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ORIGINAL RESEARCH

Scientific understanding in biomedical research

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Abstract
Motivated by a recent trend that advocates a reassessment of the aim of medical science and clinical practice, this paper investigates the epistemic aims of biomedical research. Drawing on contemporary discussions in epistemology and the philosophy of science, along with a recent study on scurvy, this paper (1) explores the concept of understanding as the aim of scientific inquiry and (2) establishes a framework that will guide the examination of its forms in biomedical research. Using the case of Tuberculosis (TB), (3) it is argued that grasping a mechanistic explanation is crucial for reaching a threshold of understanding at which we may speak of an objectual, biomedical understanding of TB.

Keywords Understanding · Biomedical research · Tuberculosis · Clinical medicine

Within just a few years, multiple editorials in prominent medical journals have issued a call to reflect on the aim of clinical medicine and medical science. Focusing on the latter matter, in a 2013 editorial, the editors of *The Lancet* clarified that they frequently confront not only queries about the rationale behind specific scientific studies but also broader inquiries regarding the overarching aim of medical science, which includes both clinical and medical laboratory research. They contend that the moment has come to rethink our approach to conducting and incentivizing research, and for this, "we need to remind ourselves about the real purpose of research" (The Lancet, 2013, p. 347; see also Thornton, 2013). The authors express concern that a significant portion of the vast sums allocated annually to biomedical research fails to

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meet its true objectives. This shortfall is attributed not only to deficiencies in research design and methodology but also to a lack of "clinical meaningfulness." Specifically, they highlight that many research projects pose questions that are not sufficiently aligned with clinical medicine and relevant to the treatment, control, prevention, or prediction of diseases. The authors note that the issues extend beyond merely reducing the potential impact of biomedical research; they suggest a fundamental misunderstanding of the very purpose of biomedical research, implying that such studies may not truly qualify as *medical*.[1]

This short *Lancet* piece highlights significant, yet often overlooked, questions concerning the epistemic aim of medical research. This paper will address these questions, positing that medical science is fundamentally engaged in inquiries aimed at achieving what we shall refer to as *biomedical understanding*. To investigate and clarify what such understanding amounts to, the paper takes inspiration from two sources. On the one hand, it draws on contemporary discussions in philosophy of science and epistemology, which have seen a renewed interest in understanding as a distinct cognitive accomplishment (Grimm, 2021; Baumberger et al., 2017), as the epistemic aim of scientific inquiry, and the measure of progress (see e.g., Potochnik, 2015; De Regt & Dieks, 2005; Elgin, 2017). Acknowledging that what constitutes proper understanding can depend on the field, as noted by scholars in the field (Strevens, 2010; De Regt et al., 2009), this paper aims to specifically articulate what understanding entails within medical science. On the other hand, this paper draws on and employs several distinctions from a recent study on scurvy (Varga, 2023). However, while that study focused on a noncommunicable condition stemming from severe dietary deficiencies, this paper shifts our focus to Tuberculosis (TB), a multifaceted and emblematic infectious disease often accompanied by stigma (WHO, 2023). TB, which is one of the oldest known infectious diseases, is caused by the bacterium Mycobacterium tuberculosis (Kapur et al., 1994; Daniel, 2006). The bacteria are transmitted when an infected individual coughs, sneezes, or speaks, allowing another person to breathe in the pathogens. Symptoms of TB can include coughing, chest pain, fatigue, fever, and night sweats and although the condition is treatable with antibiotics it remains a major global health concern.

The paper is organized as follows. It (1) explores the idea of understanding as the aim of scientific inquiry and (2) lays down a framework of understanding that will subsequently guide our exploration of its forms in medicine. Using the case of Tuberculosis (TB), (3) it is argued that grasping a mechanistic explanation is crucial for reaching a threshold of understanding at which we may speak of an objectual, biomedical understanding of TB. If evidence can be gathered to support this argument, it

[1] Interestingly, in an editorial published by the *British Medical Journal* (Marshall et al., 2018) the editors prompt a similar reflection on the purpose of clinical medicine. They challenge the prevailing emphasis on disease-centric care and encourage contemplation of whether a holistic therapeutic relationship with patients might better align with the true aim of medical practice. Though published separately, these editorials collectively highlight a growing movement towards a critical reevaluation of the aims and priorities of both medical science and clinical medicine. The question has sparked considerable interest, with various competing accounts proposing that there is a single, overarching aim (e.g., Broadbent, 2019) whereas others suggesting that medicine has multiple aims (e.g., Boorse, 2016; Brody & Miller, 1998; Schramme, 2017).

would align with the previously mentioned research on a noncommunicable disease (scurvy), suggesting a recurring pattern across various contexts of medical research.

1 The aim of scientific inquiry: constitutive aim and truth

Scientific inquiries can be viewed as extensions of our day-to-day endeavors to gather information albeit executed in a more systematic manner (see e.g., Kelp, 2021). They are goal-directed activities, implying that there is some aim that inquiry strives to accomplish. It is quite natural to assume that this description also fits medical science; however, before delving into the question of what constitutes the epistemic aim of medical science, it is crucial to first briefly clarify what medical science refers to. What sets medical science apart and qualifies something as specifically *medical* science, rather than just science in general?

