

Ethical Dilemmas in Natural Theology and Valid Inference in Clinical Trials

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Abstract

This paper discusses some aspects of natural theology (theologia naturalis), following the ideas of Baruch Spinoza. Natural theology is presented as a powerful concept capable of bridging traditional theology, ethics, and natural science, enabling original and meaningful perspectives on contemporary problems, and fostering ways of ethical engagement in the modern world. General ethical problems in clinical trials, as well as particular studies on phosphoethanolamine and hydroxychloroquine for cancer and COVID-19 therapy, are used to ground the discussion into real-life applications.

Keywords: Natural theology; Spinoza; Hermeneutics; Medical ethics; Scientific inference; Clinical trials; Phosphoethanolamine; Hydroxychloroquine.

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ויעש מֹשֶׁה נָחָשׁ נְחֹשֶׁת וַיִּשְׂמְהוּ עַל־הַנֶּסֶם וְהָיָה

אִם־נִשְׁךְ הַנְּחָשׁ אֶת־אִישׁ וְהָבִיט אֶל־נָחָשׁ הַנְּחֹשֶׁת וְחָיָה:

And Moses made a copper snake and put it on a pole, and so it was that if a snake bit a man and he looked the copper snake, then he lived.

Numbers 21:9.

Life has meaning only in the struggle.

Triumph or defeat is in the hands of the gods...

So let us celebrate the struggle!

Swahili Warrior Song, opening quotation
in *Lorenzo's Oil*, by George Miller (1992)

1 Introduction

The God of Spinoza is the all-pervading mind and power that constitutes and shapes nature the way it is – *Deus sive Natura*. Moreover, in Spinoza's view, the world is ordered by virtue of universal natural laws – *Leges naturae universales*. Hence, understanding the will of God, as it is actively manifested in the world we live in, requires the understanding of these same laws or, in other words, requires knowledge of causal relations explaining how and why nature operates the way it does – *Cognitione causae*. Furthermore, in Spinoza's view, the endeavor of learning these universal laws can be a successful enterprise, even if traveling through a gradual, progressive, or evolutionary path. Finally, the possibility of ascension in this intellectual learning path, traditionally represented in Jewish and Christian mysticism by the visual metaphor of Jacob's ladder, is the supreme manifestation of God's love for mankind – *Amor Dei intellectualis*, see Stern (2020).

To what extent can the God of Spinoza be the God of mankind? – either in religion or in science or philosophy? This is a fair question since the God of Spinoza has been seen as a problematic concept by theologians, scientists, and philosophers

alike. Theologians often perceive it as a “distant” God, a God that cannot make us special favors, a God that can not be persuaded to change his rules by ritual or prayer, a God with whom we can not bargain for super-natural interventions, see Bateson (1987, 1991). Meanwhile, positivist scientists and philosophers regard the God of Spinoza as a false idol, for it offers the hope of metaphysical understanding and legitimates causal reasoning, see Stern (2020, 2018b) for further comments.

This article argues that the God of Spinoza can fulfill a meaningful role in mankind’s science, philosophy and theology – as long as we are willing to fully embrace our learning journey on Jacob’s ladder and choose to (re)connect to this world in a meaningful and ethical way by taking responsibility for our individual and collective actions according to our best knowledge and understanding – an attitude known in Jewish tradition as **תקון עולם**, *tikun olam*; see Cooper (2013), Dreff (2019), Hong and Handal (2020), and Stern (2018a).

Moreover, this article sustains that Spinoza’s views do not constitute a break or departure but rather a continuity in well-established traditions of Jewish mysticism and philosophy, traditions that have long-standing links of communication with their counterparts in Christian and Muslim culture, see UNESCO (1986), Libera (1998) and Zauderer (2019). Furthermore, this article uses recent controversies on cancer and COVID-19 therapy as illustrative examples in real-life contexts. Finally, this article highlights some psychological polarities underlying issues under discussion and introduces some topics for further research.

2 Nature and Love – From Maimonides to Spinoza

In this section, we briefly recapitulate the development of the principles of Spinozian philosophy most pertinent to the scope of this article by tracing its antecedents in Jewish mysticism and philosophy through the works of Moshe ben Maimon (1135-1204), Abraham Abulafia (1240-1291), and Joseph Gikatilla (1248-1310); for a more detailed discussion and extensive references see Stern (2020, 2018b).

Spinoza’s principle of *Deus sive Natura* can be seen as a Latin restatement of Moshe ben Maimon’s classical principle: *ha-pe(ulot ha-)elohiyoth, ha-pe(ulot ha-*

teb'ayoth, הַפְעָלוֹת הָאֱלֹהִיּוֹת הַטְּבְעִיּוֹת, meaning: Actions of God are actions of nature. Abraham Abulafia further elucidates this statement by analyzing the etymology of the Hebrew word טְבַע, *teb'a*, meaning nature or substance. The same root, טבע, generates the verb טַבַּע, *tab'a*, meaning to stamp, to coin, to imprint, or to formulate; and the expression תְּבִיעוֹת־עֵין, *tebiyoth-ayn*, literally, eye-impression, meaning intuition or insight. Hence, Gikatilla concludes that “things”, as presented in nature, are coined, patterned, or formulated according to ideal types or abstract laws that convey the will of God. We can find a similar relation between the Latin word *causa*, meaning cause or reason, and the same word in vulgar Latin meaning a thing, like in Portuguese *cousa*, Spanish or Italian *cosa*, or French *chose*.

Jacob’s ladder, as described in Genesis 28:12, used by angels to ascend or descend between earth and heaven, is a symbolic representation of the possibility of communication and learning about the connection between worldly things and their corresponding ideal types or abstract laws. Abraham Abulafia, describes this (e)motion on Jacob’s ladder as love, namely, the love of Divine insight, *ahabah elohut sikhlut*, אַהֲבַה אֱלֹהוֹת שִׁכְלוֹת, meeting the love of human understanding, *ahabah enoshut sikhlut*, אַהֲבַה אָנוּשׁוֹת שִׁכְלוֹת. For alternative analyses of the origin of these concepts and influences on Spinoza from late medieval sources, see Fraenkel (2006), Klein (2003), Harvey (2007, 2012), Idel (2000), and Nadler (2014).

