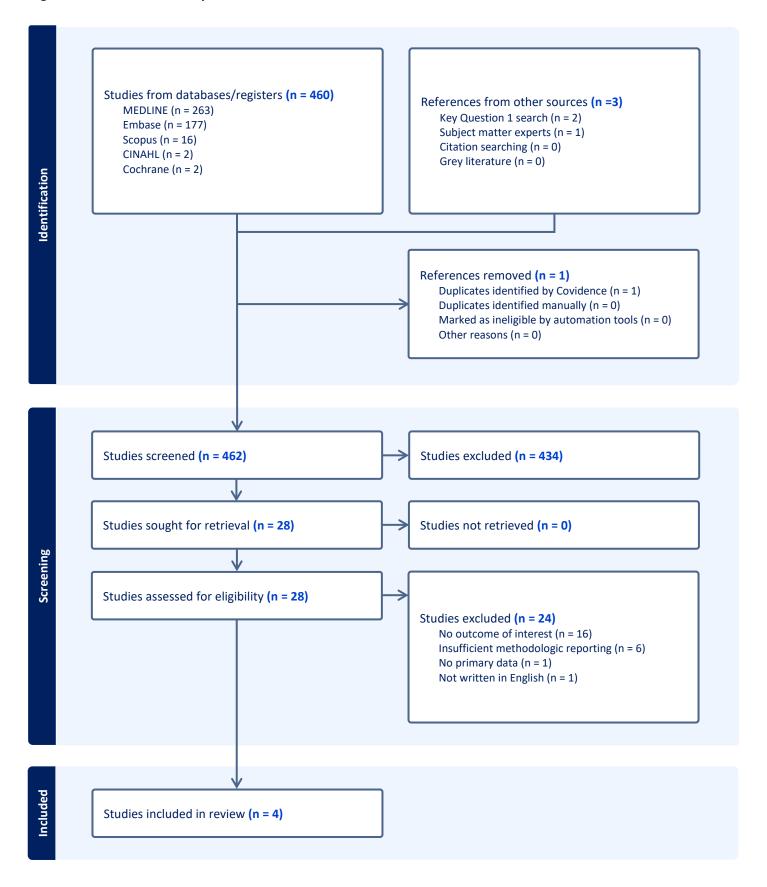


Figure 3. Results of the Study Selection Process for KQ3: Risk Period for Transmission



#### C.4. Data Extraction, Study Assessment, and Synthesis

Data from studies meeting inclusion criteria were independently extracted by two reviewers using a standardized Microsoft Excel (2021) form, and differences were reconciled by discussion. Extracted data included study characteristics, data collection and diagnostic tests, and the outcomes of interest (*Tables 3-4*). Outcome data were extracted as presented in the studies or calculated using data provided. For KQ1 and KQ2, the duration of shedding and symptoms was defined from inoculation of the participant (day zero). Shedding outcomes were extracted for viral shedding measured using any diagnostic test, and signs and symptoms included fever, flu-like symptoms, rash, and arthralgia. For KQ3, the serial interval was defined as the onset of any symptom in a primary case (day zero) to the onset of the same symptom in the secondary case. Therefore, serial intervals between transmission pairs with discordant symptoms were not extracted. The incubation period was defined as the number of days between a confirmed exposure to a primary case (day zero) and the onset of any symptom in a secondary case. The risk of bias for each study was assessed using a tool developed by the Division of Healthcare Quality Promotion at the Centers for Disease Control and Prevention, and biases of concern were recorded in the evidence tables. The signaling questions used to assess study conduct and risk of bias and results are presented are presented in *Table 5*.

The cumulative proportion of study participants with the outcomes of interest were calculated at the study-level to determine the daily change in risk of transmission from a previously healthy adult. To conservatively estimate the risk period for transmission, the shortest possible incubation period was subtracted from the longest possible serial interval. This number of days provides the longest possible contagious period using data retrieved by this review.

Data was analyzed using Microsoft Excel (2021).