Medical science, which includes clinical research and laboratory research in medicine, is fundamentally based on the life sciences. Over the past two centuries, it has extensively leveraged discoveries in biology that have identified cellular, genetic, and molecular entities and processes that help explain the development and course of diseases. While some aspects of medical science may not differ essentially from laboratory sciences within contributing disciplines such as biology, biochemistry, and physiology, medical science cannot simply be reduced to the sum of these fields. One reason is that medical research is only deemed properly *medical* when it has a specific practical orientation—that is, when it is driven by the goal of contributing to clinical medicine, which primarily focuses on the diagnosis, prevention, and treatment of disease. Without this practical focus, research might be more accurately described as biological rather than medical. Take, for example, large-scale laboratory research that aims to chart the functions of specific limbic structures in the brain. Without a practical focus on clinical applications or health outcomes, such research might be more accurately described as neurobiological rather than medical. Of course, this research could potentially yield benefits for clinical medicine in the future, but without a direct and immediate practical orientation, it would not be classified as medical research. Moreover, if we were to classify such research as medical merely based on potential future benefits, the distinction between medical and non-medical research would collapse.

Of course, this practical orientation toward health outcomes is a characteristic that biomedical research shares with related fields such as public health. However, their epistemic aims are directed towards different objectives: biomedical research typically focuses on the biological and physiological aspects of diseases at a molecular or cellular level, aiming to elucidate disease mechanisms and develop new treatments, whereas public health is primarily concerned with improving the health of populations through prevention strategies, health education, surveillance, and improving access to health care. Public health aims encompass a wide array of objectives: ensuring safe environments by controlling hazards in air, water, and food, enhancing host resistance through balanced nutrition and immunization, promoting health-supportive behaviors, and improving equitable access to health and social services (White et al., 2013; Munthe, 2008).[2]

Although both fields are dedicated to conducting research with the final aim to improve health outcomes, they operate with different priorities and methodologies, each aligned with their distinct epistemic goals. A biomedical researcher might delve into the genetic factors that contribute to the resistance of TB to antibiotics, focusing on molecular and cellular details. In contrast, public health initiatives may not require such knowledge; instead, they often concentrate on understanding societal or other health factors that hinder the implementation of vaccination programs or public campaigns aimed at increasing awareness and prevention of TB.

Having briefly clarified at least some of the aspects that set medical science apart, we can now turn to the question of its aim. As we begin to explore this, it is worth considering how plausible it is to claim that scientific inquiries in medicine are driven by a single aim. This consideration is crucial because the diversity of methods, approaches, and priorities within medical science suggests that its objectives might not be unified under a single overarching aim. In response, it is important to clarify that for the purposes of this paper, we do not assert that medical science is driven by a single aim. Instead, among potentially other aims, our objective is to explore the nature of medical science's *epistemic aim*, which also determines what counts as progress at least in this limited sense. Thus, very roughly, if A is the aim of inquiry, then medical science makes progress when A accumulates or increases (for a discussion, see Bird, 2007; Varga, 2024).

So what is the epistemic aim of scientific inquiry in medicine? According to a plausible suggestion, the aim is simply to discover truths about health and disease and correct past errors (e.g., false beliefs about diseases like scurvy or depression being caused by humoral imbalance) that were based on tradition, cognitive errors, ideologies, or religious dogma. Correspondingly, progress consists in a cumulative acquisition of true beliefs. For example, until the nineteenth century, the prevailing belief was that TB was inherited or caused by environmental factors such as bad air or poor living conditions. But already in 1720, the English physician Benjamin Marten hypothesized that TB and its symptomatic lesions in the lungs are caused by "species of Animalcula or wonderfully minute living Creatures" that can be transmitted "by very frequently conversing so nearly as to draw inpart of the breath he emits from the lungs" (cited in Cambau & Drancourt, 2014; Daniel, 2006). Supporting this hypothesis, in 1865, the French physician Jean-Antoine Villemin provided experimental evidence that TB could be transmitted. He observed that TB was more prevalent in people living close and in poorly ventilated buildings, and he noted that while TB was common among troops in barracks, it decreased during military campaigns when soldiers were not housed (Daniel et al., 1994). Thus, Marten and Villemin unearthed truths regarding TB, rectified previous mistakes, and aided in the ongoing accumulation of accurate beliefs, which constitutes progress.

On its face, the suggestion that the aim of medical research is simply to discover truths is plausible. After all, it is often said that scientific inquiries are in the "truth

[2] Munthe (2008) advocates for an integrated, multidimensional model, highlighting that recent decades have seen the introduction of new objectives focusing on autonomy and equality.

business" (Pennock, 2019; Lipton, 2004), and it is difficult to imagine that contemporary medical science would be able to achieve what it does if its claims would not at least roughly correspond to how the world actually is. Nonetheless, the acquisition of true beliefs does not seem sufficient to constitute progress.[3] Take, for instance, a scenario where Marten and Villemin arrived at the same conclusion through unreliable methods and, coincidentally, the theory they came to accept happened to be true. In that case, Marten and Villemin would have acquired a true belief, but it would not have counted as genuine progress. What would be lacking is suitable justification for holding the relevant belief. In other words, the belief that they would have acquired would not qualify as *knowledge*.

