The Real Solution Is to Avoid the Problem!

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It was with great interest that I read in this issue of the *Israel Medical Association Journal* (*IMAJ*) the article by Dovrat and colleagues [1]. This research group of virologists and clinicians recognizes the causative association between Metzitzah bePeh (MBP) and neonatal herpes simplex virus 1 (HSV-1) infections, which occur each year in small numbers when the Mohel (trained circumciser) removes blood immediately after circumcision by direct contact with his oral cavity and the open wound. To avoid neonatal HSV-1 infection, a potentially life-threatening infection with long-term side effects, Dovrat and her group performed extensive basic research to test the HSV-1 plaque-reducing effect of a 30-second incubation with Listerine®. In doing so, the infectivity of spiked viruses was reduced by more than 4 orders of magnitude but not fully eliminated. Based on their findings, they recommended that the Mohel rinse his mouth for 30 seconds with Listerine® before MBP. Moreover, since Listerine® might cause harm to the wound, they recommend a second oral rinse with water immediately after the Listerine® wash to hopefully reduce events of infection. However, they acknowledge that their solution, "cannot guarantee protection against infection to the same degree as a suction device… as virus shedding is an ongoing process, and it can return to pre-rinse levels within 60 minutes." In summary, the authors actually admit that their solution is not really an ideal solution for MBP.

THE TALMUDIC SOURCE AND THE RATIONALE BEHIND AVOIDING MBP TODAY

The controversy of neonatal complications after MBP is old [2,3]. I have presented the Talmudic sources and interesting Halachic (Jewish law) development for Hebrew readers in *HaRefuah* [4]. These basic sources are relevant to our discussion of Dovrat's article. The Talmud is concerned about the wellbeing of the sick and therefore requires the Mohel to take precautionary measures, including proper bandaging, to avoid medical complications. The Talmud states, "*Rav Pappa said: A Mohel who does not perform suction of the blood after the circumcision creates a danger to the baby, and therefore, must be removed from his position as Mohel.*" According to their understanding, removing the remaining blood from the wound prevents life-threatening complications and failure to provide proper wound care for the baby is grounds for dismissal. During the Talmudic age, oral suction was a common practice as documented, for example, in the Roman literature and therefore, MBP became common practice among Mohalim.

In the 19th century, shortly before Dr. Ignaz Philipp Semmelweis' 1846 publication linking poor hygiene as cause for morbidity and mortality, a baby in Vienna died tragically after circumcision with MBP. Rabbi Elazar Halevi Segal Horowitz, the Chief Rabbi of Vienna, contacted his teacher, the famous rabbinical authority Rabbi Moshe Sofer-Schreiber, known as the Chatam Sofer (1762–1839), who instructed him to fully abandon the MBP practice with the following Halachic reasoning (1837) [3]:

"*We do not find that 'metzitzah' (suction) has to be done specifically by the mouth, save for in the position of the Kabbalists… but we are not engaged in mystical ideas when there is any concern for physical danger. The roots 'mitz' and 'matzat' … mean 'squeezing, compressing, and suctioning something with force'…. Therefore, we may draw the blood from the 'far places' through any procedure that is effective, and we can rely on medical experts who assure us that a particular method accomplishes this... Even if oral suction had been explicitly mentioned in the Mishnah, we would be able to change it to another method which accomplishes the same…*".

The Talmud's goal of metzitzah is to remove the accumulated blood to avoid medical risks. According to modern medical standards and hygienic understanding, MBP itself can cause medical complications and undermines the basic Talmudic rationale of MBP. Indeed, some 19th century rabbis stated that a Mohel who still performs MBP should be fired, according to the Talmudic rule. Granted, many senior rabbinic authorities in the 19th and early 20th centuries did not accept the ruling or rationale of the Chatam Sofer. This position is understandable both in terms of medical understanding of the day and in the context of the period when there was serious concern of erosion of Jewish practice and tradition by heterodox movements of the time. However, nearly 200 years later, when medical knowledge has increased exponentially and the religious cultural climate is quite different, support for MBP can no longer be justified. Jewish law is concerned for any danger to life and while the incidence of neonatal infections is low, the Talmud clearly states: "Regarding saving a life, we do not follow the majority" (Talmud Tractate Yoma 84b). Therefore, the prac-

tice of MBP should be abandoned and metzitzah should only be performed with a tube, without direct oral contact and the wound. Many Rabbinic authorities [5] argue it is in keeping with the Talmudic rationale of metzitzah.

