Assisted reproduction and pandemics: lessons learned from HIV are worth remembering while battling COVID-19



We have grown accustomed to talking about pandemics. Viruses, Dr. Anthony Fauci, vaccines, and reproductive risks caused by infection, or its treatment, permeate the news, social media, and everyday conversations. COVID-19 has focused international attention on the importance of public health and safety and has forever changed the way medical care is delivered. That includes assisted reproduction. Many of us remember similar discussions over 30 years ago and from some of the same sources, including Dr. Fauci, but not related to COVID-19, rather to HIV.

Today, HIV rarely grabs headlines, yet the pandemic is still ongoing and primarily affects reproductive-aged men and women who also seek effective and safe ways to have a child. According to UNAIDS, since the first cases of HIV were reported more than 35 years ago, 78 million people have become infected, and 35 million have died from AIDS-related illnesses. Currently, 1.5 million new infections occur annually, resulting in 700,000 deaths each year (1). It is fair to say the HIV pandemic is not over, but perhaps just not as scary to most Americans now that effective medical treatments render it a "chronic condition."

Questions related to the safety and outcomes of HIVseropositive couples receiving ART treatments continue to exist, and published reports remain largely anecdotal. For instance, the recent findings by Vianna et al. (2) noted "poorer" outcomes when combining the female and male infected patients as compared with noninfected controls. However, in this series, subgroup analysis determined that these results only reflected the performance of the female patients, as when only infected men were considered, no significant differences were seen. Regardless of the differences noted, it was reassuring to read that the success rates were reasonable in all the groups that were treated and that HIV was not transmitted to uninfected partners or their offspring.

There are limitations to the evidence presented in this manner related to the retrospective review of the data, lack of matched controls in the cohort comparison, and transfer of multiple cleavage stage embryos, all of which challenge the validity of the conclusions. Problems with study design are common to most of the published literature concerning HIV-seropositive patients seeking ART. Other small clinical trials have noted similar performance among HIV-seropositive women and uninfected women, but again lack statistical power to substantiate this assumption (3). The underlying etiology for outcome differences seen by the French investigators is also speculative, but they attributed it to the use of antiretroviral therapies by participating women, which might have adverse effects on either oocyte quality or endometrial receptivity. Nearly 30 years of publications, beginning with the seminal work of "sperm washing" by Enrico Semprini (4) in 1992, have compiled a wealth of empiric information that strongly suggests that various techniques used in fertility care provide safe and efficacious alternatives to sexual intercourse in serodiscordant couples. Today, if you ask house staff in obstetrics and gynecology the simple question, "Can an HIV-serodiscordant couple safely have a child?" you typically get an immediate response, "Sure, the sperm of HIV-seropositive men can be washed and inseminated, and women can take antiretroviral medication, so their babies are uninfected." This was certainly not the answer to such an inquiry during the first half of my professional career.

Yet, even in the face of mounting evidence-based results, attitudes rooted in prejudice take time to change. Professionally we have come a long way in removing many barriers to care during the last 20 years. When I established a program for HIV-seropositive individuals at Columbia University in 1997, there were few centers in this country accepting patients, and limited treatment alternatives were available for those wishing assistance (5). Our sperm washing, in vitro fertilization/intracytoplasmic sperm injection approach, was considered experimental, and therefore, we submitted our protocols to both the university institutional review board and the medical center ethics committee for review and approval. Initially, treatment was limited to HIV-infected men, as several members of the review committee who served at that time were strongly opposed to women with HIV undertaking pregnancy attempts because of the risk of infection in the fetus. I still remember the comment from one individual who remarked, "We have enough AIDS babies in our NICU [newborn intensive care unit]."

The encouraging preliminary findings that demonstrated our early success was calendared for presentation at the Annual Meeting of AGOS in 2001 but were delayed a year due to the cancellation of the conference following the September 11th attack. The commentary and questions from academic leaders attending my 2002 AGOS presentation focused on concerns regarding safety, not efficacy, and no one questioned the ethical justification for providing access to care. However, despite endorsements by our academic leaders, not much changed after the meeting related to clinical practice as few centers felt "comfortable" with the methodology, and patients continued to be sent to Manhattan for treatment. I have no idea how many individuals simply gave up hope during those years because of the barriers to treatment, but it certainly was difficult for many patients to afford the time, money, and emotional expense incurred traveling to New York.

Even at our institution, which was more tolerant than most in accepting HIV-infected patients, another decade would pass before introducing ART treatment to HIV-infected women. Later, the addition of pre-exposure prophylaxis for patients undergoing timed intercourse and intrauterine insemination methods helped provide additional safe and affordable options.

The Ethics Committee of ASRM supports open access to care for HIV-seropositive patients. Yet, this recommendation

is still not universally embraced. There remain many ART providers who refuse to offer ART to HIV-seropositive couples, instead opting to "refer" to centers with "special expertise."

The application of core bioethical principles is central to modern public health care policy. In various and differing ways, the benefits of looking at the larger social health issues are profiled against the backdrop of potential limitations of personal freedoms, including abusive restrictions, that inherently must be balanced in formulating public policy to serve the best interest of societal well-being. Before March 2020, I gave little thought to the dichotomy that exists between individual civil rights and the collective civil liberties of a population, but pandemics quickly bring out these conflicts. Before COVID-19, for many years, the HIV/AIDS epidemic focused public attention on population health. During that time, stigmatization of entire subsets of patients occurred, and the generalized fear of contagion within our society spread well beyond at-risk individuals.

Quarantine might be considered a euphemism for denial of access, or perhaps worse, a restriction of personal freedoms. The relativism of the health risk posed by viral infections makes it very hard to legislate fairly or police adequately. As mentioned before, HIV is considered "chronic," but the acceptance of a low-risk label is largely secondary to its effective treatment, not a vaccine. I wonder if effective medication had not been introduced in the early 1990s, would we now consider it differently?

Despite concerns over the loss of personal rights and autonomy, I believe that the justice principle is of central importance in times of pandemic threat. Would anyone really argue that individuals with active and drug-resistant tuberculosis should be allowed to ride in a crowded subway car? I believe individuals lose their right to exercise full freedoms and autonomy once the welfare of the larger citizenry is at stake. This is consistent with the original Greek philosophers who judged the merit of ethics on the benefit gained by the society at large, not necessarily an individual member. This principle has also been actively espoused during the COVID-19 pandemic. It is true, "Those who cannot remember the past are doomed to repeat it." (George Santayana 1905). Lessons from the past do provide important insights into the present and the future. I would hope that COVID-19 might disappear naturally or be controlled by effective vaccines or treatments, but I have my doubts. Rather, I think it is more likely that everyone will have to deal with this virus in its present and mutated forms indefinitely. After all, as learned from our experience combating HIV, pandemics do not disappear overnight, and we need to adapt ourselves. Knowing this, and in my opinion, it would be wise to begin tracking all reproductive outcomes gathered from our COVID-19 infected patients, or those receiving vaccines, into compilations that may be freely and easily reviewed, continuously analyzed, and reported out, as we move forward.

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