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Case Report

Breakthrough Serotype 3 Pneumococcal Parapneumonic Empyema in a 9-Month-Old PCV20-Vaccinated Infant: Clinical and Sequential Serological Evaluation

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Highlights

- To our knowledge, this is the first published case of serotype 3 pneumococcal parapneumonic empyema in an infant following two doses of PCV20 in a 2 + 1 immunization schedule.
- The longitudinal serological follow-up informs the evolution of the serotype-specific antibody response after infection and booster vaccination.

What are the main findings?

- The marked serotype 3-specific IgG due to the severe infection was followed by its subsequent decline with no apparent increase after the booster dose.
- In contrast, all other tested PCV20 serotypes showed substantial antibody increases within one month after booster vaccination.

What are the implications of the main findings?

- Our findings may complement the ongoing real-world clinical experience with the newly implemented higher-valence conjugate vaccines.
- Pneumococcal serotype 3 continues to attract research interest in PCV development.

Abstract

Background: *Streptococcus pneumoniae* serotype 3 remains a leading cause of severe pneumococcal disease, including parapneumonic empyema (PPE), while vaccine escape mechanisms are not uncommon. Although such cases are not prevalent during infancy, the recent introduction of the 20-valent pneumococcal conjugate vaccine (PCV20) into national immunization schedules should be carefully monitored for breakthrough infections. We report on a case of serotype 3 PPE in a 9-month-old infant following immunization with PCV20, which was followed by sequential serological monitoring. **Case Presentation:** A 9-month-old infant presented with severe parapneumonic empyema caused by *S. pneumoniae* serotype 3. Notably, the infection occurred shortly after the inclusion of PCV20 in a 2 + 1 schedule as recommended by the Greek National Immunization Program, following the administration of the two primary doses. To investigate the immunological context of this breakthrough infection, serum pneumococcal serotype-specific antibody values were sequentially quantified at four distinct time points: 7, 51, 80, and 119 days after disease onset. The 80th-day sample was obtained before the PCV20 booster administration; the final sample was collected 33 days after the booster dose. Serotype 3-specific antibody

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concentrations were 5.19, 121.78, 19.53, and 4.10 μg/mL, respectively. **Conclusions:** Our case presents the uncommon occurrence of a serotype 3 PPE during infancy despite PCV20 vaccination. The longitudinal tracking of serotype-specific antibody levels provides interesting data on the infant's immune response to both natural infection and subsequent booster vaccination. These findings add to the experience with the newly implemented higher-valence conjugate vaccines.

Keywords: *Streptococcus pneumoniae* serotype 3; pneumococcal parapneumonic empyema; infant; PCV20; pneumococcal serotype-specific antibody concentrations; breakthrough; invasive disease

1. Introduction

An increase in the incidence of childhood pneumococcal parapneumonic empyema (PPE), particularly due to serotype 3, has been reported over the last two decades. Most cases occur between the second and fifth years of life among preschoolers who have received a pneumococcal conjugate vaccine (PCV), most commonly PCV13 in a 2 + 1 or 3 + 1 schedule [1–7]. Only a few serotype 3 PPE cases have been reported among vaccinated infants [5,7]. We describe a case of PPE caused by *Streptococcus pneumoniae* serotype 3 infection in a 9-month-old infant that occurred early after the implementation of PCV20 in a 2 + 1 schedule as per the Greek National Immunization Program (NIP), in April 2025. To our knowledge, this is the first published case of PPE in the PCV20 era in a 2 + 1 vaccination schedule, despite a complete basic series of PCV20 immunization.

2. Case

2.1. Patient Presentation

In January 2026, a 9-month-old male infant was admitted to a secondary care hospital in Central Greece with a one-week history of rhinitis, cough, progressively worsening respiratory distress, and fever which reached 39.4 °C in the four days preceding admission. No antibiotic therapy had been administered during his outpatient course of illness. Upon admission, a chest X-ray showed left-sided alveolar consolidation with pleural effusion, and intravenous (IV) cefotaxime at a dose of 200 mg/kg/day was promptly initiated. Approximately 24 h later, left-sided otorrhea was noted. The patient deteriorated clinically over the first 48 h of his hospital stay, and a repeat chest X-ray showed an increase in the parapneumonic effusion. Clindamycin was added to the antibiotic regimen, and the child was subsequently transferred to the Pediatric Ward of the University General Hospital of Larissa.