#### C.5. GRADE-ing and Recommendation Development

The quantitative findings were narratively summarized for each outcome. The strength, direction, consistency, and directness were assessed for each outcome using a modified Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach.<sup>15</sup> For this review modifications were made because the key questions do not evaluate interventions or exposures, and thus randomized controlled trials would not be the optimal study design to answer these research questions. Instead, the study types that directly answer the research question start as "high" confidence in the evidence. For key questions 1 and 2, human challenge studies reporting daily shedding and/or symptom data are the optimal study type to answer the research question and start as "high" confidence in the evidence. For key question 3, outbreak reports or case series reporting on transmission pairs are identified as the optimal study type to answer the research question. Both start as "high" confidence in the evidence in the GRADE framework. Once the confidence in the evidence was determined for the body of evidence, the GRADE Evidence-to-Decision Framework was used to guide the development of recommendations using the population perspective to make health system decisions.<sup>16,17</sup>

# C.6. Expert Review and Public Input

Draft recommendations were reviewed at a public meeting of the Healthcare Infection Control Practices Advisory Committee (HICPAC) on June 8, 2023. The associated narrative and draft recommendations were available for public comment on regulations.gov for a period of 60 days ending on April 26, 2024. The public comment period was announced in the Federal Register on February 26, 2024. No relevant public comments were received. The final guideline section and this review will be uploaded to the CDC website.

# D. Summary of Evidence

#### **D.1.** Narrative Summaries of Evidence

## D.1.a. KQ1 Duration of Shedding & KQ2 Duration of Shedding and Symptoms

KQ1: Among symptomatic adults infected with parvovirus B19, what is the duration of shedding of replication competent virus/infectious virus measured via viral culture or polymerase chain reaction (PCR)?

KQ2: Among symptomatic adults infected with parvovirus B19, what is the association between duration of symptoms and duration of shedding of replication competent virus/infectious virus measured via viral culture or polymerase chain reaction (PCR)?

There is moderate confidence in the evidence from one human challenge study<sup>3</sup> suggesting fever may indicate an individual is shedding viral DNA. This study was conducted in nine healthy adult volunteers – only five of whom were seronegative at the time of inoculation – and reported daily clinician assessments of symptoms and the collection of daily nasal washes and gargle samples to determine the presence of viral shedding using dot-blot hybridization. Of the five participants who were seronegative at baseline, four were successfully infected, and of these four, viral shedding was detected in three participants. Viral shedding was detected on days 7-11 post-inoculation, for a duration of approximately 5 days (*Figure 4*). Viral DNA was not detected in six participants, one was seronegative at inoculation and developed symptoms, one had pre-existing trace of antibody, and four participants remained uninfected after inoculation.

Among the four participants who were seronegative at inoculation and developed infection, the first episode of symptoms started with the onset of fever. Fever onset occurred between days 8-10 and resolved after 1-4 days. In one of the four patients with fever, it is possible that their fever resolved before their shedding resolved. In three of these four participants a second set of symptoms, consisting of erythematous rash, arthralgia, and mild arthritis, occurred on day 17 or 18 and lasted for 2-5 days. Importantly, this second episode of symptoms coincided with patient release, and respiratory specimens were not collected from discharged patients, preventing an assessment of viral shedding during the second episode of symptoms.

Confidence in these findings is limited by outcome measurement methods and imprecision due to small sample size. Specifically, this study was not conducted to measure an association between symptom and shedding duration and thus, did not clearly report the day shedding ended in relation to both episodes of symptoms in all participants. Viral shedding was measured using dot-blot hybridization which detects the presence of viral DNA but does not identify replication competent virus, which may have resulted in an overestimation of the duration of viral shedding among participants. Finally, the three participants experiencing rash, arthralgia, or arthritis following their flu-like symptoms were all women, limiting the generalizability of these findings. The evidence was downgraded due to a small sample size with few participants developing viremia and durations of viral shedding and symptoms were not uniformly reported for all participants.

Figure 4. Cumulative proportion (%) of participants whose shedding or symptoms resolved, measured in days from inoculation.

Study	N	Dates	Resolution of	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
Anderson 1985	9	NR	Viral shedding (n = 3)							0	0	0	0	0	100													
			Pyrexia <sup>(n=4)</sup>								0	0	25	25	75	75	100											
			Rash (n = 3)																	0	0	33	67	67	100			

<sup>^</sup>Pyrexia was reported to last 1-4 days for three participants; this figure takes a conservative approach and assigns duration as 4 days for all three of those participants.



#### D.1.b. KQ3 Risk Period for Transmission

KQ3: Among symptomatic adults infected with parvovirus B19, what is the risk period for transmission to an uninfected individual based on time since onset of symptoms in or exposure to source patients?

