Exploring the Interconnected Complexities of COVID-19

Exploring the Interconnected Complexities of COVID-19

By

Keekok Lee

Cambridge Scholars Publishing

Exploring the Interconnected Complexities of COVID-19

By Keekok Lee

This book first published 2023

Cambridge Scholars Publishing

Lady Stephenson Library, Newcastle upon Tyne, NE6 2PA, UK

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

ISBN (10): 1-5275-2532-5
ISBN (13): 978-1-5275-2532-0

CONTENTS

ACKNOWLEDGEMENTS

I would like to thank Anthony Leggett for his insightful comments and suggestions for improvement. Flaws still remain, and I am sure that many do; however, they are entirely my own responsibility.

Professor Leggett has also kindly agreed to write a Forward for the book, for which many thanks yet again.

FOREWORD

ANTHONY J. LEGGETT

In this slim and unpretentious volume, the author deploys her encyclopaedic knowledge of Chinese and Western traditions in both philosophy and medicine to place the history of the COVID-19 pandemic and efforts to combat it in a wider philosophical and sociological context. In particular she emphasizes the contrast between the more "clinical" and individualistic approach of most Western nations with the more "epidemiological" and communitarian attitudes adopted in most of the East Asian cultural sphere.

Whether or not they agree with her conclusions, readers will acquire a refreshingly different perspective on the pandemic from that which they are liable to pick up from much of the Anglo-Saxon media.

CHAPTER 1

LAYING OUT THE INTERCONNECTED THEMES FOR EXPLORATION

This book necessarily crosses disciplines as it is primarily an exploration of COVID-19 as epidemic and pandemic from the vantage point of the philosophy of disease/illness. Philosophy of medicine, thus conceived, necessarily covers the Humanities, the Social Sciences, the Life Sciences and the Health Sciences.

A lot is now known of the science of the disease, known as COVID-19, since its first appearance just over three years ago. The World Health Organisation/WHO as well as the *Lancet* have published their reports on it. What has not been done is a systematic attempt to analyse the phenomenon from the standpoint of the philosophy of disease/illness as it affects individuals and society. To do justice to the scope of the information and data, this philosophy of disease/illness must address itself not only to the issues arising from the natural sciences, such as biology, genetics, bacteriology, clinical medicine, epidemiology but must also concern itself with those arising from the social sciences, such as economics, sociology, politics, geopolitics. This means that the different strategies of coping with the epidemic/pandemic must also be contextualised in terms of the "ideological" differences between cultures and societies. In other words, the nature of a disease/illness such as COVID-19 must be understood not only in terms of objective/scientific facts but also in the inescapably value-ladenness of medicine itself, especially in a pandemic. One needs also to explore a core issue, the competing causal models. Two are identified – one which is monofactorial and where the causal arrow is unidirectional, while the other is multifactorial and where the causal arrow is bidirectional. These two models underpin respectively, by and large, the two main domains of modern medicine, Clinical Medicine and Epidemiology. Exploring them would enable one to unravel some of the complexities behind COVID-19.

This book, in the first instance, attempts to explore the nature of COVID-19 through posing the following questions:

1. What could be said to be the cause of the illness?

2. Who is likely to be infected?
3. Where is infection likely to take place?
4. When is infection likely to occur?

It will demonstrate that the four Ws listed above are interconnected (IC); that interconnectedness may be summed up as the 4**W**s+IC formula. In turn, it will show that these themes are the very ones which preoccupy biomedicine today under its two main domains of investigation, namely, Clinical Medicine and Epidemiology. However, Epidemiology is standardly portrayed as "substandard" while Clinical Medicine is put on a pedestal marked "superior" and "methodologically impeccable/privileged". [1] The book aims to challenge this standard assessment of the two domains. Indeed, it argues that the causal model underlying Clinical Medicine (standardly theorised) is too simplistic and that which underpins Epidemiology is more adequate to account for medical data and evidence, across the board. In other words, Epidemiology, far from being the "pariah" should, instead, be the standard-bearer of "scientificity" in all domains of Medical Thinking. The notion of vaccines will be explored to further bring out the interconnectivity between the two domains of Clinical Medicine on the one hand and Epidemiology on the other. It will argue that Epidemiological Thinking is Ecosystem Thinking and that Ecosystem-nesting is an appropriate analytical tool to shed light on all domains of medicine. This way of looking puts paid to the Monogenic Conception of Disease which has, since its inception in the 1890s, over roughly seven decades, powerfully impacted Clinical Medicine. (See Chapter 2.)