2.2. Personal History, Diagnostic Process on Admission

The infant was born at full term and was reported to be healthy prior to his febrile illness, with no known history of infections or family history of immunodeficiency. The infant was fully immunized according to the Greek NIP. He had received two doses of PCV20: at 3 months and 3 days of age, and again at 5 months and 6 days of age. At the time of admission to our Pediatric Ward, the patient exhibited pallor, fatigue, respiratory distress, feeding difficulties and marked spontaneous drainage of purulent material from his left ear. The respiratory rate was 40 breaths/min. He had intercostal retractions and decreased air entry with crackles over the left lung field. Pulse-oximetry oxygen saturation value (SpO_2) remained stable at 95% on supplemental oxygen administered via nasal cannula, as required.

Chest ultrasound (US) showed a large amount of pleural fluid with septation of the fibropurulent material. Despite 48 h of IV antimicrobial therapy, clinical deterioration of the patient prompted chest tube placement (Figure 1); the antibiotic regimen was temporarily escalated to IV meropenem (120 mg/kg/day) and linezolid (30 mg/kg/day). The empirical antimicrobial therapy administered was intended to cover potential pathogens [1,4], taking into account the patient's age, clinical presentation and recently identified antimicrobial resistance rates in Central Greece; nonsusceptibility of pneumococcal isolates to penicillin and cefotaxime was estimated to be approximately 15% and 5%, respectively, from January 2017 to December 2025 (authors' unpublished data).

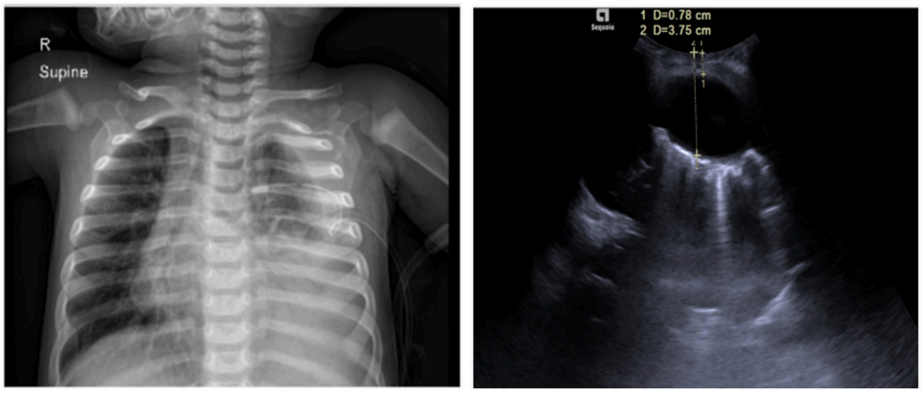


Figure 1. Radiological findings of pneumococcal parapneumonic empyema (chest X-ray and ultrasound).

Upon admission to our ward, the white blood cell count (WBC) was 11,600/mm^3 (62.8% neutrophils), platelets were 233,000/mm^3, the C-Reactive Protein (CRP) value was 253 mg/L (normal value < 5 mg/L) and the Erythrocyte Sedimentation Rate (ESR) was 68 mm in the first hour. Upon needle thoracocentesis, 45 mL viscid pleural fluid (PF) with turbid fibropurulent material was aspirated. PF analysis revealed pH 7.47, elevated values of lactate dehydrogenase (1134 U/L) and protein (3.7 g/dL), while glucose concentration was low (33 mg/dL).

2.3. Clinical and Treatment Process

Intrapleural alteplase was administered via chest tube for two consecutive days; the chest tube was removed 24 h after PF drainage had ceased; in total, 220 mL were drained through the chest tube. Acute otitis media with spontaneous perforation of the tympanic membrane and purulent ear drainage—already present upon admission to our ward—continued for a total of 5 days. The child became afebrile at the end of the fifth hospitalization day, at which time linezolid was discontinued. Skull Magnetic Resonance Imaging (MRI) with contrast enhancement revealed complete bilateral opacification of the mastoid air cells (Figure 2). When the results of microbiological and molecular studies, including *S. pneumoniae* identification, antimicrobial susceptibility testing and serotyping, and those of the initial immunological workup became available, de-escalation of the antimicrobial therapy was performed, and meropenem, which was administered for 8 days, was switched to ampicillin (175 mg/kg/day). The total duration of antimicrobial treatment in our Pediatric Ward was 14 days; oral antibiotics were not prescribed.