There is very low confidence in the evidence from three outbreak studies<sup>4,9,10</sup> reporting the serial interval for transmission pairs or cases. Serial intervals across all studies ranged from 10 to 32 days (*Figure 5A*). Secondary case symptom onset occurred 24 days after primary case symptom onset in ≥75% of all transmission pairs in all three studies. Confidence in these findings is very limited due to measurement and misclassification bias, imprecision, and inconsistency. Each study measured serial interval using different symptoms as benchmarks including rash,<sup>4</sup> muscle or joint pain;<sup>10</sup> and fever. <sup>9</sup> Only one study<sup>9</sup> attempted to link transmission pairs through molecular epidemiology and determined there were multiple circulating strains rather than an outbreak of a single strain. Confidence in these findings is limited by measurement and misclassification bias, imprecision, and inconsistency. In all three studies, the longer serial intervals of 20 days or more may represent tertiary case symptom onset, suggesting misclassification of these tertiary cases as secondary cases. Confidence in the estimate of serial interval is limited by the low number of transmission pairs. Finally, there is inconsistency in the duration of serial interval reported within and across all three studies.

There is also very low confidence in the evidence from two outbreak studies<sup>5,10</sup> reporting the incubation period for transmission pairs. These studies reported incubation periods ranging from 6 to 16 days (*Figure 5B*). Confidence in these findings is limited by inconsistency, indirectness, and imprecision. One study<sup>5</sup> reported on two outbreaks in a children's hospital where index cases were 17-year-old adolescents with sickle cell disease who were diagnosed with aplastic crisis and thus may have been infectious longer than healthy persons.<sup>18</sup> These two studies included a small number of transmission pairs and did not link transmission through genotyping.

The longest conservative serial interval was 32 days,<sup>4</sup> and the shortest incubation period was 6 days,<sup>5</sup> thus the most conservative risk period for transmission is estimated to be 26 days. The results from this review do not align with previous studies<sup>6-8</sup> reporting serial (or case) intervals of 6 to 11 days; however, those estimates were based on transmission pairs where a child was the primary case, and not an adult. While these estimates may not accurately reflect the serial interval for adult primary cases, there is very low confidence in the findings for the serial interval and the incubation period found in this review. Stronger confidence in the evidence of resolution of shedding before resolution of fever resulted in using resolution of fever – on day 14 – to estimate the risk period for transmission.<sup>3</sup>

Figure 5. Cumulative proportion (%) of symptom onset in secondary cases measured in days from A. symptom onset in the primary case or B. exposure to primary case.

Study	Pairs (N)	Dates	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
A. Serial interval: sy	mptom ons	set in index case to symptom o	onset	in se	cond	ary ca	se																				
Chen 2010	2	Mar 12 - Apr 12, 2007	0	0	0	0	0	0	0	0	0	0	0	50	50	50	50	50	50	50	50	50	50	50	50	100	
Rosenstein 2020	3	NR	0	0	0	0	0	0	0	0	0	33	33	67	67	67	67	67	67	67	67	67	67	67	100		
Shishiba 1993	8	Oct 22, 1991 - Mar 6, 1992	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	25	38	50	50	63	63	63	75	75	88
B. Incubation period	d: exposure	e to index case to symptom on	setir	seco	ndar	y cas	•																				
Bell 1989	11	Jun 6 - Jul 30, 1988	0	0	0	0	0	9	9	18	18	36	36	36	45	55	73	100									
Rosenstein 2020	1	NR	0	0	0	0	0	0	0	0	0	0	0	0	0	0	100										
		Legend: colors every 10%	0	10	20	30	40	50	60	70	90	90	100	1													

# D.2. Evidence Tables

# D.2.a. GRADE-ed Summary of Findings

#### Table 2. GRADE Table for KQ2: Duration of Shedding & Symptoms

Outcome	Summary	Studies	Risk of bias	Imprecision	Inconsistency	Indirectness	Confidence
Duration of viral shedding and fever	One human challenge study suggests that among participants who were seronegative at inoculation and successfully infected, viral shedding may occur for five days, and in 75% of patients who experienced fever, and shedding resolved with or before fever resolution.  Resolution of fever occurred by day 14 in symptomatic participants.	N = 4 seronegative participants who developed infection 1 human challenge study <sup>3</sup>		Serious concerns <sup>i</sup>	No concerns	No concerns	Moderate

#### Table 3. GRADE Table for KQ3: Risk Period for Transmission

Outcome	Summary	Studies	Risk of bias	Imprecision	Inconsistency	Indirectness	Confidence
Serial interval	Three outbreak case series report parvovirus B19 serial intervals ranging from 10-32 days.	N = 13 pairs  3 outbreak case series <sup>4,9,10</sup>	Serious concerns <sup>ii</sup>	Some concerns <sup>iii</sup>	Serious concerns <sup>iv</sup>	No concerns	Very low
Incubation period	Two outbreak case series report parvovirus B19 incubation periods ranging from 6-16 days.	N = 12 pairs  2 outbreak case series <sup>5,10</sup>	No concerns	Some concerns <sup>iii</sup>	Serious concerns <sup>v</sup>	Some concerns <sup>vi</sup>	Very low