Furthermore, the book will excavate and bring to light the values underpinning all the themes to be examined, especially with regard to how different countries/cultures respond to COVID-19. It will use mask-wearing as a case study to explore some of these differences in the core values embedded in two prominent yet different cultural/philosophical traditions in the world, namely, the modern Western (since the seventeenth century)

[1] This disparity has remarkably been commented upon by Mahbubani 2022. Mahbubani is a retired Singapore diplomat and now a renowned scholar of geopolitics. However, he has put his finger on the right spot in his comments on the COVID-19 pandemic, one of which reads: "The second way was to focus on biomedicine, with its focus on individual behavior, instead of social medicine. But understanding individual behavior is not enough to counter epidemics like COVID -19 that spread faster if we don't take care of social conditions." (Mahbubani, 2022, 248)

on the one hand and the Chinese on the other (often said to be at least three thousand years old). [2]

Chapter 2 (**The Cause of COVID-19 is SARS-CoV-2, or Is It?**) examines the following issues:

(a) Why it appears so "natural" to pick on the virus, SARS-CoV-2 as the cause of COVID-19. Can this ease be explained simply in terms of the historical contributions of medical giants such as Pasteur and Koch, under whose impetus the Monogenic Conception of Disease was formulated?
(b) It looks at the phenomenon of infected people who are asymptomatic to see if the Monogenic Conception of Disease could do justice to it. This phenomenon occurs in other cases of infectious diseases such as peptic ulcer disease, even though the infectious agent in this case is not a virus, but a bacterium, *H. pylori*.
(c) In other words, to pose the question: What could be said to be the relevant set of causal factors of COVID-19 or of peptic ulcer disease? [3] is more appropriate than posing the more simplistic question: What is the cause of COVID-19 or of peptic ulcer disease?

Chapter 3 (**Who Manifests a Disease? A Cut-and-Dry Matter?**) continues to test the validity of the Monogenic Conception of Disease by investigating how well it might fare in another context of disease-generation, when the relevant item is said to be a gene. It is tested against the disease called Phenylketonuria, said to be caused by a single defective gene. The conclusion of this exploration confirms the design flaw of the Monogenic Conception of Disease. Phenylketonuria is adequately diagnosed and treated by acknowledging the relevance both of the defective gene and a set of adverse environmental factors, that the one without the other would fail to bring on the disease. In other words, the **W**ho question, like the **W**hat question is adequately answered only in terms of the complex relationships between a factor studied in labs under Clinical Medicine as well as certain relevant factors in the environment studied by Epidemiology.

Chapter 4 (**Spatial-temporal Aspects of Disease-generation: The Where and When Questions**) tests the Monogenic Conception of Disease yet again, this time in the context of the **W**here question, to show that the flaw of the conception lies in ignoring the kind of issues raised by it. The **W**here question brings to the fore the relevance of Epidemiology to the

[2] While the Western tradition is traced back to ancient Greece, the Chinese is usually taken to be represented by the ethical thinking of Confucius (c 551 – c 479 BCE).
[3] See Mackie, 1965, 245-65; also, Chapter 5 of this book.

understanding of disease-generation and disease-transmission of a pathogenic virus, like SARS-CoV-2. At the same time, it also acknowledges the contribution of Clinical Medicine in understanding the transmission of a disease like COVID-19. In other words, it is through the joint effort of Clinical Medicine and Epidemiology that we can hope to understand and control the disease. This chapter, therefore, may also be understood as an attempt to answer the **W**hen question – a disease will become an epidemic and/or a pandemic when the relevant causal conditions happen to obtain within a certain segment(s) of the population, such as the elderly especially those with co-morbidities who are also vaccine-hesitant.