3 Guessing, Conjecturing and Speculating

Spinoza’s philosophy suggests, as the ultimate goal of our quest for understanding, the knowledge of the true causes, precise rules, and exact natural laws governing the world we live in – including of course ourselves as organisms living in it. However, for Spinoza, our journey towards such perfect understanding requires time, work, and effort. Our understanding of things starts at first with imperfect impressions and confused ideas, products of our sensory experiences and imagination, and progressively evolves to more accurate kinds of knowledge.

Metaphorically, one could compare this process as first perceiving an object by the rough outline provided by its shadow (צֶל, *tsel*); then gradually discerning more

reliable images or pictures (תְּזֵלֶם, *tzelem*); and hopping to finally grasp the object's essential characteristics (עֶצֶם, *etzem*). For the concept of essence in Spinoza, see Hübner (2015a,b) and Vinciguerra (2012a,b, 2015); for hermeneutic and analogical methods related to the last metaphor, see Hirsch and Clark (1999, p.217 and Ap.A), Klein (1987, p.547-549), Casanowicz (1893), Horowitz (2017), and Stern (2020).

In *knowledge of the first kind*, our imagination concatenates and establishes connections between sense impressions, trying to coordinate images or ideas according to some perceived order underlying our experiences. The associations established by our imagination are influenced and hence may reveal something about the objects under observation, something about our own constitution, and, most importantly, something about our habitual ways of interaction with the same objects, see Spinoza's Ethics (Part II, prop.16,17,18) and Vinciguerra (2012a, p.52-54).

The way our imagination tries to make sense of the world in this first kind of knowledge involves processes that we may call, according to the circumstances, accidental associations, dreaming, guessing, conjecturing, or speculating. Furthermore, according to Spinoza, there is nothing wrong with the “chancy”, contingent or incidental nature of the process leading to this first kind of knowledge, see Silveira (1995, Ch.VI), Spinoza and Petry (1985), and Spinoza's Ethics (Part II, prop.16,17,18). In fact, this kind of haphazard imagination seems to be essential for our creative work in the advancement of science, an idea further developed in Esteves et al. (2019) and Stern (2014, 2019).

Nevertheless, Spinoza warns us that knowledge of the first kind is prone to error, can often lead us astray, and must therefore be used with great caution. Simple trial and error is a crude (and potentially painful) method for testing the adequacy of knowledge of the first kind. Fortunately, since the time of Spinoza, mankind has perfected better methods for testing the adequacy of our ideas concerning natural laws. In statistical science, these methods include *statistical tests of hypotheses*, *design of statistical experiments*, and *design of empirical trials*; For further readings on these topics, see Fossaluza et al. (2015), Lauretto et al. (2012, 2017), Marcondes et al. (2109), Pereira and Stern (2019), Saa and Stern (2019), and Stern (2008).

Before ending this section, let us make some further comments about the dangers of using knowledge of the first kind. While camped at **צַלְמוֹנָה**, *tzalmonah* (place of shadows), one of the 42 stations of the exodus from Egypt to Israel, the Jews were afflicted by a plague of poisonous snakes. As a counter-measure ordered by God, see this article's opening quotation, Moses cast a copper snake, and then placed this symbol in public view as a warning sign of vital importance, see Stern (2020). However, what was the message being conveyed? Although this question is never explicitly answered in the biblical text, this article ventures the following interpretation:

The copper snake is a symbolic object whose very name, **נָחָשׁ נְחֹשֶׁת**, *nechash nechoshet*, echoes the thema **נחש**, a root that generates either the substantives snake and copper, or the verb **נחש**, *nichesh*, meaning to guess, to conjecture, to speculate. In these words, we also find the sub-pattern **נח**, *nach*, a verb meaning to rest, to relax or to calm down, see Hirsch and Clark (1999, p.154 and Ap.A) and Klein (1987, 411-412). Based on this philological analysis, we may interpret the aforementioned plague as the consequences of rushing to conclusions based on wild guesses, unfounded speculations, or false conjectures – fake news, to use a popular neologism. Hence, following the philosophy of Spinoza, the best remedy for this plague must have been a strong warning (conveyed by a symbolic message) to proceed with serenity and discernment, to act with prudence, to carefully evaluate working hypotheses, and to plan strategies and tactics wisely according to the best available understanding and most reliable knowledge.

4 Leadership in Times of Polar Crises

In this section, we study some examples in which potential disagreements in speculative processes as described in the last section became manifested in actual conflict. The focal points of these conflicts were polar attitudes in the development of science, opposing creative intuitions or inspired insights versus disciplined circumspection or methodological rigor. The first example concerns the role and meaning of demonstration in mathematics, a theme also explored in Stern (2011). Although

very interesting (at least for mathematicians and philosophers) this example can be studied without the danger of being entrapped by strong emotional vortexes (except perhaps the aforementioned philosophers). The next examples concern clinical trials, situations in which the well-being of patients was at stake and, in this way, were sources of commotion and political conflict in Brazil.

4.1 A Tumultuous Pupil-Tutor Interaction

In 2018 the author had the opportunity to conduct a public debate following the exhibition of the movie *The Man Who Knew Infinity* by Matthew Brown (2015), see also Kanigel (1991), Kudhyadi (2016), and Prasar (2013). The movie describes the relationship between young mathematician Srinivāsa Rāmānujan (1887-1920) and Godfrey Harold Hardy (1877-1947), his advisor at Cambridge University around the time of World War I. The debate paid special attention to the existing polarity between these scholars' personalities and attitudes.