1.1 Knowledge and understanding

What we learn from these considerations is that progress not only requires that our beliefs and theories be true but that we have attained adequate reasons for forming them. If this is correct, then it seems safe to conclude that the aim of inquiry is not merely truth, but *knowledge* (achieved by reliable means), which would mean that progress consists in the increase not of true beliefs, but of knowledge. Although this correction marks an improvement, it is necessary to supply some clarifications and caveats.

First, the aim of inquiry cannot simply be the mere accumulation of knowledge. Medical science has an expansive range of questions at its disposal, and it could potentially attain a vast pool of knowledge, but much of this potential knowledge might be trivial or inconsequential, lacking the impact or *significance* to be deemed progress. Imagine that researchers could come to know everything about some minor and transient symptom (e.g., a slight, transient change in nail coloration or longitudinal nail ridging) observed in a small subset of TB patients that are known not to have bearing on the disease's diagnosis, progression, or response to treatment. While detailed knowledge of these symptoms might add to the clinical descriptions of TB, the reason this gained knowledge is not considered significant or constitutive of true progress likely stems from its limited impact on key areas of TB research and clinical management. It lacks the potential to advance our understanding of TB (or indeed other medically relevant conditions), uncover new treatment targets, enhance diagnostic methods, or deepen our understanding of disease transmission and resistance mechanisms.

If we accept this line of reasoning, then the aim of inquiry in medicine cannot be simply to amass knowledge, but rather a selective process that prioritizes the acquisition of certain kinds of *significant* knowledge. Hence, part of the scientific endeavor involves a critical evaluation process to identify which pieces of knowledge are significant and worth pursuing. This selection process is fundamental to progress, ensuring that scientific efforts are directed toward areas of genuine importance and potential impact (Kitcher, 2001; Dupré, 2016). Identifying and focusing on significant knowledge, therefore, becomes a crucial aspect of the scientific method, guiding

[3] See Bird (2019) for a helpful discussion of an example from physics.

researchers in making meaningful advancements rather than merely expanding the repository of human knowledge.

While the aim of inquiry is *significant* knowledge, the selection process to identify which pieces of knowledge count as significant cannot be extracted from nature and is largely relative to specific interests. As Kitcher (2001, 61) stated regarding scientific inquiry in general, "significant science must be understood in the context of a particular group with particular practical interests and a particular history". In the context of TB, it is far more plausible to suggest that what constitutes significant knowledge is closely interwoven with practical concerns related to the understanding and treatment of TB.

Having discussed the issue of significance, we are now faced with a final challenge that questions the notion that the goal of inquiry in medical science is best described as the pursuit of knowledge. In recent years, numerous philosophers of science have contended that framing the aim of inquiry in terms of *understanding* offers significant benefits over viewing progress merely as an accumulation of knowledge. The advantage with comprehending progress in terms of increased understanding is that it avoids the challenges faced by accounts measuring scientific progress in terms of knowledge (see e.g., Elgin, 2007, 2017; De Regt & Dieks, 2005; Potochnik, 2017).[4] First, traditional accounts have problems explaining the significance of certain pragmatic virtues (e.g., simplicity) that do not affect the truth of claims, theories, and explanations. In contrast, an account of progress based on the notion of understanding does not face this problem, as these pragmatic virtues clearly affect the ability to understand (Dellsén, 2016). Second, traditional accounts of progress as knowledge accumulation have problems explaining abstractions, approximations, and idealizations. For example, in medicine, physiological accounts often offer idealized and simplified descriptions of organs and their functions (Ereshefsky, 2009). These provide computational tractability and improve understanding, but they also include aspects that are, strictly taken, inaccurate or false. However, such falsehoods are, as Elgin (2017) puts it, "felicitous": although they involve false representations, they also exemplify significant aspects of phenomena in a tractable manner. Several philosophers have argued that science can increase understanding and contribute to progress even if it involves departing from the truth (e.g., Elgin, 2009a, b; Strevens, 2017; Potochnik, 2015).

On an account of progress in terms of knowledge, the presence of manifest falsehoods seems incompatible with progress. However, an account of progress in terms of understanding fares better here, since understanding is compatible with a limited number of falsehoods, which are outweighed by practical advantages. Strevens argues that idealized models can provide understanding, but in a somewhat more limited way, showing why some causal factors are difference-makers and others are not (Strevens, 2017). Potochnik (2017, 102; 2015) holds that while idealizations cannot be true or approximately true, they can be epistemically acceptable. Because such idealizations are rampant in science and they always detract from the truth, truth

[4] Other accounts maintain that progress in science occurs when theories come nearer to the truth or when it accumulates solutions to scientific puzzles that are neutral about questions of truth. For a critical review, see Bird (2007).

does not seem to be a good candidate for describing the aim of science. However, given that idealizations can support understanding, it is more adequate to suppose that understanding is what science aims at.