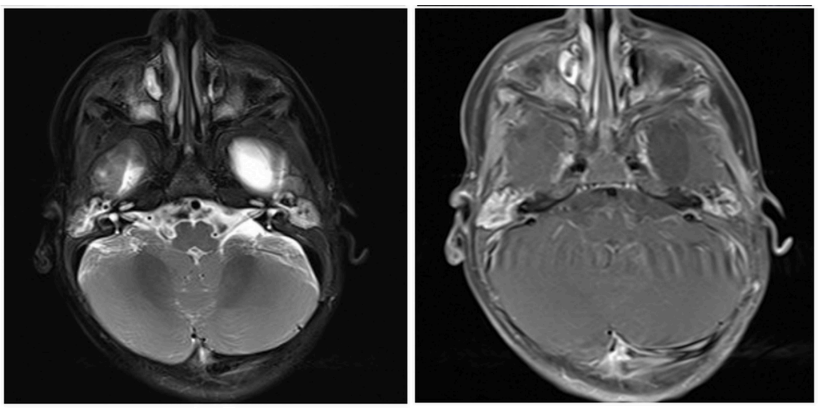


Figure 2. MRI findings of complete bilateral opacification of the mastoid air cells, with mild contrast enhancement.

Blood and pleural fluid cultures were negative. The culture of the middle ear fluid from the spontaneous tympanic perforation and RT-PCR of the pleural fluid revealed *S. pneumoniae* serotype 3.

We performed antimicrobial susceptibility testing using the isolate recovered from the culture of the middle ear fluid. The pneumococcal isolate from the ear drainage belonged to serotype 3 and was susceptible to penicillin and cefotaxime. The etiology of the pleural empyema was determined by molecular analysis of the pleural fluid by RT-PCR, while the antimicrobial susceptibility of the pathogen was assumed to be identical to that of the otopathogen.

During the child's hospitalization, postnatal CMV infection was also diagnosed. Neonatal screening, including CMV and cystic fibrosis, was negative. He was solely breastfed during the first two months of life, followed by formula. The infant had a 6 cm palpable rigid spleen, and CMV infection was confirmed by positive DNA testing of blood and urine. Thrombocytopenia and other hematological, hepatological or gastrointestinal findings were absent.

Hemoglobin electrophoresis, sickle anemia and HIV testing were negative, whereas testing of both parents did not reveal hemoglobinopathy, including thalassemia and sickle cell anemia. Cardiac ultrasound and audiological testing were normal.

2.4. Immunological Work-Up

Examination of the blood smear was negative for Howell–Jolly bodies. The immunologic workup included: (a) complete blood count, (b) serum immunoglobulin levels (IgG, IgG subclasses, IgA, IgM, IgE), (c) oxidative burst of activated neutrophils using dihydrorhodamine 123 flow cytometry assay, (d) antibody response to tetanus toxoid and to *Haemophilus influenzae* type b (Hib) conjugate vaccine, (e) lymphocyte immunophenotyping and lymphocyte subpopulations, and evaluation of the IRAK-4/MyD88-dependent pathways, (f) C3, C4, total complement activity, mannan-binding lectin pathway of complement activation, and alternative complement activity. This investigation did not reveal a specific immunodeficiency.

2.5. Sequential Serological Evaluation

A 12-plex bead-based flow analysis assay using the methodology of Lal et al. [8] was applied; the serotypes within the multiplex assay were those within PCV13 with the exception of 6A. Timing of blood sampling of immunoglobulin isotypes, IgG subclasses, antibody response to vaccines, and the 12 pneumococcal serotype-specific antibody values

are presented in relation to the initiation of the disease and the vaccination history in Table 1. The protective antibody pneumococcal cut-off level was considered ≥0.35 μg/mL.

Table 1. Immunoglobulin isotypes, IgG subclasses, antibody response to PCV20 and other vaccines in the early and late phases of the pneumococcal disease.