Chapters 2, 3 and 4 can be said to be dedicated to exploring the Monogenic Conception of Disease for two reasons: (a) from the standpoint of the history of medicine, given its powerful impact on Clinical Medicine for several decades (1876-1968), to show where its limitations lie in the context of the SARS-CoV-2/COVID-19 epidemic/pandemic and (b) also thereby, to challenge the orthodox understanding between Clinical Medicine (deemed superior) on the one hand and Epidemiology (deemed inferior) on the other. Furthermore, the book makes a distinction (in these chapters and throughout the book) between two versions of the Monogenic Conception of Disease: it calls one the Classical Version (or the non-dogmatic version) and the other, the dogmatic version.[4] It argues that Robert Koch, an acknowledged pioneer of the Age of Bacteriology failed to make such a distinction unambiguously, thereby muddying the waters.

The clarification of these matters then permits the book to move on to the next chapter. Chapter 5 (**"The Cause" in Terms of Controllability and Preventability**) examines Collingwood's Sense II of Cause, which singles out as "the cause" a factor in Mackie's account (as explored in Chapter 2) in terms of what he calls the "inus conditions". While Mackie's account is relevant to an explanatory context of disease/illness, Collingwood's is pertinent to the practical context of controlling a disease in the population. As such it cuts across the Clinical Medicine-Epidemiology divide, as an effective measure could either be a pharmaceutical (Clinical Medicine) or a non-pharmaceutical (Epidemiological) intervention.

Chapter 6 (**COVID-19, Vaccines and Vaccination: What they teach us about the nature of Medicine, Illness and Society**) in elaboration with

[4] The dates mentioned – 1876 to 1968 – are chosen for the following reasons: Koch's first pronouncement on the germ theory occurred in a paper he delivered in 1876. As we shall see, Stewart 1968 published in *The Lancet* his view that the germ theory had by 1968 (90 years after its first pronouncement) become a dogma. The critique of the Monogenic Conception of Disease undertaken in this book is, indeed, from the vantage point that it might have assumed the status of a dogma.

Chapter 5 focusses on the concept of vaccines and vaccination in order to further demonstrate that the Clinical Medicine-Epidemiology divide is unsustainable and flawed, as it is unintelligible when contextualised in either domain alone. The nature of medicine/disease/illness must be understood as being situated within society in general, and more, specifically within the different strata or classes into which society is divided. By so doing, it also challenges the highest level of probity bestowed on Clinical Medicine at the expense of Epidemiology which is considered to play the role of "Cinderella" to it as Epidemiology, given its nature, is incapable of satisfying the methodological requirements of the Randomised Controlled Trial.

Chapter 7 (**Ecosystem Thinking is Epidemiological Thinking Which is Medical Thinking**) explores in some detail the concept of Ecosystem Thinking, advanced by the author, in terms of Ecosystem-nesting in order to bring out clearly the Wholist [5] orientation of Medical Thinking in all domains. The concept of Ecosystem Thinking is advocated as an appropriate analytical research tool which can also be used outside the sphere of medicine, as it is primarily a version of Systems Thinking.

Chapter 8 (**COVID-19 and Mask-wearing: In the Context of Geopolitical and Other Values**) focusses, in the main, on mask-wearing in order to explore COVID-19 in the context of geopolitics. It explores the values embedded in the ideology of the West, as instantiated by the USA on the one hand and on the other, that of China. It proposes a spectrum with High Individualism/HI (the US) at one end and Low Individualism/LI (China) at the other. This in turn raises the issue of the relationship between Classical Liberalism with High Individualism on the one hand and Low Individualism, on the other, with some surprising conclusions. It also leaves space to discuss the relationship between self and other(s) respectively under the two versions of Individualism.

The chapter also looks briefly at another epidemiological measure which has been highly criticised by High Individualism – it is the lockdown. It shows yet again that in contrast to the high individualist vantage point, the non-pharmaceutical strategy of controlling COVID-19 via the lockdown is perfectly compatible with Low Individualism or even more strongly could be shown to be derived from its metaphysics of Wholism within which philosophical framework Epidemiological Thinking is embedded.

Chapter 9 (**Conclusion: Interconnectedness and Wholism**) maintains that the book has established, in the main, the following theses:

---

[5] This author prefers to use "Wholist" and "Wholism" instead of the more usual "Holism" for the obvious reason that the former terms make it clear that they are semantically linked with the term "whole". They also capture the ontological status of the concept behind the words better than "Holism".