The latter is not susceptible to such worries, because, in contradistinction to knowledge, understanding is only quasi-factive: it can survive false beliefs if they are not absolutely vital to the phenomenon in question. For example, Marten hypothesized that TB was caused by “species of Animalcula or wonderfully minute living Creatures” (Doetsch, 1978; Daniel et al., 1994). Strictly taken, this is false: TB was not caused by such small creatures, but by the Mycobacterium tuberculosis bacteria, which Marten had no knowledge of. Nevertheless, it is hard to deny that some progress occurred and an increase in the (objectual) understanding of TB had been obtained.

In all, as opposed to truth or knowledge, the epistemic aim of scientific inquiry is best comprehended as understanding. Comprehending progress in terms of increased understanding dovetails more closely with the pragmatic nature of medicine and has the advantage of being resistant to some of the problems that haunt accounts that comprehend progress as knowledge accumulation. If the epistemic goal of inquiry is best framed as seeking understanding, this raises questions about what understanding is in medical research. The following sections will initially delve into theories of understanding, followed by an examination of the specific nature of understanding within the realm of medicine.

2 Forms of understanding

The debates on understanding have focused on three types of understanding: *propositional understanding* (understanding that something is the case), *explanatory understanding* (understanding why something is the case), and *objectual understanding* (understanding a particular topic or subject matter) (see e.g., Kvanvig, 2003; Hannon, 2021; Grimm, 2021).[5] In what follows, we are going to be focusing on explanatory and objectual understanding, in part because propositional understanding is often largely reducible to propositional knowledge or explanatory understanding. For example, saying “he understands that he needs to come to TB screening” could amount to the attribution of propositional knowledge (“he knows that he needs to come to TB screening”) or to explanatory understanding (“he understands why it is important for him to come to TB screening”). Of course, there are many other examples of how the term “understanding” is used. But many of them are either reducible to claims about knowledge, objectual understanding or explanatory understanding. For example, when we say that a person really understands how x works, then we are attributing to this person some degree of objectual understanding of x.

[5] Practical understanding (“understanding-how”) typically involves skillful behaviors, relies often on non-propositional knowledge, and is neither explanatory nor susceptible to Gettier-style objections (Bengson, 2017). For example, a person may lack the resources to explain the workings of a device but may understand how the device works by way of her skill to adeptly use it.

To illustrate the difference between knowledge and understanding, consider the example of TB. A student of medicine may attend a lecture on infectious diseases and come to know from a reliable source that TB is caused by Mycobacterium tuberculosis. Accepting the testimony from a reliable source and even double checking it in an encyclopedia of infectious diseases, the student gains causal knowledge. But while the student now knows a proposition that picks out the cause of TB, that is not enough for explanatory understanding, which not only requires knowledge of what caused the effect, but also grasping how that cause brings about the effect (Kvanvig, 2003; Pritchard, 2010a), which many take to involves a type of "skill" (see e.g., De Regt, 2017). Understanding does not only require the possession of a theory or model, but also the skill or ability to *use* it to discern the causal relationship involved. One way to comprehend the difference is that unless explanatory understanding about *how* cause and effect are related is attained, she will be unable to address what-if-things-had-been-different questions or predict the outcomes of potential interventions (Grimm, 2011).

For another example, consider an utterly false theory leading to correct results. Charles Locock's mid-19th century discovery of the anticonvulsant effect of potassium bromide. Locock, a physician working in London, shared the widely accepted theory among his contemporaries of a causal relationship between masturbation, convulsions, and epilepsy (Ban, 2006). As bromides were known to reduce the sex drive, Locock reasoned that the ingestion of potassium bromides would control convulsions by reducing the rate of masturbation. His account of the drug's effectiveness was published in *The Lancet* in 1857, and subsequent independent studies confirmed potassium bromide's antiepileptic efficacy, albeit evidently not by reducing masturbation frequency. Through observations and inference to the best explanation, Locock had attained *knowledge that* potassium bromide reduced convulsions, and such knowledge allowed the introduction of a relatively effective antiepileptic treatment into medical practice.

Still, in an important sense, such causal knowledge does not properly close the inquiry, which would require grasping a correct explanation and attaining *understanding* of what happens and *how* cause and effect are related. Locock did not understand why potassium bromide was effective, why it failed to be effective in some people, and so on. This meant that he lacked the ability to improve the efficiency of the intervention, since he was unable to counterfactually anticipate the effects of changes he could have made with respect to the treatment. More precisely, the lack of understanding means that Locock was unable to (i) predict the changes that would occur if the factors cited as explanatory were different and (ii) to draw correct inferences about similar situations under slightly varied conditions.

2.1 Explanatory and objectual understanding

Objectual and explanatory understanding differ in several ways (Kvanvig, 2003, 2009; Hannon, 2019, 2021). Explanatory understanding involves grasping why something is the case (e.g., uncovering the causal mechanisms or reasons behind phenomena) and its scope is less expansive than that of objectual understanding (Hannon, 2021). Objectual understanding, usually expressed using the verb "understands", followed by a noun, as in the phrase “she understands TB”, entails a comprehensive grasp of a particular topic or subject matter, which includes incorporating these causal explanations into a broader context. While explanatory understanding is often necessary, it is not sufficient for objectual understanding, which requires integrating these explanatory insights within a larger framework.