#### D2.b. Extracted Evidence from Included Studies

#### Table 4. Extracted Evidence for KQ1 and KQ2

Author, Year	Population & Setting	Data collection & Diagnostic tests	Duration of symptoms	Duration of shedding
Author: Anderson <sup>3</sup>	Population: N = 9 healthy	Sampling method: Nasal wash, and gargle	Duration of pyrexia: range of 1-4	Maximum duration of shedding: 5 days
V 100F	volunteers	specimens	days; associated with headache,	
Year: 1985	Setting: Medical research unit	<b>Diagnostic tests:</b> Examined for DNA by dot- blot hybridization	itching, malaise and chills; commenced on days 8-10	DNA was detected in nasal washes and gargle specimens between 7-11 days (same time as viremia) after inoculation

<sup>&</sup>lt;sup>1</sup> Small sample size with few participants developing viremia; durations of viral shedding and symptoms not reported uniformly for all participants.

ii Differential measurement of serial interval within studies due to different symptoms used to determine 'onset' in index and secondary cases; studies may have identified tertiary cases as secondary cases.

iii Studies had small sample sizes.

<sup>&</sup>lt;sup>IV</sup> Differential measurement of serial interval between studies due to different symptoms used to determine 'onset' in index and secondary cases; wide range in reported serial intervals.

<sup>&</sup>lt;sup>v</sup> Wide range in reported incubation periods.

<sup>&</sup>lt;sup>vi</sup>Downgraded for Indirectness: one study included 17-year-old index cases.

Author, Year	Population & Setting	Data collection & Diagnostic tests	Duration of symptoms	Duration of shedding
Study design: Human challenge study	Country: England Study dates: NR; duration of 3 weeks	Symptom ascertainment: Daily examination by physician; self-reported oral temperature each morning and evening; daily symptom questionnaire	Duration of erythematous rash: range 2-3 days; commenced on day 17  Duration of arthralgia and mild arthritis: 4 days; commenced on second day of rash	from 3/4 individuals who were seronegative at start; virus was not detected in 1 seronegative volunteer, 1 volunteer with pre-existing trace of antibody, or any of the 4 volunteers who did not become infected

# **Table 5. Extracted Evidence for KQ3**

Author, Year	Population & Setting	Data collection & Diagnostic tests	Outcome definitions	Outcomes
Author: Bell <sup>5</sup> Year: 1989 Study design: Outbreak case series	Population: N = 11 HCP cases  Setting: Two units of a children's hospital  Country: Pennsylvania, USA  Study dates: June 6 – July 30, 1988	Symptoms reported: Fever, posterior cervical adenopathy, rash, pruritic rash, joint pain, malaise, anorexia, headache, myalgia  Symptom onset in infector(s): Both index cases had sickle cell disease and aplastic crisis; one reported fever, severe joint pain, headache, and evidence of pharyngitis upon admission; other reported fever on second day of hospitalization; no rash  Symptom onset infectee(s): Most common initial symptoms were malaise and fever; all HCP had low-grade fever; rash present in 10/11 which began 1-10 days after initial symptoms and lasted 1-5 days  Sampling method: Blood  Diagnostic tests: Serologic testing for anti-	Serial interval: NR Incubation period: Time interval between first exposure to a sickle cell patient in aplastic crisis and onset of symptoms in HCP	Serial interval: NR Incubation period: 6-16 days (range) Day 6: 1 HCP Day 8: 1 HCP Day 10: 2 HCP Day 13: 1 HCP Day 14: 1 HCP Day 15: 2 HCP Day 16: 3 HCP Outbreak end: NR
Author: Chen <sup>9</sup> Year: 2010 Study design: Outbreak case series	Population: N = 5 HCP cases  Setting: Two coronary care units of teaching hospital  Country: Taiwan  Study dates: March 12 – April 12, 2007	Symptoms reported: Fever, rash, facial rash (slapped cheek appearance), severe joint pain, fever, swelling of extremities  Symptom onset in infector(s): Case 2 reported fever  Symptom onset infectee(s): Cases 1 and 5 reported rash, case 3 reported fever, and case 4 reported fever and rash  Sampling method: Serum	Serial interval: Time interval between onset of fever in case 2 (hypothesized to be index case) and fever in 1) case 3 2) case 4 (and rash) Incubation period: NR	Serial interval: 12-24 days (range) 1) 12 days 2) 24 days (and rash) Incubation period: NR Outbreak end: No patient was identified as source. Hypothesized that HCP 2 propagated transmission through close contact with other staff. Reinforced hand hygiene, use of surgical masks, and disinfection using sodium hypochlorite solution ended transmission.