(a) The Monogenic Conception of Disease (held as dogma) is tested in the context of the SARS-CoV-2/COVID-19 epidemic and pandemic of the last three or so years and found to be untenable yet again. This conclusion shows the need to distinguish the Classical Version of the Monogenic Conception of Disease from the version which holds it as dogma.
(b) The causal model in Medical Thinking is not monofactorial and unidirectional but multifactorial and reciprocal/bidirectional (with feedback mechanisms.
(c) It looks at Mackie's analysis of cause in terms of "inus conditions" as well as Collingwood's in terms of controllability or preventability in order to show where their respective insights lie.
(d) The above if correct would undermine the usual division in biomedicine into two domains, Clinical Medicine and Epidemiology, with the latter perceived as "inferior" to the former, as Epidemiology cannot satisfy certain evidential and methodological requirements that the former is capable of doing.
(e) The concept of vaccines and vaccination is explored to show that it cannot be properly grasped unless understood as having a foot in either of these two domains.
(f) The concept of Ecosystem Thinking in terms of Ecosystem-nesting is a more comprehensive research analytical tool to grasp both Clinical Medicine and Epidemiology within a single philosophical-causal framework. Such a framework can do better justice to the complex interconnectedness of the four leading questions which this book has called the 4**W**s+IC formula, that is to say, in the generation of disease/illness in society, there are four interrelated aspects to be explored, namely, the **W**hat, **W**ho, **W**hen and **W**here dimensions.
(g) Ecosystem Thinking/Ecosystem-nesting also brings out clearly the value-ladenness of all forms of Medical Thinking including geopolitical values in a pandemic such as COVID-19.
(h) In addition, it briefly explores the concept of Wholism, its emphasis on the interconnectedness of its constituent parts thereby giving rise to properties which are more than the sum of the properties of its parts, as well as its underlying values which underpin Epidemiological Thinking as Medical Thinking.

CHAPTER 2

THE CAUSE OF COVID-19 IS SARS-COV-2, OR IS IT?

This chapter examines the following issues:

1. Why does it appear so "natural" to pick on the virus, SARS-CoV-2 as the cause of COVID-19?
2. Can this ease be explained simply in terms of the historical contributions of medical giants such as Pasteur and Koch, under whose impetus the Monogenic Conception of Disease was formulated?
3. Is there an alternative viable criterion of selecting a set of several relevant variables as "the cause" of a disease/an illness?
4. In other words, this chapter is an attempt to answer the **W**hat question by arguing that to pose the question: What could be said to be the relevant set of causal factors of COVID-19? is more appropriate than posing the simplistic question: What is the cause of COVID 19? and to answer it in terms of SARS-CoV-2.

The Monogenic Conception of Disease

The Monogenic Conception of Disease is based on the pioneering work of two giants, Louis Pasteur (1822-1895) and Robert Koch (1843-1910) which ushered in modern Western medicine, today called biomedicine, or more specifically the prestigious branch of it called Clinical Medicine. The conception of disease replaced the ancient paradigm of the Four Humours handed down by Ancient Greek culture.[1] Pasteur's work on microbiology

[1] Humours in this context refer to bodily fluids (blood, yellow bile, black bile and phlegm) whose exact combination determined a person's temperament, with illnesses emerging when an imbalance occurred, either when the humours were said to be in excess or in deficit. They were cosmologically linked to the stars and planets, to seasonal changes, to different stages of a person's life and so on. Other theories of disease causation down the ages included the wrath of supernatural entities such as gods, configuration of the stars or miasmas.

put the last nail in the coffin of spontaneous generation by showing that it was pathogenic micro-organisms which caused damage to the silk, wine and milk industries. We owe pasteurised milk to him. He not only uncovered harmful bacteria but also harmful viruses as well – the germ theory of disease in the new "Age of Bacteriology" marked the watershed between scientific and pre-scientific or pseudo-scientific medicine. He also pioneered vaccination, developing a vaccine against rabies, a deadly disease caused by a virus in the saliva of dogs infected by it. He played the lead role introducing the concept of the Monogenic Conception of Disease which simplistically put, says: one cause/germ (bacteria), one disease, although he left it to Koch to complete the task of filling out this grand pronouncement.

