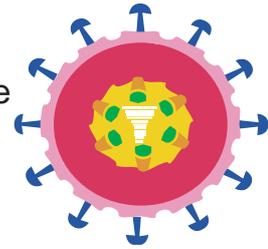




Universitaire  
Ziekenhuizen  
Leuven

Laboratory of Clinical Virology  
National Reference Center Rotavirus  
Prof. Dr. Marc Van Ranst

Rotavirus  
Surveillance  
Network  
Belgium



Dear Colleagues,

We would like to thank you again for your participation in the Rotavirus Surveillance Network Belgium, studying rotavirus incidence and the genotype distribution in Belgium. Please find enclosed the results of the analyses for the 2020-2021 rotavirus season as well as the individual rotavirus genotyping results of the samples you have sent us.

Due to the successful introduction of the Rotarix™ and RotaTeq™ vaccines onto the Belgian vaccination scheme, the number of rotavirus positive cases has strongly declined. However, we are still extremely interested in the remaining rotavirus positive cases in Belgium, both from VACCINATED and UNVACCINATED children. Since 2010 the laboratory of clinical and epidemiological virology at the KU Leuven is the national reference center for rotavirus which allows us to maintain the Rotavirus Surveillance Network Belgium for the upcoming seasons. Therefore, we hope that you will keep sending us rotavirus positive samples.

As the vaccination status of the rotavirus-positive patient is crucial for the continued monitoring of the effectiveness of the vaccines, we would appreciate if this information could be added to the samples, if available. If convenient for you, you can use the template rapport included with this letter.

Sincerely yours,

Prof. Jelle Matthijnsens  
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# Yearly report of the Rotavirus Surveillance Network Belgium 2020-2021

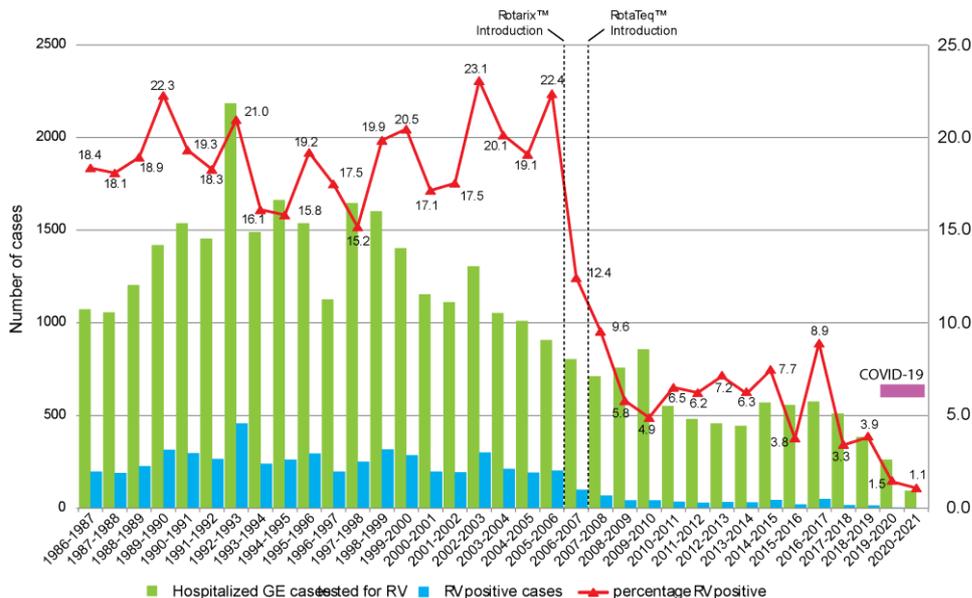
## Rotavirus surveillance in Belgium

Rotavirus incidence and genotype distribution have been monitored at the Gasthuisberg University Hospital in Leuven since the 1999-2000 rotavirus season. Rotavirus incidence has strongly decreased since the introduction of Rotarix™ (2006) and RotaTeq™ (2007) (1).

The 2020-2021 rotavirus season is the fourteenth season since the establishment of the Rotavirus Surveillance Network Belgium and many hospitals, private laboratories and pediatricians across Belgium are cooperating in this surveillance network. We received a total of 110 samples, of which 72 (65.5%) were found positive and could be (partially) genotyped. The total amount of samples received was still substantially lower than before the SARS-CoV2 pandemic (see below).

