This month’s issue features reflections on the IMGC Symposium, COVID-19 and breastfeeding, 3D printing of milk-based products, and dairy and metabolic health.

Reflections on the IMGC Virtual Symposium 2020 and a Look to the Future

This year’s IMGC Symposium was held virtually October 13-16. Like many academic and professional conferences in this year of global pandemic, “IMGC Virtual Symposium 2020” sought to bring its content to as many people as possible via Zoom and digital platforms. Yet unlike many conferences, it created a virtual space for networking and collaboration via a robust and dynamic virtual portal. Over the four days, thirty-four speakers presented 34 live talks with live Q&A to 277 registrants from twenty-five countries from North America, Europe, Asia, Australia/Oceana and Africa—making this one of the best-attended symposia for IMGC. As always, the highlight of the IMGC symposium was its ability to bring together participants from across academic, industry, and the public sectors to learn more about milk science.

Logging on to the symposium’s virtual portal brought participants to a “Lobby” that served as a launch page for the various presentations and conference events. There they could see a live Twitter feed of conference highlights, a real-time update of the day’s next presentation, and a sidebar for live networking via chat. The portal was interactive and intuitive, making it easy for participants to navigate the symposium. But most importantly, even in a virtual format, presenters and attendees were able to engage and interact, making this conference a welcome opportunity for connection in a year that has left many feeling isolated.

“I’m not sure I would have gotten to the conference this year,” explained attendee Melanie Martin during Tuesday’s Networking Session, one of the daily opportunities for informal group discussions of the day’s topics. Indeed there were many channels for real-time communication during presentations and between sessions, and the conference portal is a fascinating record of the threads of ideas and discussions that occurred over the course of the 4 days.

For regular attendees of the IMGC meeting, the conference provided a way of “coming home” to see old friends and colleagues from around the world without traveling. For new attendees, the virtual format provided a low-cost way of participating for the first time in a conference they would not ordinarily be able to attend. “What a fantastic conference!” commented Amy Skibiel of the University of Idaho in the Public Lobby Chat. “This was my first time attending and it did not disappoint! I should have been attending long ago but better late than never. Thank you to the organizers and presenters. I’m already looking forward to next year.” All attendees, old and new, can access the live oral sessions, which were recorded, until August 1, 2021. Anyone who missed the conference may register to view the recorded sessions by registering here.

As for the future and next year, in their closing remarks, IMGC founder and IMGC Director of Scientific and Strategic Development, Drs. Bruce German and Jennifer Smilowitz, respectively, discussed how IMGC will continue its place at the forefront of milk science and research, and the various upcoming projects it will host in the near future. Dr. German suggested that IMGC compose letters to NIH and to the public about breastmilk research as the “keystone research target of the 21st Century,” and milk itself as “the first line of defense for nourishment and therapeutics” in public health to assert IMGC’s position as a global leader in health research. Dr. Smilowitz highlighted the importance of SPLASH! for its contributions to research
COVID-19-positive Mothers Pass on SARS-CoV-2 Antibodies, but Not Virus, to Infants

- New research on milk from COVID-19-positive mothers supports public health guidelines that encourage continued breastfeeding during and after infection.
- Human milk does not contain viral RNA for SARS-CoV-2 and is not a source of virus transmission.
- Milk from mothers with COVID-19 contains antibodies that bind to and neutralize SARS-CoV-2 for several months after initial infection.

The pace of scientific research is usually quite slow; the time frame between applying for financial support to publishing results in scientific journals is measured in years, not months. But that was before SARS-CoV-2. The urgency to understand the who, what, why, when, and how of this novel coronavirus has accelerated the way grant money is distributed, increased scientific collaboration, and loosened requirements on when scientific papers are published online. This change of pace can clearly be seen in human milk research, resulting in a “liquid gold rush” [1] of studies focused on human milk composition and SARS-CoV-2.

The July issue of SPLASH! highlighted three SARS-CoV-2-focused human milk research projects that were just getting underway in late spring and early summer 2020. As the year comes to a close, data from these studies are already being used to answer critical questions about the composition of milk from mothers that tested positive for COVID-19.