Young Rāmānujan had brilliant intuitions that led him straight away to powerful and original conjectures. In contrast, seasoned Hardy had the discipline and the tools of formal mathematics needed to prove theorems that could validate (or, sometimes, refute) Rāmānujan's conjectures. In order to achieve their highest goals, both men had to learn from each other and work together.

Prof. Hardy had the merit of recognizing the raw talent of his future pupil by examining very unorthodox ideas presented in a letter Rāmānujan sent him from Madras. These ideas were presented using wild insights, supported by a few intuitive arguments and some application examples, but lacking any formal demonstrations. This letter was so bizarre that Hardy first suspected a practical joke played by John Littlewood, his colleague at Cambridge.

Hardy had the goodwill to invite Rāmānujan to Cambridge, the patience to act as his advisor, and, later on, the courage to fight for due recognition of his merits by the deeply prejudicial academic establishment of the time. Unfortunately, some of young Rāmānujan ways of being and consequent needs were beyond Hardy's understanding. Also, the rigid (by today's standards) habits of English society,

compounded by the stresses of war, made it difficult to accommodate the needs of a vegetarian and religious Hindu. As a consequence, Rāmānujan visit to Cambridge was a mixed (polar) blessing: On the one hand, his interaction with Hardy made his mathematical work grow and prosper; on the other hand, he had to face solitude and malnourishment, contracted tuberculosis, and, already back to India, died just a few years later.

4.2 Conflicting Goals in Clinical Trials

In 2015 the university of São Paulo was taken by a storm. Based on preliminary results published in prestigious scientific journals, some researchers had been distributing, as a dietary supplement, the substance phosphoethanolamine for its alleged therapeutic effects against cancer, see Ferreira et al. (2012, 2013). Suddenly the “good news” spread like wildfire, and the public demanded access to the wonder drug. Authorities of the highest level precipitously sanctioned special laws and approvals, expediting the usually slow and contentious process of releasing a new drug, see Escobar (2016) and Ledford (2015). The university had to work hard and fast to implement a clinical trial conforming to the golden standard of blind and randomized experiments, see Rego et al. (2017). For the rationale, history, and methods for implementing efficient, auditable, and secure randomized clinical trials, see Fossaluzza et al. (2015), Lauretto et al. (2012, 2017), Marcondes et al. (2019), Saa and Stern (2019), and Stern et al. (2008, 2020).

As so often happens in the pharmaceutical industry, phosphoethanolamine’s promising preliminary results fail to translate into a viable drug, see Oliveira and Silveira (2017). Finally, the false miracle could be sent to oblivion, not without dealing with painful ethical dilemmas and also facing some legal consequences, see Renk and Jung (2018). The scientists responsible for the original phosphoethanolamine’s project had the best of intentions and were fully convinced of the validity of their ideas for, otherwise, they would not have had the passion and drive necessary to conduct their scientific research. Nevertheless, being denied the opportunity of facing the challenges involved in the standard adversarial process

for the approval of new drugs, they fell victim to their own genuine but still not sufficiently tested beliefs.

In 2020 the world was taken by the storm of COVID-19, a pandemic illness caused by the SARS-CoV-2 virus. Notwithstanding the painful lessons learned in the recent past, politicians at the highest ranks in Brazil forced the approval of medical protocols pushing the use of another not properly tested wonder drug, in this case, hydroxychloroquine. Shortly after, anxiously awaited results of double-blinded and randomized clinical trials seemed to indicate another false miracle, see Boulware et al. (2020) and Cohen (2020).

In this context, the author was asked to advise on how to conduct a clinical study concerning the benefits of treating COVID-19 patients with hydroxychloroquine in a large hospital in Brazil. At that time, the underlying public health crisis was further complicated by the noise generated by publication of thousands of low-quality research articles, see Gale (2020a,b) and Glasziou (2020). Counting hundreds of patients, this study could have been a major contribution to medical science. Nevertheless, despite the author's best advice, the study was conducted as a non-randomized, non-blind, and partially self-selecting trial, rendering (statistically) worthless conclusions. In the discussions leading to this decision, the author often had to face emotional arguments stating that, in such difficult times, the treatment choices to be taken in the study should not be based on scientific principles, but rather on love and compassion. Unfortunately (in the author's view), the love aiming at intellectual knowledge and the greater good was less compelling than the love concerning direct and immediate personal empathy – elected as the moral guideline for this study. Under these conditions, the author had no further role in defining procedures for this study or in its statistical data analysis.

Witnessing some extremely polarized and passionate quarrels concerning the strategies used in clinical trials under intense public scrutiny made me wish for a more serene and knowledgeable (I dare to say - Spinozian) approach to the subject. Every now and then, the author had the pleasure of catching a glimpse of this spirit in the political arena; in the case of COVID-19, a few of the author's

favorite examples were Correia et al. (2020), Cuomo (2020), and Merkel (2020).

5 Relegere, Religare, and other Bifurcations

An often perplexing common trend in all cases presented in the last section is the spontaneous manifestation of religious arguments, the main topic to be studied in this section. Rāmānujan was a Brahmin deeply devoted to Namagiri, a form of the Hindu deity Lakshmi, the spouse of Mahavishnu. According to Rāmānujan, the mathematical formulas he envisioned were presented to him by Namagiri in powerful dreams and ecstatic visions; he even stated – *An equation has no meaning for me unless it expresses a thought of God*. Hence, the algebraic manipulations needed for the formal proof of these results were of secondary importance to Rāmānujan; instead, the essential truth of these theorems was “demonstrated” to him by the divine insights provided by Namagiri.

The last section mentioned the political turmoil and emotional arguments the author had to face when advising a clinical trial concerning the use of hydroxychloroquine for treating patients with COVID-19. Fortunately, this matter was under study by many institutions in different countries, data of well-controlled experiments were soon made available, and firm conclusions based on empirical evidence could be reached in a relatively short time.