## Reduction of rotavirus gastroenteritis after vaccine introduction

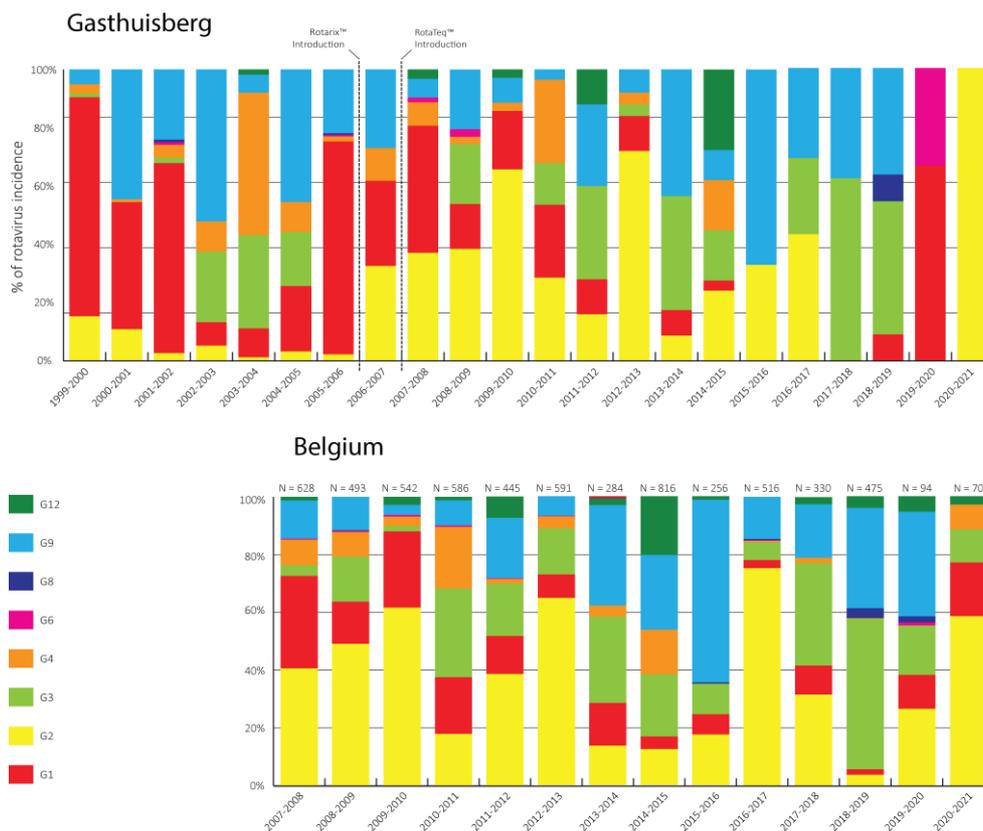
In figure 1 the number of hospitalized gastroenteritis cases (green bars), the number of hospitalized rotavirus gastroenteritis cases (blue bars) and the rotavirus positivity rate (red line) is shown for the Gasthuisberg university hospital in Leuven. Before vaccine introduction the rotavirus positivity rate fluctuated between 15.2% and 23.1%. After vaccine introduction a steep drop in the rotavirus positivity rate was observed and the rotavirus positivity rate has been more or less stable between 4.9% and 7.7% until 2014-2015. In the 2015-2016 season we only observed a positivity rate of 3.8%, which was the lowest detection rate recorded since we started monitoring at Gasthuisberg. This decrease also seems to be reflected in the number of samples that were submitted for the 2015-2016 season throughout Belgium (n=289). This is in sharp contrast to the 2016-2017 season where we recorded a positivity rate of 8.9% in Gasthuisberg (51/576), reflected in more than 900 samples send to us as part of our National Reference Centre activities. The 2017-2018 season in Gasthuisberg was an all-time low with only a 3.3% (17/510) positivity rate (and 427 samples send to the rotavirus NRC). This pattern could indicate the emergence of a bi-annual pattern, where strong and weak rotavirus seasons alternate, as had been previously observed in the USA (2). However, this did not turn out to be the case, with an incidence of only 3.9% (15/384) in Gasthuisberg (and 523 sample send to the rotavirus NRC) for the 2018-2019 season. As mentioned above, for the 2 past seasons (2019-2021) we received an all-time low number of positive cases through the rotavirus NRC (n=114; n=110, respectively), which was also reflected in only 4 and 1 rotavirus positive samples in Gasthuisberg corresponding to a 1.5% and 1.1% positivity rate (4/263, 1/94), respectively.