Is Breastfeeding a Mode of Viral Transmission?

In June, the World Health Organization (WHO) issued a statement [2] to encourage mothers that tested positive for (or suspected they had) COVID-19 to continue breastfeeding. All available evidence suggested the benefits provided by breastfeeding outweighed the potential risks of viral transmission, particularly in regions that lacked access to appropriate milk alternatives.

At the time the WHO guidelines were issued, there were over 20 publications on viral RNA from SARS CoV-2 in breast milk, but nearly all of these studies suffered from methodological issues, making it difficult to say definitively if breast milk was a source of viral transmission. In response, Dr. Michelle McGuire, Director and Professor in the School of Family and Consumer Sciences at the University of Idaho, and her colleagues quickly developed and published a best practices guide for breast milk collection during an infectious disease outbreak [3]. It included optimal methods for milk collection, handling, storage, and analysis to minimize the risks of contamination, false positives, and false negatives. Then, they put their
methods into practice in their own study [4, available as a preprint] enrolling nearly 50 breastfeeding mothers that tested positive for COVID-19.

“Our science supports the WHO guidelines,” explains McGuire. “We haven’t found any viral RNA in the [37] samples from 18 mothers.” A similar study [5] published online (as a preprint) in August came to almost the same conclusion. Only one out of 64 samples collected from 18 mothers had detectable viral RNA. Importantly, they demonstrated that the RNA was not infectious [5].

Being able to eliminate milk as a potential source for virus transmission was critical, but it is not the only risk from breastfeeding. To better inform public health policy, McGuire’s study wanted to understand the potential risk of transmission from the breast itself. Mothers that provided milk samples also supplied swabs of their areola taken before and after cleaning. Only 8 of the 70 swabs tested contained viral RNA, and only one (collected prior to cleaning) had conclusive evidence of SARS-CoV-2 RNA [4]. “At this point, we can’t say if the viral RNA is viable. We used all of the sample to perform PCR to identify viral RNA,” says McGuire. “But this was a really interesting finding and definitely something we are going to follow-up on.” In the meantime, their data suggest that washing the breast before nursing or pumping could reduce or eliminate any potential risk [4]. They found no viral RNA from swabs taken after washing, even from the mother who provided the swab with conclusive evidence of SARS-CoV-2 RNA.

**Do Mothers with COVID-19 Pass on Antibodies to SARS-CoV-2 in Milk?**

The SARS-CoV-2 virus may not pass from mother to infant in milk, but antibodies directed at the virus most definitely do. In May 2020, Dr. Rebecca Powell, Assistant Professor of Medicine and Infectious Diseases at the Icahn School of Medicine at Mount Sinai, shared the results of her lab’s preliminary study that found 80% of COVID-19-positive mothers (12 out of 15) had SARS CoV-2-reactive antibodies in their milk [6].

Now, after several more months of research and larger sample sizes, Powell can make an even more definitive statement about milk antibodies. Out of 50 milk samples, “95% generated an antibody response,” explains Powell. “And as our sample size continues to grow, this number will become even more reliable.”

Dutch researchers at the University Medical Center, Amsterdam have similar findings. Dr. Kasper Hettinga, Associate Professor in Food Sciences and Agrotechnology at Wageningen University, and colleagues found 24 of 29 mothers with confirmed cases (83%) and 6 of 9 suspected cases (67%) had SARS-CoV-2-reactive antibodies in milk [7, available as a preprint].

Powell and Hettinga both initially focused on identifying SARS-CoV-2-specific secretory immunoglobulin A (sIgA, the predominant milk antibody) in milk samples collected two months after infection. “This is when we would expect the peak antibody response,” explains Powell. But in both studies, mothers continued to send in milk samples, some up to 200 days post-infection. “Antibodies were present throughout this whole time period,” says Hettinga. “The antibody response four months after infection was the same as we saw at two months,” adds Powell. “This is different than what we see in serum, where antibodies decrease over time. The mucosal immune response seems to last much longer.”