Koch did it in 1876 in a paper about his findings on anthrax presented to members of the Botanical Institute in Breslau: "each disease is caused by one particular microbe – and by one alone. Only an anthrax microbe causes anthrax; only a typhoid microbe can cause typhoid fever" (Evans,1993, 20). It is the fulfilment of a long-cherished dream: "the final hope and aim of medical science is the establishment of monogenic disease entities" (Taylor, 1979, 21).[2]

This version of the Monogenic Conception of Disease as introduced by Pasteur and adopted by Koch as just set out above may be referred to as the Classical Version or the non-dogmatic version, as it serves to mark the establishment of a new paradigm of scientificity in Medical Thinking, abandoning older paradigms such as that of the Humours, the wrath of the gods and others for the Modern paradigm of micro-organisms as the relevant pathogenic variable.

However, in an attempt to clarify the new paradigm, Koch in 1890 embellished it with a set of methodological rules/guidelines to determine the cause of any particular disease which came to called either the Koch or the Henle-Koch postulates. They are:[3]

---

[2] The Monogenic Conception of Disease has also been used to pick out as causal agent, not only bacteria or viruses but also fungus (such as ringworm), parasite (such as Plasmodium which causes malaria), prion (misfolded protein which can cause Creutzfeldt-Jakob disease, a neurodegenerative disease), and genes (especially in the case of rare single-gene disorders, such as Down Syndrome). This larger conception of the Monogenic Conception of Disease which has evolved since Koch will be further explored in the next chapter, Chapter 3 when phenylketonuria attributed to a single defective gene will be critically examined.

[3] As presented by Cohen, 2017. See also Lee, 2012, Chapters 9 and 10.

1 The bacteria be present in every case of the disease and under circumstances which can account for the pathological changes and clinical course of the disease.
2 The parasite occurs in no other disease as a fortuitous and non-pathogenic parasite.
3 After being fully isolated from the body and repeatedly grown in pure culture, the parasite can induce disease anew.
4 The parasite can be re-isolated from an experimentally inoculated host.[4]

By so doing, Koch appeared to depart from the Monogenic Conception of Disease in its Classical Version (or its non-dogmatic version) and to transform it into a dogma. This is because, ironically, Koch realised that he could not carry out the Postulates as specified. For example, after he discovered the presence of the cholera bacteria in cholera sufferers in India as well as in the water tanks from which the victims had drawn their water, he injected the bacteria into animals rather than human beings for obvious ethical reasons. Yet, they remained stubbornly healthy (thereby falsifying Postulate 3). He also found that some people who carried the cholera germ also stubbornly showed no sign of the symptoms of cholera (thereby undermining Postulate 1 which as he had formulated it, which is misleadingly too wide). Strictly speaking, his findings had undermined two of his own postulates. This meant that the Monogenic Conception of Disease had already run into problems even as it was being launched to great acclaim.

However, can one salvage Postulate 1 in some way, by re-interpreting it as simply claiming that a factor/variable is a necessary condition of the disease and not as Koch maintained that it be "universal and necessary"? [5] In other words, in its absence the disease would not occur but its presence is not on its own sufficient to bring it about. If the concept of cause is to be understood in terms of necessary condition only, it would be a weak conception. A more robust conception would demand that the factor/ variable be both necessary and sufficient. However, Koch's own experiments had indicated that no single condition could function as both a necessary and sufficient condition for the occurrence of cholera, as he had also discovered that some people who were bearers of the cholera bacteria were asymptomatic – some other factor or factors must, therefore, be present before these bearers of the germ would develop the disease called cholera.

[4] The fourth postulate was added by later writers. See also Evans 1976 for a revised and revamped version.
[5] See Carter, 2003, 1.