Author, Year	Population & Setting	Data collection & Diagnostic tests	Outcome definitions	Outcomes
		Diagnostic tests: Immunoblotting and viral DNA extracted from serum tested via nested PCR		
Author: Rosenstein <sup>10</sup> Year: 2020 Study design: Outbreak case series	Population: N = 5 cases (n = 2 patients, n = 2 HCP, n = 1 relative)  Setting: Community-based rheumatology practice  Country: New Jersey, USA  Study dates: NR	Symptoms reported: Fever, myalgia, edema, episodic migratory pain, and malaise; no rash was reported  First symptom onset in infector(s): Index patient reported arthralgia and edema; HCP 1 reported myalgia, malaise, stiffness and arthritis  Symptom onset in infectee(s): Spouse reported malaise, myalgia, stiffness, and arthritis); HCP 2 reported episodic migratory pain  Sampling method: Blood  Diagnostic tests: IgM and IgG measured by solid phase antibody capture radioimmunoassays	Serial interval: Time interval between the onset of symptoms in 1) index patient & HCP 1 (myalgia, malaise, stiffness, arthritis) 2) HCP 1 and spouse (malaise, myalgia, stiffness, arthritis) 3) HCP 1 and HCP 2 (migratory pain, synovitis) Incubation period: Time interval between exposure to index patient 1 and the onset of symptoms in 1) HCP 1 (myalgia, malaise, stiffness, arthritis)	Serial interval: 10-23 days (range) 1) 23 days 2) 10 days 3) 12 days Incubation period: 1) 15 days (exposed on day 8 of infectious course) Outbreak end: NR
Author: Shishiba <sup>4</sup> Year: 1993 Study design: Outbreak case series	Population: N = 9 cases (n = 1 index patient, n = 8 HCP)  Setting: Neurosurgical unit of hospital  Country: Japan  Study dates: October 22, 1991 – March 6, 1992	Symptoms reported: Fever, edema, arthralgia, malaise, lymphadenopathy, and facial and extremity eruptions  Symptom onset in infector(s): Index patient reported fever with a lacy erythematous eruption 3 days later  Symptom onset in infectee(s): Patient 4 reported rash; NR for all other infectees  Sampling method: Serum  Diagnostic tests: Tested for B19 DNA by PCR and IgM and IgG seropositivity	Serial interval: Time interval between onset of rash in index case and rash in 1) HCP 1 2) HCP 2 3) HCP 3 4) HCP 4 (fever 4 days after lacy rash; face rash 2 days later) 5) HCP 5 6) HCP 6 (fever but sequence of rash and fever not reported) 7) HCP 7 8) HCP 8 Incubation period: NR	Serial interval: 16-32 days 1) 16 days 2) 16 days 3) 17 days 4) 18 days 5) 20 days 6) 23 days 7) 25 days 8) 32 days Incubation period: NR Outbreak end: NR