Perhaps even more exciting is that the virus-fighting capabilities of these antibodies don’t appear to diminish over time. Hettinga and McGuire’s research groups both report that SARS-CoV-2 sIgA were able to neutralize the virus *in vitro* [4, 7], and Hettinga shares that “the virus neutralization was stable over time, even through samples collected 200 days after infection.”

It is not possible to say whether a stable antibody response for this long is a typical response to a viral infection. “It just hasn’t been studied that thoroughly,” says Powell. “We don’t know if this is unique to SARS-CoV-2 or how sIgA works in general in milk.” To understand how long the antibody persists, both Powell and Hettinga would like to continue to follow COVID-19-positive mothers for at least the next year, if possible.
The Science Moves Forward: Milk Research during a Pandemic

Determining how long sIgA persists in milk after infection is just one of many questions McGuire, Powell, and Hettinga hope to answer about the maternal and infant response to SARS-CoV-2, and the pandemic more broadly. "Mothers and infants have been quarantined, which is a really unique situation," says McGuire. "What are the effects of the virus and this isolation on milk?" She suggests searching for unique features of milk collected during the pandemic using an "omics" approach (e.g., the metabolome, the lipidome, the glycome, and free amino-acid profiles).

Powell’s lab is developing a study using an animal model to investigate the in vivo neutralization capabilities of sIgA. Using hamsters (which Powell describes as "a surprisingly good animal model for studying SARS-CoV-2") and extracted sIgA specific to SARS-CoV-2 from human milk, the team will investigate if sIgA can prevent infection in infants and whether it can be used to treat infection in adults.

Hettinga and colleagues had also planned in vivo research trials by providing severely ill elderly (human) patients with pasteurized whole milk. Unfortunately for their research program, but thankfully for the population, the number of these types of COVID-19 patients in The Netherlands has decreased dramatically since late spring.

But the science moves on, with Hettinga’s team focused on the structure and function of milk sIgA directed at SARS-CoV-2. They have already found that mothers have unique profiles in their milk sIgA antigen-binding domains, the part of the antibody that recognizes and binds to the SARS-CoV-2 virus [7]. "Individual mothers are quite stable over time in the mass of the IgA she produces, but the mass varies a lot across the mothers in the study," explains Hettinga. Next up is determining whether this variability in mass relates to which part of the virus the antibody recognizes, to the neutralization ability of the antibody, or to the severity of the illness in the mother.

The answers to these questions, and those being asked by McGuire and Powell, are important for understanding the novel coronavirus, but speak to broader public health issues as well. "What we really want to know is, how does milk protect infants from airway infections," says Hettinga. “These studies will let us test a lot of the hypotheses. Even if COVID-19 goes away, we will always have airway infections in infants so it remains an important question to understand.”


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3D Printing Milk-based Products while Maintaining Their Nutrients

- Food printing is one of the emerging applications of 3D printing, but most existing methods either require high temperatures or additives.
- In a new study, researchers have developed a method to 3D print milk-based products with minimal additives while maintaining its temperature-sensitive nutrients.
- The technique could be used to create aesthetically pleasing, nutritionally controlled milk-based foods.

As 3D printers have become more affordable and accessible over the past 10 years, their potential applications have also increased. One emerging application of 3D printing is food printing, which could enable the creation of aesthetically pleasing food products with customized nutrients and internal structures (1-5).

3D printing of food typically requires either high-temperature or additives. “3D printing of food has been achieved by different printing methods, including the widely used selective laser sintering and hot-melt extrusion methods,” says Lee Cheng Pau, a graduate student in the lab of Assistant Professor Michinao Hashimoto of Singapore University of Technology and Design. However, these high temperature methods are not suitable for 3D printing foods such as milk (6-9). “Milk is rich in both calcium and protein, but as these nutrients are temperature-sensitive, milk is unsuitable for 3D printing using the aforementioned printing methods,” he says.