However, in spite of such flaws in Koch's reasoning, he was awarded the Nobel Prize for Medicine in 1905. A caveat must straightaway be entered. These remarks are not intended to challenge the claim that Koch (together with Pasteur) founded the germ theory of disease, a radical discovery which had far-reaching consequences for human health world-wide. Instances include the following: in 1908 the germ for polio was found to be a certain virus which led eventually to the emergence of the polio vaccine in 1958; the chance discovery of penicillin by Fleming in 1928 led to the mass production of antibiotics, post-WWll, making antibiotics the standard treatment against (bacterial) infection in Clinical Medicine. Undoubtedly, many lives have been saved and will continue to be saved in spite of the resistance to antibiotics in some cases owing to the excessive use over time of such a "magic bullet". These remarks are directed at Koch's somewhat simplistic grasp of the notion of cause in medicine, especially with the wisdom of hindsight. It is to draw attention to the difference between the Monogenic Conception of Disease held in its Classical Version (not as a dogma) and when it came to be held as a dogma.

Just as some people infected with the cholera bacterium were asymptomatic, the same holds true in the case of the coronavirus SARS-CoV-2 where some infected people are also asymptomatic. This was grasped early on in the SARS-CoV-2/COVID-19 pandemic. In the UK, towards the end of January 2020 even before the first COVID-19 case was confirmed in the country, SAGE (Scientific Advisory Group for Emergencies) warned the government that asymptomatic transmission could not be ruled out. In early to mid-February 2020, a cruise ship called the Diamond Princess had quarantined its 3,711 passengers and crew when they found 712 (19.2%) infected cases, of which 410 (331/46.5%) who tested positive, nevertheless, remained asymptomatic. On 21st February 2020, *The Journal of the American Medical Association*/*JAMA* published a paper by Chinese scientists about asymptomatic transmission of COVID-19 (see Bai, Yao, Wei, *et al*. 2020, 1406-1407). There is also evidence for presymptomatic transmission. [6] The existence of asymptomatic as well as presymptomatic cases could mean that transmission might go undetected and hence the disease could spread more widely.

[6] The term "asymptomatic" should be strictly confined to those who never develop symptoms; in this sense, we can identify who are asymptomatic only in retrospect. "Presymptomatic" should be reserved for those people who show no symptoms when they get a positive test result but who eventually develop the symptoms. In the case of SARS-CoV-2, one must wait approximately 14 days before determining whether symptoms have developed. For evidence of presymptomatic transmission, see: Accessed January 25, 2023. https://pubmed.ncbi.nlm.nih.gov/32767657/ .

In other words, the existence of asymptomatic cases should alert medical scientists to the plausible criticism that the model of causation in infectious disease could not be that endorsed by the Monogenic Conception of Disease (held as dogma) as it is too simplistic. The issue about what model of causation could be said to be more adequate is mentioned now but not pursued as its detailed exploration will take place in later chapters (from Chapter 5 onwards). Instead, one focusses, here, on testing the conception against the discovery of another pathogen, this time a bacterium, in the case of *Helicobacter pylori* by Barry Marshall (physician) and Robert Warren (pathologist) in 2005 as the cause of peptic ulcer disease, a discovery which overturned the extant explanation in terms of stress, spicy foods and/or too much acid in the stomach. In this context, the discovery amounts to the Classical Version of the Monogenic Conception of Disease.

However, to go beyond the enunciation of it as the Classical Version could be misleading and runs into the danger of adhering to the Monogenic Conception of Disease as dogma. Let us pose the question: Is *H. pylori* a sufficient condition of peptic ulcer? To say, that it is, entails that every person (ascertained by the usual means such as through endoscopy) who has *H. pylori* in the stomach would have the disease called peptic ulcer disease whose symptoms include the following: belching, feeling pain, sick, vomiting, sometimes bleeding via vomiting blood or passing blood in bowel movements. What does medical data in fact show? It shows that 90% of people known to have *H. pylori* infection do not develop gastritis or peptic ulcers. Only 10% do. As a matter of fact, roughly 80% of the world's population harbours *H. pylori* of which only 10% have the disease. In other words, large numbers are asymptomatic. To say that the factor X (the cause) is a sufficient condition for Y (the effect) is to say that the occurrence of X guarantees the occurrence of Y. However, we have just shown that the presence of X (*H. pylori*) fails invariably to guarantee Y (the effect/peptic ulcer disease).