In contrast, the phosphoethanolamine case was of only local (national) interest and became a source of long and protracted conflicts. In the author’s view, the culminating point of these conflicts was the public hearing on 29/10/2015 at the Brazilian Federal Senate, see TVSenado (2015). On the one hand, several patients gave passionate testimonies, shedding bitter tears and asking for human and heavenly mercy; on the other hand, some patients took the opposite attitude, calmly but resolutely presenting subjective experiences as objective truth. On the one hand, some researchers presented summaries of their findings reported in articles published in prestigious scientific journals; on the other hand, other researchers told tall tales of heroic combat against evil interests, all for the good of patients, for the glory of national science, or in the fulfillment of divine missions. On the one

hand, some officials of regulatory agencies confirmed their commitment to international standards cast in stone; on the other hand, experts of the same agencies revealed gems of creative hermeneutics and pathways for flexible interpretations of underlying legal texts. Finally, senators of the republic asserted their responsibility as legislators, but also considered the possibility of dispensing altogether with existing regulations by proclaiming an *ad hoc* law, which they ended up doing shortly after.

The author is fully convinced that most testimonies given in the aforementioned cases were genuine and sincere, even if misguided from a scientific point of view. As already mentioned, a remarkable characteristic of those testimonies was the spontaneous emergence of religious symbolism, manifested either in the form of immediate allegories or in the form of more elaborate arguments intertwined with religious language. Moreover, these powerful symbolic messages found strong resonance in popular opinion. Furthermore, this symbolic content was reclaimed in the political arena, where it was skilfully recycled by rhetorical argumentation that, in turn, had the power to mobilize legislative action (with foreseeable electoral repercussions). Hence, in the author's opinion, the psychological forces at play in this scenario deserve serious attention, which shall be given in the sequel.

5.1 Ambiguous Etymologies

In western tradition, the word *religion* has two conjectured etymological derivations, namely, either from the Latin word *relegere* or from the word *religare*, see Azevedo (2010), Derrida (1998, p.36-37), Hoyt (1912), Jung (1991, vol.V par.669 p.1929, vol.XI par.982 p.5480), and Ramsey and Ledbetter (2001, p.2). The word, *religare* (from the root **leiĝ*), meaning to reconnect, points to a strong and direct link, either to God or to fellow human beings. The second is often the preferred interpretation in pastoral practice, where it is used to stress the importance of healthy social ties in the community that, in turn, should provide indirect access to heavenly rewards.

Meanwhile, the word *relegere* (from the root **leĝ*), meaning to read again,

points to diligent examination and research. However, *relegere* hides, again, a dual or bifurcated interpretation: On one hand, *relegere* suggests a privileged path of divination, inspired guessing or intuitive understanding. This ancient path corresponds to Roman practices where auspices and oracula read (*legere*) sacred signs collected from nature. On the other hand, it suggests an *intellectual* path that may be associated to study of *legated* tradition, to formal *legal* reasoning, etc. Finally, from Francis Bacon (1608) to Alfred Whitehead (1917, p.44), the metaphorical image of Jacob's Ladder has been refitted as the *Scala Intellectus sive Filum Labyrinthi*, in which scientists and philosophers can ascend by careful readings and *intelligent* interpretations from the “book of nature”, see Stern (2020).

The last paragraphs reveal dual or bifurcated aspects of religion, that sometimes appear to be incompatible and antagonistic, and sometimes appear to be complementary and possibly synergistic. It is remarkable that a single word, namely religion, is so semantically overloaded and that, furthermore, the same word is used to express polar or antithetic meanings – a phenomenon known as *enantiosemy*. Ogneva (2012) gives a historical account of enantiosemy and related concepts like polysemy and ambiguity in the field of linguistics. Biblical hermeneutic has long ago recognized this phenomenon, known as סְתִירָה עֲצֻמִית, *sthirah* (*atsmith*, or self-contradiction. For example, the word בָּרַךְ, *barech*, is used in the biblical text with the alternate meanings of kneeling, blessing or cursing; while the word שָׁכַח, *shachach*, has the double meaning of finding and forgetting. Interestingly, the very word סְתִירָה, *sthirah*, also carries an enantiosemy, for the root סָתַר can assume either the form לְסַתֵּר, *listor*, to contradict or refute, or the form לְהַסְתִּיר, *lehastir*, to hide or conceal, see Abel (1884), Apeh and Tobin (1991), Casanowicz (1897), Horn (1989), Klein (1987), Landau (1896), Nöldeke (1910) and Finkin (2005).

5.2 From Words to Dreams, or Vice-Versa

The linguistic entanglement of polar meanings by enantiosemy may seem paradoxical, but this kind of entanglement is in fact a typical (or archetypical) pattern found in the phenomenology of psychological processes. Sigmund Freud (1910)

has studied enantiosemy (Gegensin) in primal words (Urwörten), following the linguistic studies of Abel (1884). In this short paper, Freud first recalls his previous finding that dreams often disregard logical negation by condensation (Verdichtung) or amalgamation of contrary or contradictory meanings in a single representation; in his own words – *They [dreams] show a particular preference for combining contraries into a unity or for representing them as one and the same thing*, Freud (1900). Finally, Freud (1910) recognizes the phenomenon of enantiosemy as a specular image in linguistics of his recently discovered dream mechanisms, and closes the paper with the following conclusion: *We psychiatrists cannot escape the suspicion that we should be better at understanding and translating the language of dreams if we knew more about the development of language.*

Later on, Carl Gustav Jung conceived a form of characterizing psychological types by a system of symmetrical modal polarities, see Jung (1991, vol.VI), Stern (2022), Wilde (2011). Furthermore, Jung characterized the phenomenon of *enantiodromia* as attitudinal “runs” between antithetic polarities, usually from a bright spot in the conscious mind to its antipodal point in unconscious shadow, see Jung (1991, vol.V par.581 and vol.VI). For example, several aspects of the pupil-tutor case presented in the last section can be analyzed in the context provided by the *Puer-Senex* relation described in Jung (1991, vols. V, VI, XI).