Days Elapsed Between Disease Onset and Blood Sampling	**7**	**51**	**80**	**119**	**175**	**206**
Days elapsed between the most recent PCV20 dose and blood sampling	Since 2nd dose				Since booster dose	
	130	174	203 * (pre-booster)	33 (post-booster)	89	120
Days elapsed between the most recent DTPa-IPV-HBV-Hib dose and blood sampling	Since 3rd dose					Since booster dose
	103	147	176	215	271 (pre-booster)	30 (post-booster)
Immunoglobulin isotypes and IgG subclasses (mg/dL)						
IgG	811	942	884	659	762	767
IgM	105	94	90	112	106	77
IgA	291 §,¥	68	46	66	82	68
IgG1	528	594	517	390	555	478
IgG2	98	88	95	88	86	91
IgG3	74	54	49	40	51	47
IgG4	1	1	1	1	2	3
Antibody response to vaccines						
Anti-Pnc (μg/mL)	54	>270	>270	240	212	132
Anti-Tetanus-toxoid (IU/mL)	0.2	1.5	1.8	1.3	1.1	>7
Anti-Hib (μg/mL)	0.5	1	0.7	0.5	0.5	>9
Pnc serotype-specific Abs (μg/mL)						
1	0.15	0.23	0.14	3.23	-	-
3	5.19	121.78	19.53	4.10	-	-
4	0.14	0.3	0.21	3.36	-	-
5	0.05	0.13	0.05	0.87	-	-
6B	0.16	0.20	0.12	5.39	-	-
7F	0.28	0.54	0.36	1.34	-	-
9V	0.05	0.15	0.05	3.36	-	-
14	1.43	2.53	1.66	13.20	-	-
18C	0.05	0.16	0.05	1.41	-	-
19A	0.05	0.10	0.05	1.26	-	-
19F	0.26	0.35	0.21	9.05	-	-
23F	0.05	0.05	0.05	1.42	-	-

DTPa-HBV-Polio-Hib: 6-valent vaccine against diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and *Haemophilus influenzae* type b; Pnc: pneumococcus; Abs: antibodies; * pre-booster at 11.9 months; § normal range of IgA: 13–69 mg/dL (6–11 mos).
¥ Speculative high IgA interference in the initial ELISA measurement of IgG antibodies

Of note is the very high IgA level measured in the first sample; it is plausible that IgA may have led to interference with the IgG concentrations for tetanus toxoid, Hib and serotype-specific pneumococcal antibodies. The high serotype 3 antibody concentration (5.19 μg/mL) measured was most likely due to an anamnestic response to the serotype 3 polysaccharide from the recent infection, since the infant was primed with two doses of PCV20. We were unable to accurately evaluate the 11—additional to serotype 3—serotype-specific pneumococcal concentrations in the initial serum sample. It is plausible that removal of the IgA in the initial sample would have restored the IgG levels against tetanus toxoid, Hib and serotype-specific pneumococcal antibodies; however, this cannot be easily performed on small volumes of sera. Due to the inadequate volume of the stored sampling material, we cannot verify this hypothesis. Interestingly, the level of IgA had substantially declined in the three samples obtained after the initial one (Table 1). We maintain that removal of IgA interference restored the detectability of IgG concentrations, thus substantially elevating

the levels against tetanus toxoid, Hib and serotype-specific pneumococcal antibodies within 6 weeks.

2.6. Clinical Follow-Up

At the one-month post-discharge follow-up, the patient was well; he had a normal respiratory clinical examination and chest X-ray. Spleen rigidity regressed. Neurological development and milestones were normal for his age. The ENT physical examination was normal.

3. Discussion

The novelty of our study lies in the serial measurement of pneumococcal serotype 3-specific antibody concentrations during the child's infection and recovery. On the other hand, ours is a single-case study, while the 'clinician's approach' to the patient did not allow for pre-infection testing for antibody concentrations, which would have been valuable. The high antibody concentration (121.78 μg/mL) found at the age of 11 months is most likely induced by the serotype 3 infection; this value declined in the following two months. The concentrations of the other 11 of 12 serotypes of PCV20 measured—other than serotype 3—were decreased just before the PCV20 booster dose. These low values may be attributed, at least partially, to the infant's age, i.e., the later months of the second semester of life; they substantially increased within one month after the booster dose, except for the serotype 3 value. Serotype 3 IgG concentrations (μg/mL) declined from 19.53 immediately before the booster dose to 4.10 at one-month post-booster immunization. However, this value is well above the putative protective level of 0.35 μg/mL, while this threshold does not establish individual protection.