**Table 6: Internal Validity Assessment of Studies Examining Key Questions** 

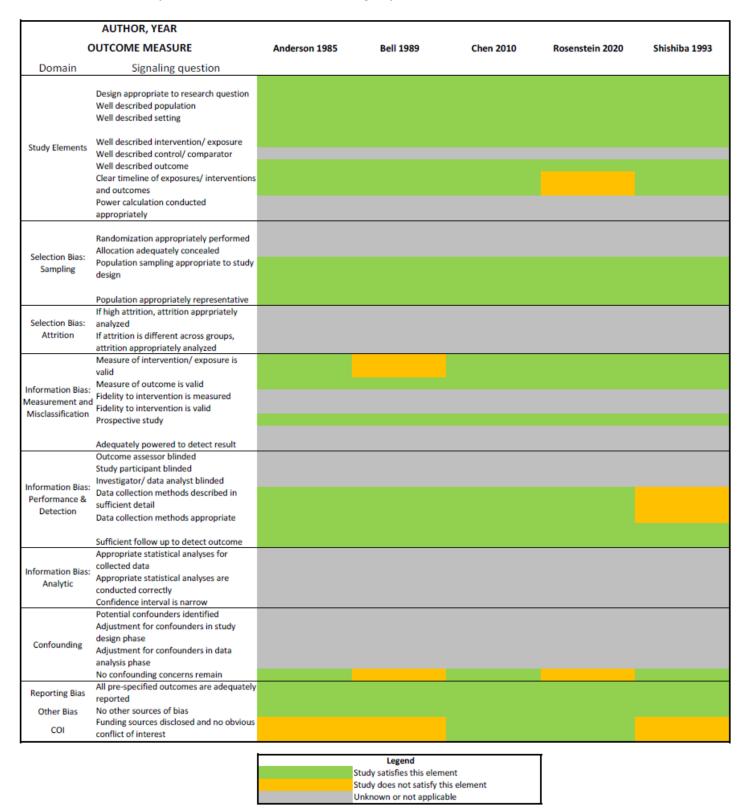


Table 7. Primary Search of MEDLINE (OVID), Embase (OVID), Cochrane Library, CINAHL (Ebsco), and Scopus for KQ1: Duration of Shedding

Database	Strategy	<b>Records</b> 04/03/2025
Medline (OVID) 1946-	<ol> <li>exp Erythrovirus/ OR Parvovirus B19, Human/</li> <li>(erythrovirus* OR parvovirus B19* OR parvovirus B 19* OR B 19 virus*).ti,ab,kf,hw.</li> <li>1 OR 2</li> <li>exp virus shedding/</li> <li>(shed* OR replica* OR competent OR infectiousness OR infectivity OR contagiousness OR ((viral or virus) ADJ5 (emission* or emit*)) OR viable OR viability).ti,ab,kf,hw.</li> <li>exp Polymerase Chain Reaction/ OR exp clinical laboratory techniques/</li> <li>(polymerase chain reaction OR PCR OR RT-PCR OR RT-qPCR OR qPCR OR sero* OR serum OR specimen* OR sample* OR test* OR assay* OR clinical technique* OR lab* OR cultures OR detect*).ti,ab,kf,hw.</li> <li>4 OR 5 OR 6 OR 7</li> <li>3 AND 8</li> </ol>	3276
Embase (OVID) 1974-	<ol> <li>exp Erythrovirus/ OR Human Parvovirus B19/</li> <li>(erythrovirus* OR parvovirus B19* OR parvovirus B 19* OR B 19 virus*).ti,ab,kf,hw.</li> <li>1 OR 2</li> <li>exp virus shedding/</li> <li>(shed* OR replica* OR competent OR infectiousness OR infectivity OR contagiousness OR ((viral or virus) ADJ5 (emission* or emit*)) OR viable OR viability).ti,ab,kf,hw.</li> <li>exp Polymerase Chain Reaction/ OR exp laboratory technique/</li> <li>(polymerase chain reaction OR PCR OR RT-PCR OR RT-qPCR OR qPCR OR sero* OR serum OR specimen* OR sample* OR test* OR assay* OR clinical technique* OR lab* OR cultures OR detect*).ti,ab,kf,hw.</li> <li>4 OR 5 OR 6 OR 7</li> <li>3 AND 8</li> <li>limit 9 to "remove medline records"</li> <li>limit 10 to conference abstract status</li> <li>10 NOT 11</li> </ol>	711 - duplicates =521 unique items
Cochrane Library	#1 [mh Erythrovirus] OR [mh "Parvovirus B19, Human"] #2 (erythrovirus* OR "parvovirus B19" OR "parvovirus B 19" OR "B 19 virus"):ti,ab,kw #3 #1 OR #2 #4 [mh ^"virus shedding"] #5 (shed* OR replica* OR competent OR infectiousness OR infectivity OR contagiousness OR ((viral or virus) NEAR/5 (emission* or emit*)) OR viable OR viability):ti,ab,kw #6 [mh ^"Polymerase Chain Reaction"] OR [mh ^"clinical laboratory techniques"] #7 ("polymerase chain reaction" OR PCR OR RT-PCR OR RT-qPCR OR qPCR OR sero* OR serum OR specimen* OR sample* OR test* OR assay* OR (clinical NEXT technique*) OR lab* OR cultures OR detect*):ti,ab,kw #8 #4 OR #5 OR #6 OR #7 #9 #3 AND #8	- duplicates =30 unique items
CINAHL (EBSCOHost)	(MH Erythrovirus) OR (MH "Parvovirus B19, Human")  (erythrovirus* OR "parvovirus B19*" OR "parvovirus B 19*" OR "B 19 virus*")  S1 OR S2  (MH "virus shedding")  (shed* OR replica* OR competent OR infectiousness OR infectivity OR contagiousness OR ((viral or virus) N5 (emission* or emit*)) OR viable OR viability)  (MH "Polymerase Chain Reaction") OR (MH "clinical laboratory techniques")	98 - duplicates =28 unique items