Finally, Jorge Forbes and Newton da Costa, see Forbes et al. (1983, 1987) investigate the use of heterodox logics (like paraconsistent, paracomplete, or non-reflexive) to describe the manifestation of contradictory logical modalities in the practice of psychoanalysis confirming, in this context, the convenience of speaking about alethic, epistemic, deontic and doxastic modalities using logics where notions like negation or conflation are severely weakened (relative to classical logic) or even completely absent; for related aspects in non-standard logics and inference see Béziau (2012, 2015), Borges and Stern (2007), Bueno-Soler and Carnielli (2016), D’Ottaviano and Gomes (2017), Dubois and Prade (2012), Esteves et al. (2019), Gargov (1999), Varzi and Warglien (2003) and Stern et al. (2004, 2017, 2020a, 2022) and references therein.

It should be remarked that the aforementioned authors in the field of psychology work in very distinct and often incompatible theoretical frameworks. Nevertheless, the fact that the psychological phenomena under scrutiny deserved the attention of so diverse schools of thought could be taken as an indication of the relevance and importance of the same topics. Furthermore, it is interesting to see how the historical development of these schools makes them pay attention to oppositional structures turning around a cycle that goes from psychological functions, to narratology, linguistics, logic, and back to psychology.

The psychological aspects of polar relations under examination and their pragmatic impact on the implementation of clinical trials are reflected in some topics for further research given in the next section. These topics stand at the intersection of science, law, and psychology, requiring and leading to *ethical conscience* – as preconized by Gustav Jung in the following quotation. I believe this quotation also reinforces the need to integrate diverse and complementary perspectives in the discussion of the complex problems under consideration.

The concept and phenomenon of conscience thus contain, when seen in a psychological light, two different factors: On the one hand, a recollection of, and admonition by, the mores; on the other, a conflict of duty and its solution through the creation of a third standpoint. The first is the moral, and the second is the ethical, aspect of conscience. A conflict of duty and its solution through the creation of a third standpoint [...is...] the ethical aspect of conscience. The nature of the solution is in accord with the deepest foundations of the personality as well as with its wholeness; it embraces conscious and unconscious and therefore transcends the ego. Jung (1991, vol.X, par.857, p.4759)

6 Further Research and Final Remarks

From 2016 to 2020, the author served as head of his Institutes's Research Committee (CPq) that, up to the end of his term, also doubled as the Institute's Ethics

Committee (recent regulations now require the Ethics Committee to be a separate entity). During this time, the author had to be aware of some research projects under the supervision of ethics committees of other Institutes, and was also asked to advise on the aforementioned clinical trial on hydroxychloroquine.

Even in situations where it seems (in someone's perspective) that it is possible to decide from a purely scientific point of view the right course of action, the communication of this decision to the target group is far from a trivial task. For example, this communication often requires the translation of arguments stated in technical language (for example, in defining statistical models and demonstrating its theoretical properties) to alternative forms of discourse that are more amenable to colleges of other areas or to subjects involved in an experiment.

A particularly sensitive topic concerns the need to make sure that patients involved in a clinical trial are sufficiently informed about experimental procedures and risks involved. The primary goal of a well-designed clinical trial is efficient and reliable statistical inferences about the (relative) efficacy of alternative treatments (possibly including placebo – the null treatment). Hence, the main goal of such a study can *not* be that of offering the best possible treatment and comfort for the patients involved. For starters, despite strong personal opinions about it, “what's best” is (scientifically) uncertain, hence the need for statistical experiments in the first place. Moreover, most of the time, well-designed clinical trials must rely on double-blind and randomized attribution of treatments, procedures that may seem perplexing to patients and caretakers alike.

I believe the signing of the term of consent that allows a patient to participate in a clinical trial should not be a meaningless ceremonial procedure demanded by legal protocol, but the culmination of a process that shares, in a form understandable to laymen, the best scientific information available, including potential conflicts of interest and often misunderstood ethical aspects of clinical trials. Moreover, the considerations on polar aspects of the human psyche made in the last section suggest that limiting this process to the dissemination of technical papers risks future backlash of unattended aspects left in the shadows. Patients' fears, anxieties, and

hopes should also be accessed, analyzed, and integrated into their decision process in order to minimize post hoc hesitation or regret. Furthermore, patients should not be expected to speak their mind in (pseudo) scientific language, but rather be welcome to express themselves and find some dialogical engagement using their preferred concept and word palette. Accordingly, our first topic for further research concerns interdisciplinary approaches for handling complex and multifaceted aspects of human participation in clinical trials having in mind the implementation of stable scientific studies where all those who choose to participate do so in a well-informed, well-aware, and co-responsible way.

Our second topic of further research concerns the scope and language of scientific education campaigns. This topic deserves urgent attention during the present COVID-19 pandemic, due to the spread of disinformation in the form of anti-vaccine campaigns and organized resistance against social isolation measures. Some efforts in this direction focus on disseminating scientific doctrine to the layman, while either ignoring or being hostile to any form of non-scientific reasoning. The author is convinced that a preferable course of action would acknowledge the inherent polarities of the human psyche, recognize the importance of alternative ways of perceiving and conceiving human life, and find ways to effectively communicate and positively engage alternative *weltanschauungen*, always respecting, nevertheless, the limits imposed and the specificities of the pertinent scientific disciplines.

The aforementioned topics of further research are in line with the general approach of natural theology (*theologia naturalis*): Neither does this approach provide a master key to the universe, nor does it give immediate access to its general laws; neither does it promise super-natural solutions for particular problems, nor does it supply a theodicy able to justify human sufferings, nor does it provide a simple answer to the meaning of life. Nevertheless, this approach offers real opportunities for engaging in the struggle of human life in a considerate, meaningful, ethical and responsible way and, in so doing, celebrate the struggle, as commanded by the second opening quotation of this article.