**Fig. 1.** Number of hospitalized gastroenteritis cases (green bars) and number of hospitalized GE cases tested rotavirus positive (blue bars) per season at the Gasthuisberg university hospital from 1986-1987 until 2020-2021. The red line indicates the percentage rotavirus positive tested in a particular season. Black dotted lines indicate the vaccine introductions in Belgium.

## Rotavirus G-genotype distribution

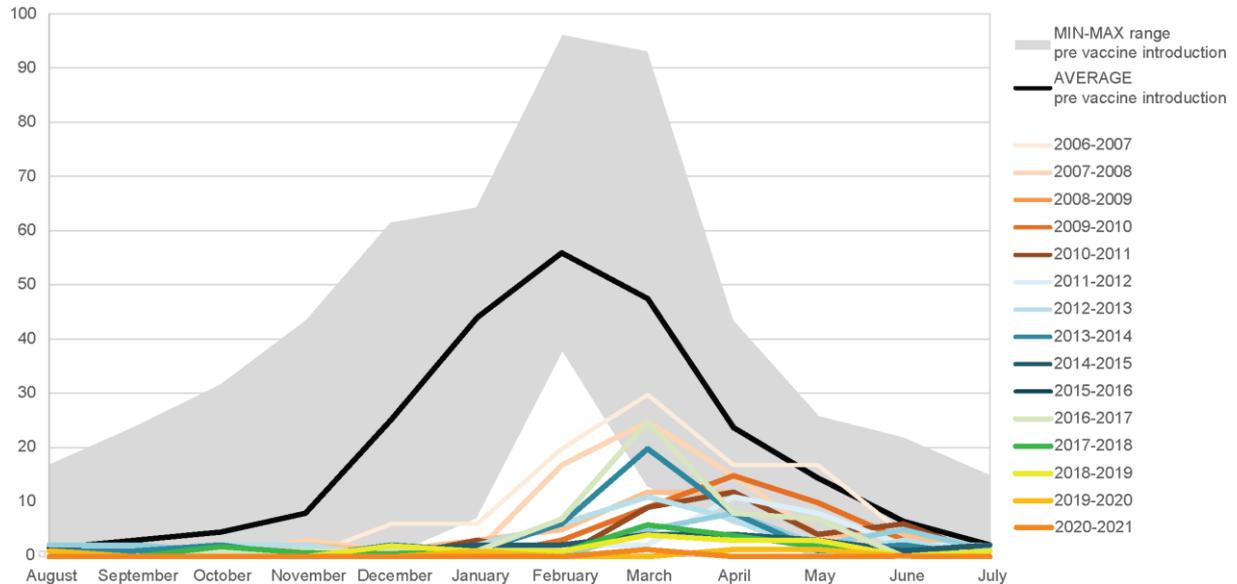
The G-genotype distribution of rotavirus samples collected at Gasthuisberg and by the Rotavirus Surveillance Network Belgium are shown in figure 2. Before vaccine introduction a fluctuating pattern of genotype predominance was seen (G1, G4 and G9) in conjunction with a low prevalence of the G2 genotype. After vaccine introduction a prolonged but fluctuating increase in the prevalence of G2 genotypes was observed. In general, the national surveillance data display a similar genotype distribution as was observed at the Gasthuisberg university hospital, although the low number of rotavirus positive cases in Gasthuisberg the last 6 seasons makes a comparison not very reliable. During the 2017-2018 season an increase of G9 and mainly G3 at the expense of G2 was noted. This trend further continued into the 2018-2019 season which was dominated by G3 (G3P[4]: 1.3%; G3P[8]: 50.1% and G3P[14]: 0.2%) and G9 (G9P[4]: 13.4% and G9P[8]: 21.1%). The remaining genotype combinations represented each less than 5% of the samples for this season: G1P[8] (2.5%), G2P[4] (3.8%), G4P[6] (0.2%), G8P[8] (3.3%) and G12P[8] (4,2%). Despite the low number of rotavirus positive samples in the 2019-2020 season, the genotype distribution was in line with that of the 2 previous seasons with multiple co-circulating strains, without a clear dominant genotype. The last 2020-2021 season was again dominated by G2P[4] (55.6%; n=40). Smaller numbers of G3P[8] (n=8), G4P[8] (n=6), wildtype G1P[8] (n=3) and G9P[8] (n=2) were identified. Three samples remained partially typed. Interestingly, also 10 vaccine-derived G1P[8] strains were identified. The age of these 10 infants ranged from 2 to 3 months. For 7 of these infants the available vaccination data indicated a recent vaccination (4-9 days prior to sample collection), for 2 no or incomplete vaccination information was available, and for 1 it was indicated that it was not vaccinated.