To illustrate the difference, imagine that our student has now acquired knowledge of a vast number of isolated facts about TB, such that her peers would not hesitate to say that she has knowledge about TB. Nonetheless, this would not imply that the student understands TB, which would attribute to the student a more profound penetration of TB, a sort of epistemic acquaintance that is more profound than knowing particular propositions (Kvanvig, 2003, p. 191; Strevens, 2017). Her objectual understanding of TB is gradable and can always become more profound along various dimensions (Bengson, 2017).

Often, achieving (full) objectual understanding is the aim of inquiry, and reaching it justifiably concludes the investigation of the topic (Kvanvig, 2013). If we think of medical research, objectual understanding seems to better capture the primary aim of inquiry and the conditions under which it can be concluded. To take the example of TB, researchers not only want to understand why it arises or why certain characteristic biochemical reactions occur but also why it leads to the characteristic symptoms, why it has varied effects on individuals, how it relates to other conditions, and so on. Even though single research projects cannot take on such a large task, the ultimate goal seems to go beyond obtaining explanatory understanding of features of TB to systematically *understanding TB*, which means attaining some level of coherence and completeness in terms of knowledge, as well as in taxonomies and classifications.

A prevalent perspective posits that achieving objectual understanding marks the endpoint of inquiry and legitimately closes the investigation into the subject (Kvanvig, 2013; Carter and Gordon 2014). This perspective aligns well with medicine, where an objectual understanding of a condition, rather than just its explanation, is often the ultimate aim. In their pursuit of understanding TB, researchers aim to grasp not just its origins, but also its manifestations, correlations with other conditions, its varied effects on individuals, and the most useful systematic categorization of its characteristic symptoms and signs.

Some argue that objectual understanding is not merely a subset of explanatory understanding, in part because it is possible to achieve objectual understanding of indeterministic systems where explanatory relations do not obtain (Kvanvig, 2009). But even if this turns out to be false (see e.g., Khalifa, 2013, ch. 4), maintaining this distinction conserves the intuition that when we attribute to somebody objectual understanding of a subject matter (as opposed to explanatory understanding), we imply that the agent’s epistemic commitments relevant to the subject matter form a coherent network. Also, the distinction upholds the idea that objectual understanding’s factivity requirement is more lenient, making it less susceptible to peripheral falsehoods compared to explanatory understanding (see e.g., Elgin, 2017; Bamberger, Beisbart, & Brun 2017; Kvanvig, 2009).

2.2 Grasping explanations and context-dependency

Both explanatory and objectual understanding go beyond mere knowledge by encompassing an additional cognitive achievement, often referred to as a form of "grasping" (e.g., de Regt, 2009; Strevens, 2017; Grimm, 2014; Elgin, 2017; for a critique, see Khalifa, 2013, ch. 3). The objects of grasping are "explanatory and other coherence-making relationships" (Kvanvig, 2003, p. 192). There is no clear agreement on the precise meaning of "grasping" (Hannon, 2019), but for our purposes we might conceptualize it as a form of cognitive control that agents develop through the active engagement of their epistemic agency in delineating conceptual and explanatory links. Importantly, while grasping enables agents to mentally map a relational assembly (Grimm, 2014), it is not reducible to the experience of understanding (e.g., an "aha" moment): good explanations do not necessarily trigger a sense of understanding, while inadequate explanations sometimes do (Trout, 2002). While philosophers commonly concur that what is being grasped are explanations, aligning with the notion that the primary purpose of scientific explanation is to foster understanding (Lipton, 2001), opinions differ on what kind of explanations lead to understanding, such as deductive-nomological explanations (Hempel & Oppenheim, 1948), or mechanistic explanations, which explain phenomena by specifying the mechanisms that produce them (Salmon, 1984; Machamer et al., 2000).[6]

Importantly, what counts as understanding, is – at least in a limited sense – *context-sensitive*. This can be interpreted in several ways. First, some argue that understanding is context-sensitive in the sense that the criteria for understanding can evolve even within a single scientific discipline (for historical examples, see De Regt, 2017; De Regt et al., 2009). This is in part because the capacity of an explanation to lead to understanding is partially contingent upon the disciplinary background and knowledge of individuals seeking to understand.

Second, and more importantly for our aims here, some hold that context-sensitivity is linked to the nature and aim of the particular scientific inquiry. For example, Craver (2013; Kendler et al., 2011) contends that mechanistic explanations are inherently contextual and "perspectival", as they are framed within a specific explanatory framework that is chosen based on explanatory interests. While this point may be limited to mechanistic explanations, there are indications that objectual understanding displays some context-sensitivity across scientific fields. To illustrate this with a medical example, consider the study of cholesterol metabolism in medical science and chemistry. In medical science, a significant level of objectual understanding of cholesterol metabolism arguably encompasses an understanding of how cholesterol levels are regulated (e.g., by diet, genetics) and how they can be modified through interventions or lifestyle changes to reduce the risk of disease. From the perspective of chemistry, objectual understanding of cholesterol metabolism does not necessarily relate to cardiovascular health but instead focuses on explaining the biochemical pathways of cholesterol breakdown and synthesis, elucidating the precise molecular interactions involved. Thus, what constitutes some sufficient level of objectual

[6] A mechanism is typically defined as "a structure performing a function in virtue of its component parts, component operations, and their organization" (Bechtel & Abrahamsen, 2005, p. 423).

understanding in medicine might differ from that in chemistry, primarily because the explanatory goals and interests in medicine are intrinsically tied to practical applications and clinical medicine. There is no inherent tension between context-sensitivity and objectual understanding: even if the threshold for sufficient objectual understanding can be consistent across disciplines, the kinds of explanations needed to reach this understanding vary according to the specific context and the explanatory, practical and other goals of each field.