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References

- C. Abel (1884). *Über den Gegensinn der Urworte*. Leipzig: Wilhelm Fridrich Verlag.
- D. Adams (1979). *The Hitchhiker's Guide to the Galaxy*. London: Pan Books.
- E. Aphek, Y. Tobin (1991). Semantic Polarity and the Origin of Language. *Studies in Language Origins*, 2, 263-284.
- C.A.de Azevedo (2010). The Search of the Concept of Religio: Between Relegere and Religare. *Religare*, 7, 1, 90-96.
- F. Bacon (1608). *Scala Intellectus sive Filum Labyrinthi*. Reprinted and translated as: *A Escada do Entendimento ou o Fio do Labirinto*. *Skepsis*, 2008, 3/4, 197-203.
- G. Bateson, M.C. Bateson (1987). *Angels Fear: Towards an Epistemology of the Sacred*. NY: Macmillan.
- G. Bateson (1991). *A Sacred Unity: Further Steps to an Ecology of Mind*. NY: Harper-Collins.
- J.Y. Béziau (2012). The Power of the Hexagon. *Logica Universalis*, 6, 1-43.
- J.Y.Beziau (2017). A Chromatic Hexagon of Psychic Dispositions. p.273-288 in M.Silva ed. *How Colours Matter to Philosophy*. Synthese Library, 388; Cham: Springer.
- W.S. Borges, J.M. Stern (2007). The Rules of Logic Composition for the Bayesian Epistemic e-Values. *Logic Journal of the IGPL*, 15, 5-6, 401-420.
- D.R. Boulware, M.F. Pullen, A.S. Bangdiwala, K.A. Pastick, S.M. Lofgren, E.C. Okafor, et al. (2020). A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for COVID-19. *New England Journal of Medicine*, doi:10.1056/NEJMoA2016638
- M. Brown (2015). *The Man Who Knew Infinity*. Burbank, CA: Warner Bros.
- J. Bueno-Soler, W. Carnielli (2016). Paraconsistent Probabilities: Consistency, Contradictions and Bayes' Theorem. *Entropy*, 18, 9, 325, 1-18;
- I.M. Casanowicz (1893). Paronomasia in the Old Testament. *Journal of Biblical Literature*, 12, 2, 105-167.
- I.M. Casanowicz (1897). Landau, Die Gegensinnigen Wörter im Alt und Neuhebraischen. *The American Journal of Semitic Languages and Literatures*, 13, 3, 231-233.
- M.S. Cohen (2020). Hydroxychloroquine for the Prevention of COVID-19 - Searching for Evidence. *New England Journal of Medicine*, doi:10.1056/NEJMe2020388
- L. Cooper (2013). The Assimilation of Tikkun Olam. *Jewish Political Studies Review*, 25, 3/4, 10-42.
- L.C. Correia, I.A. Pena, F.L.A. Fernandes (2020). Kit COVID: O que diz a Medicina Baseada em Evidências. *Ciência USP debate*, 22/07/2020; retrieved from youtu.be/hcrrb04BuE-o
- A. Cuomo (2020). Governor Andrew Cuomo press briefing, 3/29/2020; retrieved from youtu.be/scrn2mAxMU
- J. Derrida (1998). Faith and Knowledge: The Two Sources of Religion at the Limits of Reason Alone. p.1-78 in J. Derrida, G. Vattimo; *Religion*; Cambridge: Polity Press.

- E. Dreff (2019). The Love of God as a Consistent Jewish Response to Modernity. *Religions*, 10, 5, 324.1-324.10.
- I.M.L. D'Ottaviano, E.L. Gomes (2017). *Para além das Colunas de Hércules: Uma história da paraconsistência - De Heráclito a Newton da Costa*. Coleção CLE, v. 80, Campinas: Editora da UNICAMP.
- D. Dubois, H. Prade (2012). From Blanché Hexagonal Organization of Concepts to Formal Concept Analysis and Possibility Theory. *Logica Universalis*, 6, 1, 149-169.
- H. Escobar (2016). Brazil President Signs Law Legalizing Renegade Cancer Pill. *Science*, doi:10.1126/science.aaf9915
- L.G. Esteves, R. Izbicki, R.B. Stern, J.M. Stern (2019). Pragmatic Hypotheses in the Evolution of Science. *Entropy*, 21, 883, 1-17.
- A.K. Ferreira, R. Meneguelo, A. Pereira, O.M. Filho, G.O. Chierice, D.A. Maria (2012). Anticancer Effects of Synthetic Phosphoethanolamine on Ehrlich Ascites Tumor: An Experimental Study. *Anticancer Research*, 32, 1, 95-104.
- A.K. Ferreira, B.A.A. Santana-Lemos, E.M. Rego, O.M.R. Filho, G.O. Chierice, D.A. Maria (2013). Synthetic Phosphoethanolamine has in Vitro and in Vivo Anti-Leukemia Effects. *British Journal of Cancer*, 109, 11, 2819-2828.
- J. Finkin (2005). Enantiodromia: Enantiosemeia in Arabic and Beyond. *Bulletin of the School of Oriental and African Studies*, 68, 3, 369-386.
- J.F. Forbes, N.C.A.da Costa (1987). Sobre Logica e Psicanálise. *FALO – Revista Brasileira do Campo Freudiano*, 1, 103-111.
- J.F. Forbes, I. Villalba, N.C.A.da Costa (1983). Da Nossa Responsabilidade. *Atas da II Jornada de Psicanálise da Biblioteca Freudiana Brasileira*; retrieved from www.psicanaliseslacaniana.com/estudos/documents/danossaresponsabilidade.pdf
- V. Fossaluzza, M.S. Lauretto, C.A.B. Pereira, J.M. Stern (2015). Combining Optimization and Randomization Approaches for the Design of Clinical Trials. *Springer Proceedings in Mathematics and Statistics*, doi:10.1007/978-3-319-12454-4_14
- C. Fraenkel (2006). Maimonides' God and Spinoza's Deus sive Natura. *Journal of the History of Philosophy*, 44, 2, 169-215.
- S. Freud (1900, 1957). *Die Traumdeutung*. Translated as: The Interpretation of Dreams. vols. IV & V in Standard Edition of Complete Psychological Works. London: Hogarth.
- S. Freud (1910, 1957). *Über den Gegensinn der Urworte*. Translated as: The Antithetical Meaning of Primal Words. pp.155-161, vol.XI in Standard Edition of Complete Psychological Works. London: Hogarth.
- R.P. Gale (2020a). Conquest of COVID-19. Publish it to Death? *British Journal of Haematology*, doi:10.1111/bjh.16905.
- R.P. Gale (2020b). *20.000 Papers Published in 6 Months: Was it Worth it?* Presentation and discussion held on 09/07/2020 at ANM – the Brazilian National Academy of Medicine; retrieved from <https://youtu.be/73PoPHdmYmo>
- G. Gargov (1999). Knowledge, Uncertainty and Ignorance in Logic: Bilattices and Be-