Inability to respond to a specific PCV serotype after PCV vaccination of children who have previously suffered pneumococcal disease by the same vaccine serotype has been noted in several studies during the PCV7 era, mostly in the case of serotype 6B, and to a lesser extent with serotypes such as 4, 14, 18C and 23F. The mechanism of this decreased response has been attributed to the exhaustion of existing memory B cells, which are not replenished following disease [9,10]; direct memory B cell assessment was not performed in our patient. Another potential explanation is that the overwhelming number of bacterial inflammation-derived antibodies cannot be increased further by the minute amount of antigen introduced by the vaccine. The distinctive biology of serotype 3, particularly the release of capsular polysaccharide [11], leads to a functional defect which has been shown experimentally to interfere with antibody-mediated killing (opsonophagocytic assay, OPA) and protection [12]; OPA was not performed in our patient.

A causal relationship between postnatal CMV infection and the development or severity of pneumococcal disease cannot be established; in particular, the timing of CMV acquisition relative to the pneumococcal infection remains uncertain, while the extensive immunological evaluation did not identify a specific underlying immunodeficiency. The postnatal CMV infection, noted four months after administration of the second PCV20 dose of the basic immunization, does not appear to have interfered with the PCV20 immunogenicity. Interestingly, two studies in Gambian infants did not show decreased responses to *Haemophilus influenzae* type b, tetanus toxoid, or serogroup C meningococcal or measles vaccination in CMV-seropositive infants [13,14].

It should be noted that the 2 + 1 PCV20 Greek NIP vaccination schedule does not conform to the 3 + 1 PCV20 EMA directive; however, the 2 + 1 PCV20 schedule is currently also implemented in other countries including Portugal, Israel, Brazil and Australia. Currently, there is no way of knowing if a third primary dose would have prevented or at least alleviated the severity of pneumococcal disease in the infant.

4. Conclusions

We report on a case of a serious serotype 3 pneumococcal infection presenting as parapneumonic empyema in a 9-month-old infant who had received two primary PCV20 doses as part of a 2 + 1 vaccination schedule. We believe that the longitudinal tracking of serotype-specific antibody levels in our patient provides instructive data on the immune responses of the infant. Our findings may complement the ongoing real-world clinical experience with the newly implemented higher-valence conjugate vaccines.

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Data Availability Statement: The data presented in this study are available on request from the corresponding author due to privacy and legal restrictions.