3 Biomedical understanding

While the presented account of understanding does not purport to capture the intricacies of philosophical debates on the topic, it serves as a basis for exploring what it means to possess objectual understanding of a disease within the medical field. This will be referred to as *biomedical understanding* (see Varga, 2023, 2024). To grasp what biomedical understanding entails, let us revisit the history of TB research.

Before the 19th century, tuberculosis (TB) was thought to result from heredity or environmental causes like bad air. Marten's initial hypothesis that "minute living creatures" could spread TB was later validated by Villemin, who in 1865 provided experimental evidence of TB's transmissibility. He linked its higher incidence to crowded, inadequately ventilated environments and noted a decrease in TB cases among soldiers when they were not confined to cramped barracks (Daniel et al., 1994; Bynum, 2012). Moreover, by removing liquid from tuberculous cavities of individuals who had died of TB and injecting it into healthy animals, Villemin successfully transmitted the disease from humans to rabbits, from cows to rabbits, and from rabbits to rabbits. Throughout his studies, he used the same amount of liquid and animals of similar origin, age, and habitat conditions, such that "everything indeed other than inoculation, were identical" (Villemin 1868/2015, 257). While not all animals developed symptoms, autopsies three months later revealed that the vast majority developed extensive TB with massive dissemination of tubercles to the organs (Villemin 1868/2015; Barnes, 2000).

Clearly, Villemin's findings helped distinguish between variables that had a direct effect on the development of TB and those that were correlated with it (e.g., certain professions, poverty, poor living conditions). However, while Villemin attained an important piece of explanatory understanding, it would be unwarranted to say that he obtained objectual understanding of TB in any noteworthy sense. Given that the explanatory goals and interests in medicine are closely tied to practical applications, such a claim might seem excessive because the explanatory understanding Villemin obtained did not form a coherent network that would have allowed him to consider how possible medical interventions could limit control the progression and spread of TB. After all, Villemin did not understand under what conditions TB developed, how it transmitted, and what the agent of the disease was, except that the tubercle (nodular lesion) contained it.

Let us now look closer at some shortcomings that could have prevented him from attaining objectual understanding of TB in any substantial sense. The first shortcoming stems from an incomplete understanding of the causal agent. Villemin lacked comprehension with respect to two critical aspects of the causal connection: stability and specificity (see Woodward, 2010). A causal link between the injected substance and TB is considered stable if the counterfactual dependence remains consistent across various background situations. Villemin's studies did not provide much evidence with respect to stability, because they did not involve testing under different background circumstances. In addition, specificity refers to the grain level of counterfactual dependencies between the inoculated substance and TB. Because Villemin inoculated the same amount of substance in each case, his studies offered no knowledge about the extent to which the intensity of tuberculization depends on the amount of substance inoculated. Villemin had no way of determining whether the counterfactual dependencies between the inoculated substance and TB are fine-grained, in which case intervention on the inoculated substance would enable more precise control over how TB develops.

Moreover, Villemin's incomplete understanding of the causal agent prevented him from ruling out the possibility that experimentally induced tuberculosis might follow a different pathway from ordinary TB or could even be a distinct disease altogether. When injecting liquids from organisms that succumbed from TB, one could argue that the effects obtained were not due to TB, but to the injection containing some "cadaveric material." Although Villemin could show that the number and extent of lesions on the lungs are not correlated with the number and extent of lesions developed at the injection site, he himself noted a crucial limitation: "should we consider the entire chain of phenomena observed in experimental tuberculosis as the result of a traumatism due to inoculation? This is an enigma that we cannot resolve" (Villemin 1868/2015, 259).

The second shortcoming concerns a lack of knowledge about the relevant mechanism. The causal knowledge Villemin attained did not permit "tracing" the causal process (Steel, 2008), which would have assisted grasping coherence-making relationships and comprehending how the elements of TB are configured. This seems to necessitate some degree of explanatory understanding and discerning the mechanism that is responsible for linking cause and effect. A mechanism for phenomenon P consists of parts and processes that are structured in a way such that they are responsible for P (Glennan et al., 2021). Explanations in the biomedical sciences are most frequently mechanistic, explaining a disease by identifying the spatiotemporal structure of a mechanism that is responsible for that disease and its symptoms (Thagard, 2005; Darrason, 2018; Williamson, 2019). Villemin's study establishes a coarse-grained difference-making relationship, but it does not amount to biomedical understanding because it fails to discern the correct mechanism.