- yond. *Journal of Applied Non-Classical Logics*, 9, 2-3, 195-283.
- P.P. Glasziou (2020). Waste in COVID-19 Research: A Deluge of Poor Quality Research is Sabotaging an Effective Evidence Based Response. *BMJ*, doi:10.1136/bmj.m1847
 - W.Z. Harvey (2007). Idel on Spinoza. *J. Study of Religions and Ideologies*, 6, 18, 88-94.
 - W.Z. Harvey (2012). Gersonides and Spinoza on Conatus. *Aleph: Historical Studies in Science and Judaism*, 12, 2, 273-297.
 - S.R. Hirsch, M. Clark (1999). *Etymological Dictionary of Biblical Hebrew: Based on the Commentaries of Samson Raphael Hirsch*. Jerusalem: Feldheim Publishers.
 - B.A. Hong, P.J. Handal (2020). Science, Religion, Government, and SARS-CoV-2: A Time for Synergy. *Journal of Religion and Health*, doi:10.1007/s10943-020-01047-y
 - E. Horowitz (2017). *How the Hebrew Language Grew*. NY: Ktav.
 - S.F. Hoyt (1912). The Etymology of Religion. *Journal of the American Oriental Society*, 32, 2, 126-129. doi:10.2307/3087765
 - K. Hübner (2015a). Spinoza on Essences, Universals, and Beings of Reason. *Pacific Philosophical Quarterly*, 96, 2, 58-88.
 - K. Hübner (2015b). On the Significance of Formal Causes in Spinoza's Metaphysics. *Archiv für Geschichte der Philosophie*, 97, 2, 196-233.
 - M. Idel (2000). Deus sive Natura – The Metamorphosis of a Dictum from Maimonides to Spinoza. p.87-110 in R.S. Cohen, H. Levine (2000). *Maimonides and the Sciences*. Boston Studies in the Philosophy of Science, v.211.
 - C.G. Jung (1991). *C.G.Jung Collected Works*. London: Routledge. vol.V - Symbols of Transformation, vol. VI - Psychological Types, vol. X - Civilization in Transition, vol. XI - Psychology of Religion: West and East. German titles in *Gesammelte Werke* by Patmos-Verlag, 1989: Bd.05 - Symbole der wandlung, Bd.06 - Psychologische Typen, Bd.10 - Zivilisation im Übergang, Bd.11 - Zur Psychologie westlicher und östlicher Religion.
 - R. Kanigel (1991). *The Man Who Knew Infinity: A Life of the Genius Ramanujan*. NY: Washington Square Press.
 - E. Klein (1987). *A Comprehensive Etymological Dictionary of the Hebrew Language*. Jerusalem: CARTA.
 - J.R. Klein (2003). Spinoza's Debt to Gersonides. *Graduate Faculty Philosophy Journal*, 24, 1, 19-43.
 - N. Kudhyadi (2016). *Srinivasa Ramanujan: The Man and his Legacy*. Mumbai: PSBT; retrieved from youtu.be/K5jsgBvJMUc
 - E. Landau (1896). *Die Gegensinnigen Wörter im Alt und Neuhebraischen: Sprachverleichend dargestellt*. Berlin: S. Calvary.
 - M.S. Laretto, F. Nakano, C.A.B. Pereira, J.M. Stern (2012). Intentional Sampling by Goal Optimization with Decoupling by Stochastic Perturbation. *American Institute of Physics Conference Proceedings*, doi:10.1063/1.4759603
 - M.S. Laretto, R.B. Stern, K.L. Morgam, M.H. Clark, J.M. Stern (2017). Haphazard Intentional Allocation and Rerandomization to Improve Covariate Balance in Experiments.