Methods that don’t require high heat, such as cold extrusion, generally require additives to modify the rheology—or flow—of the ink and stabilize the printed structures (10,11). For example, previous studies have 3D printed milk with additives such as Xanthan gum (12). “Optimizing these additives is a complex and judicious task,” says Pau.

The researchers characterized milk inks made with different concentrations of commercially available milk powder in water. “Extensive characterizations of the formulated milk ink were conducted to analyze their rheological properties and ensure optimal printability,” says Pau. The researchers found that milk ink consisting of either 70 or 75 weight/weight percent milk powder in water was suitable for direct ink writing 3D printing, with the former being less viscous and thus easier to extrude than the latter.

Pau and his colleagues were able to use both these milk ink formulations to successfully 3D-print mesh structures as well as complex structures—such as a 3D model of a couch—that were stable enough to hold their shape. “The texture can vary depending on the final shape and size,” says Pau.

The researchers were also able to demonstrate multi-material printing using multiple syringes containing milk ink and other edible inks. The researchers printed a 3D structure of a couch with milk ink and chocolate inks at different layers, or a milk ink structure with different fillings. “For instance, the milk powder can be 3D printed as a rigid enclosure and filled with soft fillings such as blueberry syrup, chocolate syrup and maple syrup,” says Pau.
This kind of multi-material printing could be used to create a nutritious and visually appealing meal that combines different food inks and maintains milk’s temperature-sensitive nutrients. The method could also be extended to 3D print other edible inks at room temperature and with minimal additives, which could have a variety of applications in creating customized food products.

“This novel yet simple method can be used in formulating various nutritious foods including those served to patients in hospitals for their special dietary needs, or dairy manufacturers or restaurants to create 3D milk products,” says Pau. “Personal use of 3D printing in the kitchen, for the purpose of cooking, is also possible,” he says. “There are ongoing plans for commercialization,” says Pau.

The study thus expands the possibilities of 3D food printing by demonstrating a relatively simple way to modify the rheology of food inks with minimal additives without degrading their heat-sensitive nutrients.


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The Effects of Dairy on Metabolic Risk Depend on the Type of Dairy Product Consumed

- Investigations of the effects of dairy products on cardiometabolic risk often have mixed or inconclusive results.
- A new study investigated the association between habitual consumption of various types of dairy products and markers of metabolic risk and adiposity (body fatness).
- Data from a large cohort of more than 15,000 adults from the European Prospective Investigation into Cancer and Nutrition–Norfolk (EPIC-Norfolk) study in the United Kingdom were evaluated.
- Different types of dairy products have different health effects, with fermented dairy products such as yogurt or low-fat cheese showing the most beneficial associations with metabolic risk.
- Dairy consumption and cardiometabolic risk are most likely linked through the adiposity and lipid pathways.

Researchers have long been interested in understanding the effects of different types of dairy products on cardiometabolic health (1–3). Studies have looked at the effects of consuming different types of dairy on metabolic markers such as body weight, body fat, lean mass, or cholesterol. Although some studies have found that dairy products are associated with lower cardiometabolic disease incidence, other study results have been mixed or inconclusive (4–10). As a result, there’s still a lot researchers don’t know about the effects of long-term habitual dairy consumption on cardiometabolic risk, or the potential pathways linking the two.
A new study led by Professor Nita Forouhi at the University of Cambridge investigated associations between habitual consumption of various dairy products and markers of metabolic risk and adiposity (body fatness) among adults in the United Kingdom (11). “We wanted to expand the understanding about a link between different types of dairy products and health,” says Forouhi. “Diet is a dynamic behavior, which might change over time, therefore it would be informative to assess how the change in dairy consumption would influence the change in intermediate markers of longer term disease,” she says.

Forouhi and her colleagues examined associations between changes in dairy consumption, assessed with a food-frequency questionnaire, and parallel changes in cardiometabolic markers. “We tested the parallel change of types of dairy consumption and the body’s metabolic markers of risk, which has not been done much in past research as this is more complex,” says Forouhi (10,12-14). “This approach can help to give results in observational studies, such as ours, to be closer to those from clinical trials, which are considered a better form of study design but are notoriously difficult to perform well for nutritional factors,” she says (15).

