At least instinctively, it would be hard to imagine a greater halachic challenge than ingesting the ova (eggs) of a parasitic whipworm harvested from the feces of a pig. For that matter, it would seem at least as far-fetched to imagine that the intake of worm eggs could provide genuine therapeutic benefit. However, as recent clinical studies have demonstrated, swallowing large quantities of certain worm eggs induces an immunological reaction that is both beneficial and safe for persons suffering from inflammatory bowel disease (“IBD”). Moreover, when one examines the pertinent halachic considerations, there would seem to be ample reason why observant Jews would have to recourse to this potentially important new treatment that may alter the natural course of these diseases.

**Overview: The use of helminths to treat IBD**

Recent studies have shown that helminths (parasitic worms that live inside a host) interfere with the human immune system response at several levels and can protect against outbreaks of various auto-immune indications. In particular, published clinical data demonstrates that administering to patients the ova of a porcine (pig) whipworm will induce down-modulation of the auto-immune response that causes IBD, including Crohn’s disease (“CD”) and ulcerative colitis (“UC”). This whipworm helminth, *Trichuris suis*, the ova which are referred to herein as “TSO,” is non-pathogenic in nature, non-reproductive in humans, and can be produced in pharmaceutical quality and quantities through a process acceptable to drug regulators. Ingestion of these helminths is believed to boost production of regulatory T-lymphocytes, thereby inducing a state of increased tolerance to self-antigens and reducing, if not eliminating, the symptoms of these diseases.

**IBD: Symptoms and Pathogenesis**

CD and UC are chronic inflammatory disorders that affect the intestines. Crohn’s disease is a chronic relapsing inflammatory reaction that can affect any segment of the gastrointestinal tract. Abdominal pain and diarrhea are the core symptoms, and extra-intestinal manifestations of the disease are common. UC is an inflammatory bowel disease that differs from CD in that it mainly affects the colon, and is accompanied by ulcers characteristic of the disease. The nature and extent of inflammation (shallow, mucosal) differs from that seen in CD, in which inflammation is usually found deep in the tissue. The main symptom of Crohn’s disease is diarrhea mixed with blood [1].

The exact pathogenesis of IBD is unknown. However, it is thought to result from an excessive immune response to contents of the intestinal lumen (such as bacterial antigens). Genetic factors appear to play some role, but their relevance in UC in particular is limited. Rather, as described below, environmental factors, including the patient’s level of hygiene and exposure to helminths seem to play a more important role than genetic factors in the pathogenesis of IBD [2].
TNF-α antagonists infliximab (marketed as Remicade®) and adalimumab (marketed as Humira®) have been approved to treat adult and pediatric patients with moderate-to-severe CD, and adult patients with moderate-to-severe UC [1, 3].

The remission induction rates from these treatment modalities are sub-optimal. Indeed, despite recent treatment advances, most patients suffer a low quality of life and often require surgery, especially when they develop complications such as fistula, abscesses, or bowel obstruction. In addition, oral and biological immunosuppressive agents have adverse safety profiles when used continuously, including heightened risk of severe infections (including tuberculosis) and lymphomas, as well as congestive heart failure and a lupus-like syndrome. Finally, while current therapies may treat symptoms of IBD, there is no clinical evidence that they positively influence the natural course of the disease. Consequently, even the newer biological agents are not recommended as first-line therapy, and physicians cite the need for more efficacious therapy to avoid these complications [3].

The “Hygiene Hypothesis”

Helminths are a species of parasitic worms. People acquire helminths naturally through contact with contaminated food, water, or soil. The colonization of helminths within humans is most common in children living in tropical areas with poor sanitation. Helminths and humans co-evolved over time. Until the advances of medicine in the twentieth century, humans routinely carried helminths and the human immune system adapted for them. Interestingly, prior to the twentieth century, autoimmune diseases such as IBD were largely nonexistent, and they remain nonexistent today in third world countries where hygienic conditions are less advanced. This inverse correlation between exposure to helminths and autoimmune diseases is often referred to as the “Hygiene Hypothesis.” The “Hygiene Hypothesis” posits that the loss of exposure to these organisms has adversely impacted our immune systems, provoking an outbreak of excessive immune responses that cause auto-immune disease, including IBD. More than a mere hypothesis, robust epidemiological data shows that exposure to helminths protects entire populations from auto-immune diseases, including multiple sclerosis, asthma, other allergic diseases and excessive inflammation [4, 5].

The intake of TSO as a proxy for exposure to helminths

For a helminth species to serve as a natural immune modulator (and thus treat IBD in humans), it must be suited for medicinal application. T. suis is uniquely suited to play that role for several reasons. First, although T. suis is not a human parasite (but rather a porcine parasite), its ova can colonize a human host for several weeks before being eliminated from the body without any specific therapy. Second, T. suis cannot replicate in humans. Third, eggs that are shed in the stool cannot colonize another human host because they are not yet embryonated. Also, because TSO require a 3 to 6 week incubation in moist soil to mature, inadvertent spread to others is highly unlikely. Finally, T. suis can be isolated and purified free of other agents and organisms [6].