We could say that the lack of such a mechanism has crucially impacted Villemin's ability to gather sufficient evidence for explanatory understanding. There are two possibilities here, depending on which thesis one subscribes to regarding the role of mechanisms in establishing causal claims (for discussions, see Russo & Williamson, 2007; Illari, 2011; Williamson, 2019). According to a strong thesis, establishing a causal relationship requires not only difference-making evidence but also evidence of a mechanism composed by entities (such as proteins) and processes (such as protein expression) that together link cause and effect. If one accepts the strong thesis, then Villemin has not met the criteria for establishing a causal relationship because he had no knowledge of the mechanism. According to a weaker thesis, difference-making can serve as evidence for a causal relationship. However, evidence of a mechanism, combined with difference-making evidence, significantly increases certainty that the observed correlation is not merely spurious and that the effect can be attributed to the experimental intervention rather than to confounding variables.

Having examined these two shortcomings, it appears likely that each has contributed to the failure to attain objectual understanding. However, it is unclear whether any of these factors are essential for achieving objectual understanding. In the sections that follow, we will explore the historical development of tuberculosis research to further investigate this issue.

3.1 Koch and beyond

A significant breakthrough with respect to the first two shortcomings came with Robert Koch's 1882 discovery of the bacterium Mycobacterium tuberculosis (MTB) as the causative agent of TB (Keshavjee & Farmer, 2012).[7] Koch formalized a set of "postulates" for establishing causation, which required (a) coincidence of bacteria and disease, (b) isolation of bacteria in a pure culture, and (c) induction of disease by inoculation with bacteria from pure culture. As to (a), Koch was able to show that the MTB were always present in TB (but not in normal states), that they preceded tubercle formation, and that their number covaried with TB being progressive or quiescent. As to (b), Koch managed to isolate individual colonies of MTB in pure culture that allowed studying their growth characteristics. As to (c), he inoculated animals with MTB obtained from various origins (induced disease, spontaneous disease, and artificial culture). Koch found that injections led to the formation of tubercles with similar characteristics, and the number of tubercles corresponded to the amount of the inoculum used (Blevins & Bronze, 2010).

While Koch's postulates can be interpreted in various ways (e.g., Broadbent, 2009), some have argued that Koch's experimental distinction of causal from correlational relationships are best captured by the interventionist account of causation (Ross & Woodward, 2016). Interventionism posits that causal relationships are those that can be potentially harnessed for manipulation and control: very roughly, if intervening on C reliably leads to changes in E, then C is the cause of E. Woodward (2003) outlines the necessary and sufficient criteria for establishing causation as follows: C causes E if and only if (i) there is some possible intervention on C such that (ii) were this intervention to occur, there would be an association or correlation between C and E. The account highlights idealized experimental intervention as appropriate for the purposes of determining whether C causes E, as it eliminates possibility of confounding. As the induced change is not correlated with potential confounders, the presence of a correlation between C and E upon intervention on C means that C has a causal influence on E.

Interventionism fits Koch's postulates, particularly his emphasis on (c), i.e., the induction of disease into a healthy animal by inoculation with bacteria from pure culture. In fact, Koch clearly maintains that determining causality between MTB and

[7] For his research, Koch earned the Nobel Prize in 1905.

TB “can only be decided by inoculating pure bacilli,” thus step (c) (quoted in Ross & Woodward, 2016, p. 44).[8] Of course, (b) can be seen as a procedure to ensure that (c) obtains the characteristics of a proper intervention: it excludes the possibility that confounding factors are contained in the inoculated material. Causal claims can only be established if the intervention is associated with a change in the incidence of TB (e.g., its presence, absence, rate of occurrence). In accordance with (M), if the inoculation of substances had not led to the occurrence of disease, Koch would not have identified them as the cause of the disease.

Although the discovery of the causal agent addressed the first shortcoming in Villemin’s research, it alone was insufficient to resolve the second shortcoming concerning the mechanism. However, this is clearly a significant issue, in part because it connects with important questions from a clinical perspective. Without an understanding of the mechanism, questions about what holds together the symptoms of TB, whether certain characteristics (e.g., diarrhea) are parts of TB or caused by TB, how MTB is disseminated to other organs, why most individuals with latent infection do not develop the disease, cannot be answered.

3.2 Twentieth-century discoveries

In the twentieth century, a notable breakthrough came with the identification of the mechanism through which MTB interacts intricately with the host’s immune system, leading to TB. Roughly, when MTB reaches the lungs, it is taken up by macrophages, which are immune cells that engulf and destroy foreign particles. However, MTB is able to survive and replicate within the macrophages, which leads to the formation of granulomas that surround the infected macrophages to contain the infection. MTB is sometimes able to resist destruction and containment, eventually causing the macrophages to burst and release more bacteria into the surrounding tissue. The infected tissue becomes inflamed, leading to the formation of the characteristic lesions, or granulomas, in the lungs and other organs. The granulomas can restrict the infection, leading to a latent TB infection, or they can break down, releasing MTB into the lungs, where it can be coughed up and spread to others (for reviews, see Delogu et al., 2013; Yan et al., 2022).