The researchers were also interested in teasing apart the effects of different types of dairy products. “Prior research from us and others had indicated that yogurt and cheese consumption might be favorably associated especially with type 2 diabetes,” she says. “Since there is sparse research on why that might be, we studied links with intermediate markers of disease processes such as body fatness, blood fats and blood sugar,” says Forouhi.

The researchers evaluated data from the European Prospective Investigation into Cancer and Nutrition–Norfolk (EPIC-Norfolk) study in the United Kingdom (16). “In the EPIC-Norfolk Study we had a rich data source on a large number of adults with data collection at two time points, which enabled us to do our research among more than 15,000 people with diet and other parameters measured an average of 3.7 years apart,” says Forouhi.

Their approach was not without its limitations. “Our study is observational, meaning we did not do a clinical trial of a dietary intervention with changing people’s consumption of different types of dairy products,” says Forouhi. “We have to be careful about the interpretation of findings as we cannot conclude about a cause and effect because other factors may interfere,” she says. “However we did the best we can to try and account for many such factors such as underlying other health behaviors and social and other dietary factors as well as age, sex and body mass index of the participants,” says Forouhi.

The new study found that different types of dairy products have different health effects, with fermented dairy products such as yogurt or low-fat cheese showing the most beneficial associations. “Of all the dairy types, fermented dairy products—including all yogurt or low-fat cheese—showed the most beneficial associations, with a lower increase in body weight and body mass index (BMI),” says Forouhi. “In general, low-fat dairy products were associated with a better blood fat profile,” she says. In contrast, increasing total high-fat dairy consumption was associated with higher increases in adiposity measures such as body weight or BMI and major lipid (or blood fat) markers.

The findings highlight differences among various types of dairy products. “Not all dairy products are equal for health,” says Forouhi. “There are differences in the health effects of different types of dairy products so we should think about individual types rather than all in the same category,” she says. “Our research findings also complement results from clinical trials, as we assessed the habitual consumption over longer periods of time,” says Forouhi.

The researchers also attempted to identify pathways linking dairy consumption to metabolic disease. “Of all the cardiometabolic markers we examined, including body fatness, blood fats, blood sugar, and blood
pressure, dairy products were mostly associated with adiposity and lipids, making them the most likely pathways linking dairy consumption to cardiometabolic disease,” says Forouhi. “We previously showed that higher consumption of fermented dairy products was related with lower risk of future type 2 diabetes, and now our current study highlights that the body’s pathways that underpin this link are likely to be through body fat and blood fats,” says Forouhi (17).

Forouhi and her colleagues are planning to conduct follow-up studies. “We think it is really important to do follow up research as we still have further to go before we can make definitive dietary recommendations to the public,” she says. “For example, we are using blood metabolomics data, which refers to the group of small molecules in our body, to identify potential markers that may reflect dairy consumption,” says Forouhi. “This could open up a future way, together with other blood markers of dairy fat, to test links with diabetes and other diseases using objective methods,” she says.

“We are also using genetic data to identify potential predictors of dairy consumption and use them in a method called Mendelian randomization, which allows us to explore whether the associations under study may be about cause and effect,” says Forouhi. “This can also help to get results that can approximate the findings from clinical trials, which are very hard to do in nutritional research,” she says.

The researchers also suggest that it would be important to study other populations and countries, and to look at fermented and non-fermented dairy types separately rather than all dairy combined into one category. “Also, it would be really helpful to look at the effects of different types of dairy products on the gut, the gut microbes, and the gut microbiome that can influence health outcomes,” says Forouhi.

Forouhi’s research methodology could also help inform how follow-up studies are conducted. “The methods we used can inform better conduct of future research,” says Forouhi. “In nutritional research, to increase the confidence in findings, it is important to have consistency of results between different types of studies,” she says. “Our findings complement prior evidence and this is important for increasing our scientific understanding because previously there has been a lot of confusion about dairy products and health outcomes.”

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