TSO are produced through the colonization of young pathogen-free pigs with T. suis from a master ova bank. Ova are then harvested from the feces of these pigs, incubated to maturity and heavily processed to remove any pathogens. Ova then are extensively tested to assure uniformity. They are then used to repopulate the master ova bank and are processed further into a final formulation of the “drug product,” which is a clear tasteless and odorless liquid [6].

TSO ova are essentially microscopic in nature, measuring about 24 μm x 54 μm. Once ingested by humans, the ovum hatches to release a single T. suis larva. In about two months, the larva matures, migrating from the small bowel to the cecum and ascending colon. The body of a mature adult whipworm is about 1 cm in length. It has a thin hair-like appendage that attaches to the host, giving it a “whip-like” appearance. Like most helminths, T. suis cannot mature outside of a host [6].

TSO’s assumed mechanism of action

TSO therapy seeks to leverage the strong influence that helminths exert on the human immune system. The key immune response associated with helminth infection is increased production of regulatory T-lymphocytes (“T-reg” cells) [7-9]. T-reg cells are immune cells that suppress inappropriate activation of the immune system, thereby dampening or preventing autoimmune responses. By boosting T-reg cell production, helminth therapy causes improved control of IBD symptoms. In addition to up-regulating T-reg cell production, persons infected with helminths also tend to shift away from a Th1 immune response (cellular immunity) to a Th2 immune response (humoral immunity) [6, 9]. This shift from Th1 dominance towards Th2 appears to decelerate immunological disorders, like IBD, aggravated by a Th1 imbalance.

Halachic considerations regarding the intake of TSO

The Torah makes clear that “of all that creeps in the water and of all the living creatures that creep in the waters . . . you shall not eat of their flesh” (Leviticus 11:10-11). While there is little question that the ingestion of a mature whipworm would run afoul of this proscription, swallowing TSO to treat IBD would appear to present a very different
halachic situation, including for reasons of (i) the size of TSO, (ii) the primitive stage of development of the eventual worm, (iii) the manner of TSO ingestion, and (iv) the severity of IBD as a disease state. Each of these is discussed in sequence, below.

(As a preliminary matter, the fact that TSO are harvested from pigs (and pigs feces, at that) should not, in itself, pose a halachic concern. While *T. suis* are colonized inside of pigs, the TSO are distinct from and do not acquire the status of their pig hosts. Moreover, the extensive purification process of the TSO required by regulatory authorities, described above, all but ensures the absence in the drug solution of even a trace of pig cells).

(i) TSO would appear to be too small to have halachic relevance

Focusing on the TSO itself, it would appear that their microscopic size should remove them from halachic concern. As various authors have noted, including in articles published in the aftermath of the “discovery” several years ago of copepods in New York City drinking water, organisms that are visible only through magnification are arguably not proscribed by the Torah. For example, there are extensive halachic summaries set forth by Rabbi J. David Bleich [10], Dr. Harvey Babich [11] and Dr. Yosef Levi [12], each of which, in turn cites numerous classic and contemporary sources opining that organisms not visible to the human eye do not carry significance in the eyes of halacha. These include (a) Rav Yechiel Mechel Epstein, who writes in *Aruch HaShulchan* (Yoreh Deah 84:36) that, even if magnification confirms the presence of tiny organisms in water, “the Torah did not forbid that which the eye cannot perceive, for the Torah was not given to angels. For, if not so, many scientists have written that the entire atmosphere is also full of extremely minuscule creatures, and that when a person opens his mouth he swallows a number of them. . . . Even if this is so, since the eye cannot perceive them, it is of no significance”; (b) Rav Shlomo Kluger, in *Teshuvos Tuv Ta’am vs-Da’as* (Mahadura Tinyana, Kuntres Acharon, Siman 53), who explains that vision achieved solely through magnification is not vision according to halacha and is thus not a necessary form of examination; (c) Rav Ovadia Yosef, in *Yechaveh Da’as* (vol. 4, responsum 47) (citing, among others, the Meorei Or, Chelek Kan Tahor, Chulin 58b, and 88a, that “those very small remosim [crawling objects] that are not seen in vinegar and flour other than through a microscope, are not something regarding which the rabbis are concerned at all, and it is only regarding those that are visible to the eye are we concerned about the prohibition of *tolaim* [worms]”); and (d) Rav Moshe Feinstein in *Igros Moshe*, who concludes that the halachic definition of death is not affected by information learned only through radiographic means just as vinegar is permitted even though microscopic magnification would reveal the presence of insects, because “[t]hese are not the sheratzim which the Torah forbade. Using magnification is not mentioned in the Gemora. Our forefathers did not use a microscope and it is clear that they kept all the mitzvos and did not fail anywhere, even by way of oness.” (Yoreh Deah, vol. II, responsum 146).