- American Institute of Physics Conference Proceedings*, doi:10.1063/1.4985356
- H. Ledford (2015). Brazilian Courts Tussle over Unproven Cancer Treatment. *Nature*, 527, 7579, 420-421.
 - A.de Libera (1998). *A Filosofia Medieval*. São Paulo: Edições Loyola.
 - D. Marcondes, C. Peixoto, J.M. Stern (2019). Assessing Randomness in Case Assignment: The Case Study of the Brazilian Supreme Court. *Law, Probability and Risk*, 18, 2-3, 97-114.
 - A. Merkel (2020). Chancellor Angela Merkel press briefing, 3/18/2020; retrieved from youtu.be/F9ei40nxKDC
 - G. Miller (1992). *Lorenzo's Oil*. Universal Pictures.
 - S. Nadler (2014). *Spinoza and Medieval Jewish Philosophy*. Cambridge Univ. Press.
 - Th. Nöldeke (1910). Wörter mit Gegensinn. p.67-108 in *Neue Beiträge zur semitischen Sprachwissenschaft*. Strassburg: Karl J. Trübner.
 - A. Odone (2011). *L'Olio de Lorenzo: Una Storia d'Amore*. Milano: Mondadori.
 - S.V. Ogneva (2012). On History of Enantiosemy and its Types. *Russian Linguistic Bulletin*, 3, 7, 102-106.
 - A.G. Oliveira, D. Silveira (2017). O Fim da Expectativa e Realidade em Torno do Efeito Anticancer da Fosfoetanolamina? *Infarma - Ciências Farmacêuticas*, 29, 2, 87-89.
 - C.A.B. Pereira, J.M. Stern (2020). The e-value: A Fully Bayesian Significance Measure for Precise Statistical Hypotheses and its Research Program. *São Paulo Journal of Mathematical Sciences*, doi:10.1007/s40863-020-00171-7
 - N. Pondé, F. Ades, E.de Azambuja (2016). Threat Posed by Unproven Drugs in Medical Oncology. *Cancer Horizons*, doi:10.1136/esmopen-2016-000064
 - V. Prasar (2013). *The Genius of Srinivasa Ramanujan*. Pune: IISER; retrieved from youtu.be/SYB00jhAMsM
 - E. Ramsey, S. Ledbetter (2001), Studying Religion: Issues in Definition and Method. p.1-14 in I.S. Markam, T. Ruparell (eds.); *Encountering Religion: An Introduction to the Religions of the World*; Oxford: Blackwell Publishers.
 - J.F.M. Rego, G. Lopes, R.P. Riechelmann, C. Sternberg, C. Ferrari, G. Fernandes (2017). A “Miracle” Cancer Drug in the Era of Social Media: A survey of Brazilian Oncologists’ Opinions and Experience with Phosphoethanolamine. *Revista da Associação Médica Brasileira*, doi:10.1590/1806-9282.63.01.70
 - A.A. Renk, P. Jung (2018). Caught by Uncertainty: The Lessons from the “Cancer Pill” Case for Precaution. *Revista Eletrônica do Curso de Direito da UFSM*, 13, 1, 159-182.
 - O.T. Saa, J.M. Stern (2019). Auditable Blockchain Randomization Tool. *Proceedings*, doi:10.3390/proceedings2019033017
 - N.da Silveira, (1995). *Cartas a Espinoza*. Rio de Janeiro: Livraria Francisco Alves.
 - B. Spinoza (1677, 2008). *Ethica: Ordine Geometrico Demonstrata / Ética: Demonstrada Segundo a Ordem Geométrica*; Edição Bilingüe Latim - Português. São Paulo: Autêntica.
 - B. Spinoza, M.J. Petry (1985). *Spinoza's Algebraic Calculation of the Rainbow and Calculation of Chances*. Dordrecht: Martinus Nijhoff.

- J.M. Stern (2004). Paraconsistent Sensitivity Analysis for Bayesian Significance Tests. *Lecture Notes in Artificial Intelligence*, 3171, 134-143.
- J.M. Stern (2008). Decoupling, Sparsity, Randomization, and Objective Bayesian Inference. *Cybernetics and Human Knowing*, 15, 2, 49-68.
- J.M. Stern (2014). Jacob's Ladder and Scientific Ontologies. *Cybernetics and Human Knowing*, 21, 3, 9-43.
- J.M. Stern, R. Iznicki, L.G. Esteves, R.B. Stern (2017). Logically Consistent Hypothesis Testing and the Hexagon of Oppositions. *Logic Journal of the IGPL*, 25, 5, 741-757.
- J.M. Stern (2018a). Verstehen (causal/ interpretative understanding), Erklären (law-governed description/ prediction), and Empirical Legal Studies. *J.of Institutional and Theoretical Economics – Zeitschrift für die Gesamte Staatswissenschaft*, 174, 1, 105-114.
- J.M. Stern (2018b). Karl Pearson and the Logic of Science: Renouncing Causal Understanding (the Bride) and Inverted Spinozism. *South American Journal of Logic*, 4, 1, 219-252, 2018.
- J.M. Stern (2020). Jacob's Ladder: Logics of Magic, Metaphor and Metaphysics. *Sophia*, 59, 365-385. doi:10.1007/s11841-017-0592-y
- J.M. Stern, M.A. Simplicio, M.V. Silva, R.A.C. Pfeiffer (2020). Randomization and Fair Judgment in Law and Science p.399-418 in J.A.de Barros, D. Krause, eds. *A True Polymath: A Tribute to Francisco Antonio Doria*. Rickmansworth, UK: College Publications.
- J.M. Stern (2022). Color-Coded Epistemic Modes in a Jungian Hexagon of Opposition; to appear in *Studies in Universal Logic*; Cham, Switzerland: Birkhäuser.
- TVSenado (2015). Debate sobre a Fosfoetanolamina, Senado Federal. Reunião Conjunta das Comissões de Ciência e Tecnologia e Assuntos Sociais, 29/10/2015; retrieved from youtu.be/jLX0_bt8Gh0
- UNESCO (1986). Averroes and Maimonides: Two Master Minds of the 12th Century. *The Courier*, Special issue, Sept. 1986.
- A.C. Varzi, M. Warglien (2003). The Geometry of Negation. *Journal of Applied Non-Classical Logics*, 13, 1, 9-19.
- L. Vinciguerra (2012a). *La Semiotica di Spinoza*. Pisa: Edizioni ETS.
- L. Vinciguerra (2012b). Mark, Image, Sign: A Semiotic Approach to Spinoza. *European Journal of Philosophy*, 20, 1, 130-144.
- L. Vinciguerra (2015). *Spinoza*. Roma: Carocci.
- A.N. Whitehead (1917). *The Organization of Thought, Educational and Scientific*. London: William and Norgate.
- D.J. Wilde (2011). *Jung's Personality Theory Quantified*. Berlin: Springer.
- D.L.R. Zauderer (2019). *Metaphor and Imagination in Medieval Jewish Thought: Moses ibn Ezra, Judah Halevi, Moses Maimonides, and Shem Tov ibn Falaquera*. Cham: Palgrave.