THE CLINICAL EXPERIENCE AND PUBLICATION

During my residency in pediatrics in Jerusalem over 25 years ago, I treated several babies presenting with severe neonatal HSV-1 infections. As a religious Jew with rabbinical training and certification by the Chief Rabbinate of Israel, I was aware of MBP and its rare medical risks. This training enabled me to already identify these babies in the emergency department and to promptly add antiviral agents to their treatment plan for neonatal sepsis, which at times required weeks to resolve. It was disturbing to me, in the modern era, to have to treat the outcome of a glaring dismissal of contemporary infectious disease and modern wound care protocols. Unfortunately, for the most part, parents are not even informed by the Mohel about MBP and its risks nor are they offered a choice of metzitzah by a tube as a valid Halachic alternative. Would they have been aware of their choices, they may not have agreed to MBP. Instead of enjoying their new baby, the parents experience unnecessary trauma. In my publication in *Pediatrics* [6], I presented eight cases of proven neonatal HSV-1 infection after MBP. The article was published with the ultimate goal of increasing awareness among pediatricians worldwide of the MBP practice and to prompt adequate antiviral treatment. To this day, the paper remains the central scientific reference for medical and legal discussions relating to MBP [6]. Due to the deep uneasiness associated in sharing the historical practice of MBP with a global medical readership, I first consulted with a group of virologists, pediatricians, and a leading rabbinical authority (Rabbi Prof. M. Tendler, OBM) before publishing and concluded that my fundamental medical and ethical responsibility is to avoid the potential risks to newborns by MBP. This responsibility is in keeping with the clear statement by Maimonides (1138–1204): "*Danger to life is a factor that overrides everything else. It is possible to circumcise after the appointed time, but it is impossible to restore a life that has been lost*" (Hilchot Milah 1:18). Furthermore, one should never conceal clinical observations for social-political reasons. One needs to be more concerned "not to become for one moment a wicked man before God" (Mishna Eduyot 5:6).

REFLECTIONS AND OPEN QUESTIONS

After describing the relevant Talmudic and Halachic sources and the medical background, I close with some reflections and open questions.