**Fig. 2.** (Top) G-genotype distribution from positive rotavirus cases isolated at the Gasthuisberg university hospital from 1999–2000 until 2020–2021. Black dotted lines indicate the vaccine introductions in Belgium. (Bottom) G-genotype distribution from positive rotavirus cases collected by the Rotavirus Surveillance Network Belgium from 2007-2008 until 2020-2021.

## Seasonality

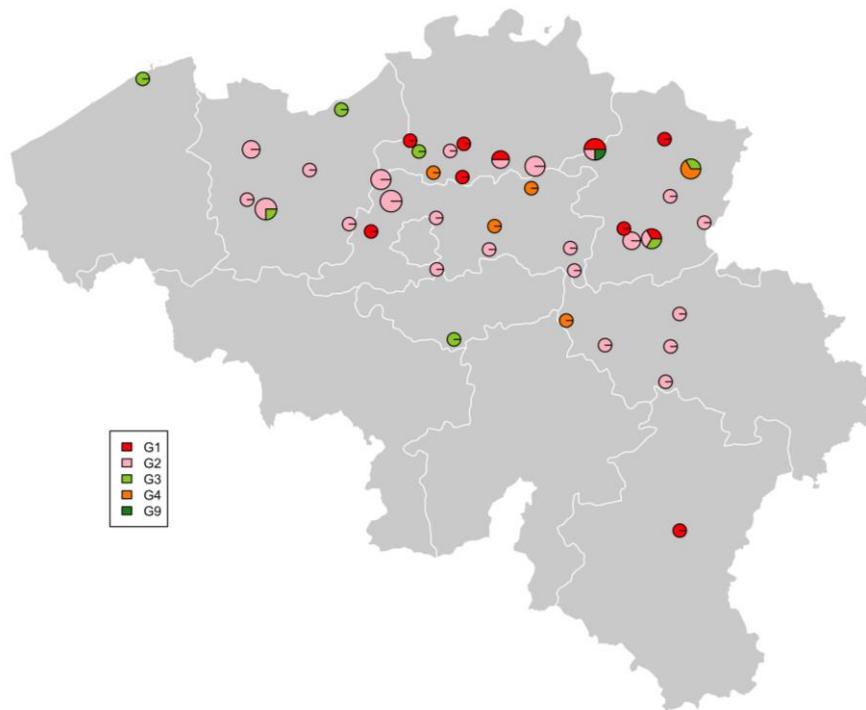
In addition to a decline in the number of rotavirus positive cases, the rotavirus season was found to be shortened and delayed after vaccine introduction in Gasthuisberg. Before vaccine introduction the rotavirus season started in November and the peak incidence of rotavirus infections occurred in February. In the seasons after vaccine introduction, the rotavirus season typically started in the beginning of a calendar year and the peak incidence was delayed to March or April (Fig. 3). In the current unusual 2020-2021 season we cannot really speak about a season anymore, since only 1 positive case was found in March.



**Fig. 3.** Number of hospitalized GE cases tested rotavirus positive at the Gasthuisberg university hospital per month of year. The black line indicates the median number of rotavirus positive cases in a particular month from 1986–1987 until 2005–2006. The shaded area indicates the minimum and maximum number of rotavirus positive cases in a particular month from 1986–1987 until 2005–2006. The colored lines indicate the number of rotavirus positive cases in a particular month in post-vaccine introduction seasons.