The mechanism was elucidated over several decades through the significant contributions of numerous researchers. Therefore, it is challenging to pinpoint exactly when and by which researchers a threshold was crossed, marking a stage at which we may speak of researchers having attained objectual understanding of TB. However, once a mechanistic explanation became available that referenced the configuration and activities of component entities, and identified both the normal functioning of macrophages and how MTB disrupts this process, it seems quite intuitive to say that researchers had achieved a significant level of objectual, biomedical understanding of TB. Researchers have progressed beyond merely explaining various aspects of TB; they have crossed a threshold into systematically, objectually *understanding TB*.

[8] It makes sense to think that had Koch adhered to a view of causation as merely regularities involving necessary and sufficient conditions that could be discerned through observation, he would not have emphasized (c).

Of course, while this assertion may seem intuitively appealing, it alone raises a crucial question: what is it about mechanistic explanations that renders them necessary for achieving a significant level of objectual understanding? In what follows, the aim will be to show that mechanistic explanations have enabled achieving a level of coherence and integration, offering clear potential to refine theoretical frameworks and clinical practices, and to facilitate the development of more comprehensive taxonomies and classifications. But before doing so, it is worth emphasizing that a sufficient level of objectual biomedical understanding of TB has been achieved, not merely by grasping the relevant mechanistic explanations, but also by integrating this with other pieces of knowledge and understanding already obtained.

For this, we may start by noting how a mechanistic explanation not only overcomes the second shortcoming observed in the research of Villemin and Koch but also enables new insights that carry profound implications for diagnosis, treatment, and prevention strategies, directly affecting patient care and public health initiatives. This underscores an earlier argument that what constitutes a sufficient level of objectual understanding in medicine is context-sensitive and closely linked to a practical orientation. Let us now review a couple of important implications for research and clinical settings.

First, grasping the relevant mechanistic explanation, researchers were able to chart a much more fine-grained intricate web of counterfactual dependencies, which paves the road towards enhanced intervention possibilities concerning TB. Researchers can formulate new hypotheses around potential interventions, such as enhancing the macrophages' capability to eradicate MTB or inhibiting MTB's ability to prevent acidification within macrophages (for a review of current research, see e.g., Bo et al., 2023).

Second, comprehending the mechanism significantly enhances the ability to interpret and address a range of clinically relevant issues. It provides a unified view of TB, clarifying how its various elements are interrelated, and explaining how seemingly disparate symptoms are interconnected through a common cause. This comprehensive insight into the relationships between TB symptoms and the disease process improves diagnostic accuracy and aids in refining diagnostic criteria. It enables healthcare providers to more effectively differentiate TB from other conditions with similar symptoms, thereby reducing the risk of misdiagnosis. Moreover, this understanding is crucial in explaining why some individuals with latent TB infections do not progress to active disease, a key factor in managing public health risks.

Overall, comprehending the mechanism of TB has facilitated a significant milestone, crossing a threshold into what we may describe as an objectual, biomedical understanding of TB. This had key implications for identifying new treatment targets, enhancing diagnostic methods, and deepening our knowledge of disease transmission and resistance mechanisms—all of which are vital for improving clinical interventions and formulating effective public health strategies. Crossing this threshold is an important milestone, but it is entirely consistent with recognizing that further exploration and deeper understanding may still be necessary. It does not in any way imply that researchers have reached a final stage in their inquiry that would conclude investigation into TB. Indeed, as researcher recognize, many questions remain (for a recent review, see e.g., Bloom, 2023; WHO, 2023), driving increasingly detailed and nuanced insights to continuously refine existing approaches to treatment and prevention.

4 Concluding remarks

In light of the recent calls to reexamine the foundational aims of medicine, both in research and clinical practice, this paper emphasizes the importance of understanding as a unifying aim in these domains. As underscored by recent editorials cited in the introduction, there is an imperative to revisit not only the practical aims that medicine seeks, but also its epistemic aims. This is particularly salient in a time when the very essence of what constitutes medical science and clinical medicine is under scrutiny. Accordingly, this paper concentrated on the relevant epistemic aims. By exploring different forms of understanding, the paper uses TB as a focal point to argue that a grasp of mechanistic explanations is crucial for reaching a threshold of understanding at which we may speak of an objectual understanding of TB.

An important limitation of this paper is its focus on a single case: TB. Consequently, there are notable constraints on the breadth of conclusions that can be drawn. However, there are at least some reasons to believe that the findings may have broader applicability. One such reason is that an earlier study on noncommunicable diseases (Varga, 2023) have reached similar conclusion. That study revealed that in the case of scurvy, a mechanistic explanation of the condition is necessary for biomedical understanding, but this is not sufficient for understanding in a clinical setting. This earlier study, which examined an emblematic noncommunicable disease, reached a similar conclusion to the current study that focuses on a representative communicable disease. This suggests a potential pattern across various contexts of biomedical research. That said, additional research is required to reinforce this point by investigating whether these conclusions are applicable across a wide spectrum of diseases, including those that are rarer and less prominent. Additionally, it is worth noting that this might differ significantly for conditions where mechanistic explanations have proven challenging to establish. Mental disorders could serve as critical test cases to explore the applicability of our findings in contexts where the underlying mechanisms are less understood.

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