- In a joint statement paper based on the expert medical opinion and practical guidance in Jewish law of ultra-orthodox Rabbis, the Israeli Ministry of Health and the Israeli Chief Rabbinate/ Ministry of Religious Affairs support MBP [7]. The authors attempted to deny the causative association between MBP and neonatal infection, while at the same time, admitted the potential risks and recommend the use of Listerine® rinse in keeping with the recommendations of Dovrat et al. [1] to avoid virus transmission by MBP. With all due respect to these rabbis and consultants, is it not time to promote use of a tube for metzitzah, as dictated by contemporary medical knowledge, supported by the Chatam Sofer and many other Rabbinical authorities [8] and as recommended by rabbinical leaders in other countries? Is it not time for the Israeli Ministry of Health to critically revise their recommendations and to consult independent pediatricians with expertise in virology and infectious disease to formulate professional guidelines? In sharp contrast to this statement paper, the Rabbinical Council of America (RCA) declared already in 2005, after a fatal outcome following MBP in New York, which states that it is "firmly of the opinion that in light of current realities and medical knowledge it is proper, and preferable, to use a tube" [9].
- Translating Dovrat's study [1] of Listerine® treatment of HSV-1 samples to clinical guidelines to reduce neonatal infection is neither a logical conclusion nor a clinically practical solution. Furthermore, scientifically the quality of their research might be questioned: The experimental design poses critical gaps in its modeling of saliva-borne HSV-1, a liquid far more viscous than the tested aqueous cell culture fluid with implications on virus diffusion rates. Furthermore, the authors' suggestion to rinse with water immediately after the Listerine® wash would likely leave minimal residual Listerine® in the oral cavity, further calling the translatability of their experimental findings into question. In addition, the extent of the wash and rinse will naturally differ between Mohalim, as will the timing of the procedure with respect to the actual MBP, introducing critical variability into the proposed protocol. In fact, Dovrat et al. acknowledged that Listerine® rinse "cannot guarantee protection against infection to the same degree as a suction device" and that neonatal infection might occur at a "low incidence … due the rare practice of MBP". Furthermore, the Mohel's compliance to perform mouth rinses diligently just before the circumcision may be low and difficult to monitor. In summary, using the tube instead of MBP as per RCA and most rabbinical authorities remains the only correct solution, not the Listerine® solution.
- Should signed parental consent be required prior to MBP?
- What is the legal and Halachic liability of the Mohel if MBP caused morbidity, long-term side effects or even mortality?
- Last, Jewish sources spanning from the Bible, Talmud, and rabbinic responsa to modern literature, provide

many meaningful and relevant messages for contemporary clinicians, particularly, the sanctity of human life. I actively engage in researching and relaying these messages to medical students and the medical community [10]. I deeply regret these discussions on an unnecessary practice of MBP, which seems to be based on a blatant misrepresentation of the Talmudic source and results in a polarization of Jewish society. According to the interpretation of the Talmudic source by the Chatam Sofer, RCA, and many rabbinic authorities, this conflict can be easily resolved in compliance with the fundamental Talmudic value of protecting human life.

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Capsule

T cell-independent muscle loss

Although recent data suggest the involvement of autoimmune mechanisms in the pathophysiology of sporadic inclusion body myositis (IBM), the role of T cell–mediated autoimmunity remains to be elucidated. **Britson** and co-authors developed a humanized xenograft rodent model of IBM that recapitulates the main hallmarks of the disease. The authors showed that T cell depletion was able to reduce major histocompatibility complex class I (MHC-I) upregulation within myofibers but did not reduce pathology of the transcriptional protein TDP-43 or rimmed vacuole formation. The results indicated that in this xenograft model, loss of TDP-43 function, and muscle degeneration in IBM occured independently of T cell infiltration.

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Capsule

Optimization of non-coding regions for a non-modified mRNA COVID-19 vaccine

The CVnCoV (CureVac) mRNA vaccine for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was recently evaluated in a phase 2b/3 efficacy trial in humans. CV2CoV is a second-generation mRNA vaccine containing non-modified nucleosides but with optimized non-coding regions and enhanced antigen expression. **Gebre** and co-authors reported the results of a head-to-head comparison of the immunogenicity and protective efficacy of CVnCoV and CV2CoV in non-human primates. The authors immunized 18 cynomolgus macaques with two doses of 12 µg lipid nanoparticle-formulated CVnCoV or CV2CoV or with placebo (n=6 per group). Compared with CVnCoV, CV2CoV induced substantially higher titers of binding and neutralizing antibodies, memory B cell responses and T cell responses as well as more potent neutralizing antibody responses against SARS-CoV-2 variants, including the Delta variant. Moreover, CV2CoV was found to be comparably immunogenic to the BNT162b2 (Pfizer) vaccine in macaques. Although CVnCoV provided partial protection against SARS-CoV-2 challenge, CV2CoV afforded more robust protection with markedly lower viral loads in the upper and lower respiratory tracts. Binding and neutralizing antibody titers were correlated with protective efficacy. These data demonstrate that optimization of non-coding regions can greatly improve the immunogenicity and protective efficacy of a non-modified mRNA SARS-CoV-2 vaccine in non-human primates.

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