## Geographic distribution of genotypes

In figure 4 the geographic G-genotype distribution across Belgium is shown based on the available postcode provided with the samples from the 2020-2021 season, showing regional differences in the prevalence of the major genotypes. Due to the low number of samples, it is difficult to observe clear patterns.



**Fig. 4.** G-genotype distribution across Belgium based on provided postal area codes of samples.

## Conclusions

This year (as was also the case last year) we received a very low number of samples due to the SARS-CoV2 pandemic. We still believe that the main drivers are: 1) the varying restriction measures in place to limit physical interactions between people, as well as increased hygiene measures, which prevented the spread from SARS-CoV2, but also many other pathogens including rotavirus; 2) parents may have been more reluctant to go to the hospital with their infants with a (mild) case of gastroenteritis, during the pandemic; 3) due to the very high burden on medical personnel, sending rotavirus positive samples to the Reference center was not a priority.

It will be hard to predict what the effect of the pandemic will be on future rotavirus seasons, but it could be speculated that due to a decreased circulation of rotavirus - due to physical distancing - an increasing number of susceptible infants could be accumulating. This in combination with further relaxations of measures implemented to restrict the pandemic, might result in more severe rotavirus seasons to come.

However, both Rotarix™ and RotaTeq™ still perform very well in the prevention of rotavirus gastroenteritis. The previously proposed bi-annual pattern in rotavirus epidemics, does not seem to hold true in the last seasons. An increase in the prevalence of the G2P[4] genotype after vaccine

introduction was observed in the 6 seasons post vaccine introduction but this was less pronounced between 2013 and 2016. However, G2P[4] re-appeared stronger than ever reported before in Belgium in the 2016-2017 season, with more than 70% of rotavirus cases caused by this genotype, and also the 2017-2018 season was dominated by G2 together with G3. In the 2018-2019 season G2 was the lowest since the start of the rotavirus surveillance in Belgium. In the 2019-2020 season G2 was again found in a quarter of the rotavirus positive samples, and this increasing tendency seems to continue in this last year with more than 50% of the cases being caused by G2 rotavirus strains. As also described for previous seasons, despite the use of both live attenuated vaccines for more than a decade in Belgium now, there is very little evidence of their circulation in the human population.

In order to keep evaluating the effects of vaccination on the rotavirus population, and to monitor the possible appearance of animal-like genotypes into the human rotavirus population, it will be important to continue the rotavirus surveillance in Belgium. Belgium is one of the few countries in the world with a very long track record of rotavirus genotyping in a country with a very high rotavirus vaccination coverage, which makes it ideally suited to investigate the impact of the vaccines on the rotavirus genotype distribution in the long run.

We would also like to encourage you to take a closer look at the following manuscript which was recently published. In this paper we investigate the presence of other enteric pathogens in alleged “rotavirus break through cases”.

High Prevalence of Coinfecting Enteropathogens in Suspected Rotavirus Vaccine Breakthrough Cases. Simsek C, Bloemen M, Jansen D, Beller L, Descheemaeker P, Reynders M, Van Ranst M, Matthijssens J. *J Clin Microbiol.* 2021 Nov 18;59(12):e0123621. doi: 10.1128/JCM.01236-21. Epub 2021 Sep 29.

In case you do not have access to this paper, and would like to have an electronic copy, feel free to send an email to: [jelle.matthijssens@kuleuven.be](mailto:jelle.matthijssens@kuleuven.be)

## References

1. Zeller M, Rahman M, Heylen E, De Coster S, De Vos S, Arijs I, et al. Rotavirus incidence and genotype distribution before and after national rotavirus vaccine introduction in Belgium. *Vaccine.* 2010 Nov 03;28(47):7507-13. PubMed PMID: 20851085.
2. Leshem E, Tate JE, Steiner CA, Curns AT, Lopman BA, Parashar UD. Acute gastroenteritis hospitalizations among US children following implementation of the rotavirus vaccine. *Jama.* 2015 Jun 09;313(22):2282-4. PubMed PMID: 26057291.