	("polymerase chain reaction*" OR PCR OR RT-PCR OR RT-qPCR OR qPCR OR sero* OR serum OR specimen* OR sample* OR test* OR assay* OR "clinical technique*" OR lab* OR cultures OR detect*)  S4 OR S5 OR S6 OR S7  S3 AND S8  Limiters - Exclude MEDLINE records	
Scopus	TITLE-ABS-KEY(erythrovirus* OR "parvovirus B19*" OR "parvovirus B 19*" OR "B 19 virus*") AND TITLE-ABS-KEY(shed* OR replica* OR competent OR infectiousness OR infectivity OR contagiousness OR ((viral or virus) W/5 (emission* or emit*)) OR viable OR viability OR "polymerase chain reaction*" OR PCR OR RT-PCR OR RT-qPCR OR qPCR OR sero* OR serum OR specimen* OR sample* OR test* OR assay* OR "clinical technique*" OR lab* OR cultures OR detect*) AND NOT INDEX(medline)	935 - duplicates =228 unique items

# Table 8. Primary Search of MEDLINE (OVID), Embase (OVID), Cochrane Library, CINAHL (Ebsco), and Scopus for KQ2: Duration of Symptoms and Duration of Shedding

Database	Strategy	<b>Records</b> 02/10/2025
Medline (OVID) 1946-	<ol> <li>exp Erythrovirus/ OR Parvovirus B19, Human/</li> <li>(erythrovirus* OR parvovirus B19* OR parvovirus B 19* OR B 19 virus* OR B19 virus*).ti,ab,kf,hw.</li> <li>1 OR 2</li> <li>Symptom*.mp</li> <li>exp virus shedding/</li> <li>(shed* OR replica* OR competent OR infectiousness OR infectivity OR contagiousness OR ((viral or virus) ADJ5 (emission* or emit*)) OR viable OR viability).ti,ab,kf,hw.</li> <li>5 OR 6</li> <li>3 AND 4 AND 7</li> </ol>	24
Embase (OVID) 1974-	<ol> <li>exp Erythrovirus/ OR Human Parvovirus B19/</li> <li>(erythrovirus* OR parvovirus B19* OR parvovirus B 19* OR B 19 virus*).ti,ab,kf,hw.</li> <li>1 OR 2</li> <li>Symptom*.mp.</li> <li>exp virus shedding/</li> <li>(shed* OR replica* OR competent OR infectiousness OR infectivity OR contagiousness OR ((viral or virus) ADJ5 (emission* or emit*)) OR viable OR viability).ti,ab,kf,hw.</li> <li>5 OR 6</li> <li>3 AND 4 AND 7</li> </ol>	- duplicates =24 unique items
Cochrane Library	#1 [mh Erythrovirus] OR [mh "Parvovirus B19, Human"] #2 (erythrovirus* OR "parvovirus B19" OR "parvovirus B 19" OR "B 19 virus"):ti,ab,kw #3 #1 OR #2 #4 Symptom*:ti,ab,kw #5 [mh ^"virus shedding"] #6 (shed* OR replica* OR competent OR infectiousness OR infectivity OR contagiousness OR ((viral or virus) NEAR/5 (emission* or emit*)) OR viable OR viability):ti,ab,kw #7 #5 OR #6 #8 #3 AND #4 AND #7	duplicates =3 unique items

CINAHL (EBSCOHost)	S1 (MH Erythrovirus) OR (MH "Parvovirus B19, Human") S2 (erythrovirus* OR "parvovirus B19*" OR "parvovirus B 19*" OR "B 19 virus*") S3 S1 OR S2 S4 (TI Symptom*) OR (AB Symptom*) OR (SU Symptom*) S5 (MH "virus shedding") S6 (shed* OR replica* OR competent OR infectiousness OR infectivity OR contagiousness OR ((viral or virus) N5 (emission* or emit*)) OR viable OR viability) S7 S5 OR S6 S8 S3 AND S4 AND S7 S9 Limiters - Exclude MEDLINE records	- duplicates =0 unique items
Scopus	TITLE-ABS-KEY(erythrovirus* OR "parvovirus B19*" OR "parvovirus B 19*" OR "B 19 virus*") AND TITLE-ABS-KEY(symptom*) AND TITLE-ABS-KEY(shed* OR replica* OR competent OR infectiousness OR infectivity OR contagiousness OR ((viral or virus) W/5 (emission* or emit*)) OR viable OR viability)	5 - duplicates =2 unique items