According to the *Aruch HaShulchan* (Yoreh Deah 84:36), “that which the eye can see, even [if only] against the sun and even if it is the tiniest of the tiny, is a veritable insect.” Based on this, it would appear extremely unlikely that TSO is visible at all to the human eye. In the view of Answers.com, a 20 µm particle would not be visible to the human eye, which is unable to see anything smaller than a human hair, whose width ranges from 40 to 120 microns [13]. “Therefore, if we were going to create a definition of visible artifacts based on the smallest possible size viewable by the human eye, I would have to conclude that it is about as wide as a hair (40-120 microns) and as long as the head of a pin or about 1,500 microns.” [14] Based on that, insofar as the narrower dimension of TSO is barely more than 20 microns (and the wider dimension only 50 microns), it is virtually inconceivable that TSO would be visible to the human eye and should thus be halachically permissible.

(ii) Does TSO run afoul of the Torah’s admonition against “creeping objects”?

Even to the extent that TSO might be deemed visible to highly sensitive vision - and all signs suggest that it is not - there is an argument that TSO still may not fall within the prohibition against creeping objects. Rav Ovadia Yosef, writing in the *Yechaveh Da’as*, cites the *Mareh Cohen* on Zevachim 72a, who explicates the Shulchan Aruch’s teaching that a “beriah” (a living creature), due to its complete and distinctive form, is forbidden from the beginning of its creation. According to the *Mareh Cohen*, that statement does not mean that a beriah is forbidden from the time it is created in the “womb”, but rather from the time that it emerges in the “avir haolam”, i.e., the atmosphere of the world. Evidence of that conclusion is rooted in the discussion in Chulin 89b that “Gid Hanashheh” (consumption of the sciatic nerve) is not prohibited while the animal is still in utero. TSO, which are merely ova from which larvae have yet to emerge, may well be halachically permissible for the reason that it too does not constitute a beriah.
Further, it would appear that a characteristic feature central to “creeping objects” is just that - an ability to move upon the earth, which would not be the case with respect to ova. The Aruch Hashulchan’s explication of the prohibition against microorganisms is amplified by Rav Shmuel Wosner (in Teshuvos Shevet Halevi, vol. VII, responsum 122). Rabbi Wosner addresses the issue of insects that appear visible to the naked eye but which, upon examination, can be seen only as specks or black dots not recognizable as insects. Since they cannot be recognized as insects absent perceivable limbs, antennae or discernible body parts, Rav Wosner regards them as permissible. See also the reported view of Rav Shlomo Zalman Auerbach that an organism that cannot be perceived as living or mobile is not regarded as a “creeping thing that creeps upon the earth” (Leviticus 11:41) [15].

This line of reasoning too may protect the permissibility of TSO insofar as ova plainly are not mobile or recognizable as insects. But see Chazon Ish (Yoreh Deah 14:6), “[even] if the eye does not recognize it because of its small size, if it is yet whole it does not become nullified by virtue of rabbinic decree because of the law of beriah.”

(iii) Ingestion of TSO may not constitute halachic “achilah”

The definition of eating according to halacha is discussed in the Talmud (Chullin 103b). One view focuses on the enjoyment of forbidden foods “by the intestines,” while the other view regards the prohibition as forbidding “enjoyment by the palate.” Since Rambam, Hilchos Maacholos Asuros, 14:3, ties the prohibition against forbidden foods to enjoyment by the palate; it would appear that there is no biblical prohibition with regard to any foodstuff not swallowed by mouth. For that reason, if food is placed directly into the stomach or intestines, no prohibition is involved (according to the Teshuvos of the K’Sav Sofer, Orach Chayim responsum 96), and there is no prohibition against non-kosher ingredients in medications taken by injections, suppositories and the like (according to the Seridei Aish, vol. 2, responsum 59) [16]. Accordingly, there may be an argument that the ingestion of unhatched larvae within ova equates to a delivery mechanism through which the “enjoyment” of the “creeping thing” may occur in the intestines, but not in the palate.

(iv) The IBD patient arguably constitutes a “cholel sheyash bo sakana”

For a seriously ill patient, all prohibitions in the Torah are set aside except for idolatry, murder and forbidden sexual relations. Accordingly, when a patient is seriously ill, if permitted items are not available, he may be given less forbidden foods and ultimately prohibited items as well. See Pesachim 24b to 25a; Rambam, Mishneh Torah, Yesodei Hatorah, 5:6-8; Tur, Shulchan Aruch, Yoreh Deah 155:3 [17]. A patient with moderate to severe IBD would likely fall into this category.