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Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Syrogiannopoulos, G.A.; Michoula, A.N.; Tsimitselis, G.; Vassiou, K.; Chryssanthopoulou, D.C.; Grivea, I.N. Pneumonia with empyema among children in the first five years of high coverage with 13-valent pneumococcal conjugate vaccine. *Infect. Dis.* **2016**, *48*, 749–753. [CrossRef] [PubMed]
2. Krenke, K.; Sadowy, E.; Podsiadły, E.; Hryniewicz, W.; Demkow, U.; Kulus, M. Etiology of parapneumonic effusion and pleural empyema in children. The role of conventional and molecular microbiological tests. *Respir. Med.* **2016**, *116*, 28–33. [CrossRef] [PubMed]
3. Silva-Costa, C.; Brito, M.J.; Pinho, M.D.; Friães, A.; Aguiar, S.I.; Ramirez, M.; Melo-Cristino, J.; Portuguese Group for the Study of Streptococcal Infections; Portuguese Study Group of Invasive Pneumococcal Disease of the Pediatric Infectious Disease Society. Pediatric complicated pneumonia caused by *Streptococcus pneumoniae* serotype 3 in 13-valent pneumococcal conjugate vaccinees, Portugal, 2010–2015. *Emerg. Infect. Dis.* **2018**, *24*, 1307–1314. [CrossRef] [PubMed]
4. Liese, J.G.; Schoen, C.; van der Linden, M.; Lehmann, L.; Goettler, D.; Keller, S.; Maier, A.; Segerer, F.; Rose, M.A.; Streng, A. Changes in the incidence and bacterial aetiology of paediatric parapneumonic pleural effusions/empyema in Germany, 2010–2017: A nationwide surveillance study. *Clin. Microbiol. Infect.* **2019**, *25*, 857–864. [CrossRef] [PubMed]
5. Strachan, R.; Homaira, N.; Beggs, S.; Bhuiyan, M.U.; Gilbert, G.L.; Lambert, S.B.; Macartney, K.; Marshall, H.; Martin, A.C.; McCallum, G.B.; et al. Assessing the impact of the 13 valent pneumococcal vaccine on childhood empyema in Australia. *Thorax* **2021**, *76*, 487–493. [CrossRef] [PubMed]
6. Syrogiannopoulos, G.A.; Michoula, A.N.; Moriondo, M.; Nieddu, F.; Syrogiannopoulou, T.G.; Anthracopoulos, M.B.; Petinaki, E.; Azzari, C.; Grivea, I.N. Childhood invasive pneumococcal disease and acute otitis media in Central Greece during 2005–2024—A report at the doorstep of the new multivalent PCV era. *Vaccine* **2025**, *52*, 126765. [CrossRef] [PubMed]
7. Arrieta, A.C.; Osborne, S.; Grant, L.R.; Gessner, B.D.; Blaschke, A.J.; Hulten, K.G.; Nieves, D.J.; Miller, A.; Bender, C.; Isturiz, R.; et al. Parapneumonic empyema complicating community-acquired pneumonia: Etiology in the era of pneumococcal vaccination and role of molecular diagnosis. *Pediatr. Infect. Dis. J.* **2025**, *44*, 622–629. [CrossRef] [PubMed]
8. Lal, G.; Balmer, P.; Stanford, E.; Martin, S.; Warrington, R.; Borrow, R. Development and validation of a nonaplex assay for the simultaneous quantitation of antibodies to nine *Streptococcus pneumoniae* serotypes. *J. Immunol. Methods* **2005**, *296*, 135–147. [CrossRef] [PubMed]

9. Borrow, R.; Stanford, E.; Waight, P.; Helbert, M.; Balmer, P.; Warrington, R.; Slack, M.; George, R.; Miller, E. Serotype-specific immune unresponsiveness to pneumococcal conjugate vaccine following invasive pneumococcal disease. *Infect. Immun.* **2008**, *76*, 5305–5309. [CrossRef] [PubMed]
10. Tamura, K.; Matsubara, K.; Ishiwada, N.; Nishi, J.; Ohnishi, H.; Suga, S.; Ihara, T.; Chang, B.; Akeda, Y.; Oishi, K.; et al. Hyporesponsiveness to the infecting serotype after vaccination of children with seven-valent pneumococcal conjugate vaccine following invasive pneumococcal disease. *Vaccine* **2014**, *32*, 1444–1450. [CrossRef] [PubMed]
11. Linley, E.; Bell, A.; Gritzfeld, J.F.; Borrow, R. Should pneumococcal serotype 3 be included in serotype-specific immunoassays? *Vaccines* **2019**, *7*, 4. [CrossRef] [PubMed]
12. Choi, E.H.; Zhang, F.; Lu, Y.J.; Malley, R. Capsular polysaccharide (CPS) release by serotype 3 pneumococcal strains reduces the protective effect of anti-type 3 CPS antibodies. *Clin. Vaccine Immunol.* **2015**, *23*, 162–167. [CrossRef] [PubMed]
13. Miles, D.J.C.; Sanneh, M.; Holder, B.; Crozier, S.; Nyamweya, S.; Touray, E.S.; Palmero, M.S.; Zaman, S.M.A.; Rowland-Jones, S.; van der Sande, M.; et al. Cytomegalovirus infection induces T-cell differentiation without impairing antigen-specific responses in Gambian infants. *Immunology* **2008**, *124*, 388–400. [CrossRef] [PubMed]
14. Holder, B.; Miles, D.J.C.; Kaye, S.; Crozier, S.; Mohammed, N.I.; Duah, N.O.; Roberts, E.; Ojuola, O.; Palmero, M.S.; Touray, E.S.; et al. Epstein-Barr virus but not cytomegalovirus is associated with reduced vaccine antibody responses in Gambian infants. *PLoS ONE* **2010**, *5*, e14013. [CrossRef] [PubMed]

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