# Table 9. Primary Search of MEDLINE (OVID), Embase (OVID), Cochrane Library, CINAHL (Ebsco), and Scopus for KQ3: Serial Interval

Database	Strategy	<b>Records</b> 04/03/2025
Medline (OVID) 1946-	<ol> <li>exp Erythrovirus/ OR Parvovirus B19, Human/</li> <li>(erythrovirus* OR parvovirus B19* OR parvovirus B 19* OR B 19 virus*).ti,ab,kf,hw.</li> <li>1 OR 2</li> <li>Onset OR (begin* ADJ5 symptom*) OR (start* ADJ5 symptom*) OR (show* ADJ5 symptom*)</li> <li>(transmi* OR shed* OR contagiousness OR emission* or emit* OR duration OR competenc* OR viable OR viability OR infecti*).ti,ab,kf,hw.</li> <li>3 AND 4 AND 5</li> </ol>	263
Embase (OVID) 1974-	<ol> <li>exp Erythrovirus/ OR Human Parvovirus B19/</li> <li>(erythrovirus* OR parvovirus B19* OR parvovirus B 19* OR B 19 virus*).ti,ab,kf,hw.</li> <li>1 OR 2</li> <li>Onset OR (begin* ADJ5 symptom*) OR (start* ADJ5 symptom*) OR (show* ADJ5 symptom*)</li> <li>(transmi* OR shed* OR contagiousness OR emission* or emit* OR duration OR competenc* OR viable OR viability OR infecti*).ti,ab,kf,hw.</li> <li>3 AND 4 AND 5</li> <li>Limit 6 to "remove medline records"</li> </ol>	- duplicates =177 unique items
Cochrane Library	#1 [mh Erythrovirus] OR [mh "Parvovirus B19, Human"] #2 (erythrovirus* OR "parvovirus B19" OR "parvovirus B 19" OR "B 19 virus"):ti,ab,kw #3 #1 OR #2 #4 (Onset OR (begin* NEAR/5 symptom*) OR (start* NEAR/5 symptom*) OR (show* NEAR/5 symptom*)):ti,ab,kw #5 (transmi* OR shed* OR contagiousness OR emission* or emit* OR duration OR competenc* OR viable OR viability OR infecti*):ti,ab,kw #6 #3 AND #4 AND #5	duplicates =2 unique items
CINAHL (EBSCOHost)	S1 (MH Erythrovirus) OR (MH "Parvovirus B19, Human") S2 (erythrovirus* OR "parvovirus B19*" OR "parvovirus B 19*" OR "B 19 virus*") S3 S1 OR S2 S4 (TI (Onset OR (begin* N5 symptom*) OR (start* N5 symptom*) OR (show* N5 symptom*))) OR (AB (Onset OR (begin* N5 symptom*) OR (start* N5 symptom*)	8 - duplicates =2

	OR (show* N5 symptom*))) OR (SU (Onset OR (begin* N5 symptom*) OR (start* N5 symptom*) OR (show* N5 symptom*)))  S5 (TI (transmi* OR shed* OR contagiousness OR emission* or emit* OR duration OR competenc* OR viable OR viability OR infecti*)) OR (AB (transmi* OR shed* OR contagiousness OR emission* or emit* OR duration OR competenc* OR viable OR viability OR infecti*)) OR (SU (transmi* OR shed* OR contagiousness OR emission* or emit* OR duration OR competenc* OR viability OR infecti*))  S6 S3 AND S4 AND S5	unique items
Scopus	Limiters - Exclude MEDLINE records  TITLE-ABS-KEY(erythrovirus* OR "parvovirus B19*" OR "parvovirus B 19*" OR "B 19 virus*") AND TITLE-ABS-KEY(Onset OR (begin* W/5 symptom*) OR (start* W/5 symptom*) OR (show* W/5 symptom*)) AND TITLE-ABS-KEY(transmi* OR shed* OR contagiousness OR emission* or emit* OR duration OR competenc* OR viable OR viability OR infecti*) AND NOT INDEX(medline)	61 - duplicates =16
		unique items

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