Although IBD does not typically lead to death, there is a modest incidence of death resulting from bleeding and infection in severe cases (as well as from adverse events, including cancer, brought on by immune systems compromised from current IBD treatments) [1]. According to Teshuvos Shevet Halevi (vol. 2 responsum 32), a patient who has a peptic ulcer is considered to be seriously ill. Therefore, even where there is no danger if he does not drink milk, he is allowed to do so one hour after having eaten meat. Insofar as IBD, especially if it is not properly treated, can accelerate death, the ingestion of TSO may be permissible as well based on the patient’s serious state of disease.

To be clear, intake by a seriously ill patient of forbidden matter is permissible only to the extent that a permitted remedy is not available or is not effective (Ramoh, Yoreh Deah 155:3; Kitzur Shulchan Aruch 192:5). Moreover, one may not seek to heal a patient with a forbidden remedy unless the remedy has been reasonably tested or is otherwise deemed effective (Teshuvos Chasam Sofer, Yoreh Deah 339 (even if it is not fully proven, a dangerously ill patient may be fed a medicine of doubtful efficacy if it has been tested and the physician claims that it is beneficial). In this case, the efficacy of TSO in published clinical trials, coupled with its pristine safety history - especially by comparison with the adverse safety profile of immunosuppressive agents - would seem to justify on a halachic basis the intake of TSO by IBD patients.

Researchers have performed at least four clinical trials with TSO to treat IBD (the “Existing Studies”) - two open-label studies in patients with CD and one open-label study and one randomized controlled trial in patients with UC [6, 18]. In these Existing Studies, TSO was shown to be a safe and effective treatment for CD and UC, including in patients also using steroids and or anti-inflammatories.

Specifically, researchers first conducted two pilot studies, enrolling 4 refractory (i.e., patients who had relapsed on currently approved therapies) CD and 3 refractory UC patients who had failed high dose steroid and immunosuppressives, treating them with a single dose of 2,500 ova and observing them for 12 to 15 weeks. Three of the 4 CD patients achieved a clinical remission within 8 weeks of the single dose (as measured by a standard index of clinical symptoms used for determining how CD responds to treatments) [6, 19]. After 8 weeks, the effect waned and two of the patients...
relapsed. (This time frame was assumed to correlate with the fairly rapid loss of *T. suis* from its human hosts). Of these four patients, the one who had not responded was treated with 2,500 ova every 3 weeks and then achieved a durable response lasting over 3 months. One of the patients who had a remission from a single dose and relapsed at 12 weeks was treated with 2,500 ova every 3 weeks, and achieved a remission lasting over one year.

Based on that pilot data, an open-label single-arm study was conducted in 29 refractory CD patients who were treated with 2,500 ova every 3 weeks for 24 weeks [18, 19]. Therapy with TSO was associated with substantial and sustained improvement. At 12 weeks, 66% of patients had achieved remission and 76% had responded; at 24 weeks, 73% had achieved remission and 80% had a meaningful response. These results are better than those observed with anti-TNF antibodies and affected more durable and stable remissions [20].

Results achieved in the UC pilot study were similar: three patients with refractory UC were treated with a single oral dose of 2,500 TSO and observed every two weeks for 12 weeks [6]. All 3 patients achieved remission with a single dose by week 8, and 2 were treated in maintenance with 2,500 ova every 3 weeks, remaining in remission for more than a year [6, 19]. A randomized, double-blind, placebo-controlled study with a crossover period then was conducted in 54 active UC patients [19]. Patients ingested placebo or 2,500 TSO in suspension on a bi-weekly basis. After the first 12 weeks of treatment, placebo-treated patients were switched to TSO for a second 12-week interval and TSO patients were switched to placebo [20]. The blind nature of the study was maintained during the crossover phase.

Of the 54 patients enrolled in the study, 24 received placebo and 30 received TSO during the first 12 weeks of the study. A significantly higher number of patients treated with TSO (43.3%) responded than with the placebo (16.7%). In addition, there were significant differences in most of the signs and symptoms of the disease, including that TSO-treated patients had statistically significant improvements in stool frequency, blood in the stool, mucosal appearance, and overall assessment compared with baseline values.

No drug-related adverse events were reported in any of the Existing Studies, which spanned the oral administration of TSO to approximately 82 patients with IBD (33 patients with CD, 49 patients with UC), including at least three IBD patients who received tri-weekly TSO for at least one year [6, 18, 19]. No ova or parasites were detected in the stools of patients who received TSO, despite exams at baseline and every six weeks [18, 21]. Given the statistically significant efficacy reflected in the Existing Studies and its flawless safety profile, the ingestion of TSO by IBD patients would appear to be permissible as a proven remedy for a *choleh sheyaish bo sakana*. 
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