If not a sufficient condition, is it, then, a necessary condition? It appears not. First, let us distinguish between the sufferers in two very different contexts: (a) 90% of peptic ulcer disease in the world are caused by *H. pylori* infection – sufferers in developing countries are, in the main, caused by such infection; (b) however, this leaves 10% of sufferers, living primarily in the developed world whose disease is not caused by *H. pylori* infection. Their ulcers are caused by excessive use of NSAIDs (non-steroidal anti-inflammatory drugs such as aspirin, ibuprofen, naproxen sodium). About 30 per cent of regular NSAID users have one or more ulcers. It follows that the peptic ulcer disease can occur even in the absence of the putative cause, *H. pylori*.

If above criticism is plausible, that *H. pylori* is neither a necessary nor a sufficient condition of peptic ulcer disease, then the Monogenic Conception of Disease is severely undermined, not only more than a hundred years ago when Koch singled out the cholera bacterium, as the cause of cholera but also about two decades ago when adherence to the Monogenic Conception of Disease (held beyond the Classical Version) seems to have failed yet again to obtain in the causal relation between peptic ulcer disease and *H. Pylori.*

Mackie, 1974, exploring the notion of cause in the explanatory/ scientific context argues that no factor should be singled out as "the cause" as each of several relevant factors identified, taken on its own, is neither necessary nor sufficient, although each is a necessary component of this particular complex. In other words, all identified factors form a complex set of "inus conditions". For instance, should we wish to explain why a person exposed to SARS-CoV-2 succumbs to COVID-19, we may find a set of relevant conditions such as the person's age, health-status (any co-morbidities), past illnesses (which may have lingering effects), place and kind of employment, lifestyle characteristics such as diet, and so forth. Of course, in any one case of infection, not all of these conditions would obtain but it is certainly the case as indicated by the data that any one case of infection would involve one or more of such factors apart from exposure to and infection by SARS-CoV-2. According to Mackie, "inus" stands for "an insufficient but necessary part of an unnecessary but sufficient complex".

Take this example from Wulff 1984, 169-177 to illustrate what could be meant by "inus conditions". A male patient presents himself with a stiff neck and a high temperature. The doctors put him through certain diagnostic tests from the results of which, they diagnosed meningitis as his spinal fluid contained pneumococci. His records showed that he had no spleen as it had been removed [7] following an accident earlier on in his life and that he had not been vaccinated against pneumococcal infections. What then is "the cause" of his meningitis should we follow the Monogenic Conception of Disease (beyond its Classical Version)? The removal of the spleen? or the failure to vaccinate him against pneumococcal infections following the splenectomy? Or is it the pneumococci in his spinal fluid? Strictly speaking, adherence to the Monogenic Conception of Disease permits one in logic to opt for one of the three mentioned factors, namely, the pneumococci in the patient's spinal fluid. The important point to grasp is that each of these three conditions, on its own, is neither necessary nor sufficient for the patient's

[7] People whose spleen has been removed are prone to an increased incidence of pneumococcal infections as well as to other sorts of infection such as sepsis.

suffering from meningitis. All three factors in combination cause the meningitis – this complex set of relevant factors constituted a set of "inus conditions" of the patient's meningitis. To labour the point, each of the said variables occurring in the set of "inus conditions", on its own, is neither a necessary nor a sufficient condition of the meningitis diagnosed in the patient.

The Henle-Koch postulates were formulated in the 1890s and a lot of water has passed under the bridge of what today we call biomedicine. As Cohen 2017 puts it:

> Koch's postulates were invaluable at the time they were developed and remain largely valid for a relatively small number of defined circumstances in which bacteria can be precisely tied to the cause of a particular clinical syndrome. But in a world in which virus cause cancer and noncultivable bacteria can be demonstrated by molecular probes, Koch's postulates are no longer fit for purpose. … Their main purpose now is to provide a framework to ensure that scientific rigor is applied when proposing an organism as the cause of a disease – exactly as Koch intended when he first conceived them.

Stewart 1968 (already mentioned in the last chapter) has put the point well – that the conception has become a dogma. He wrote:

> The germ theory of disease – infectious disease is generally caused by transmission of an organism from one host to another – is a gross oversimplification. It accords with the basic facts that infection without an organism is impossible and that transmissible organisms can cause disease; but it does not explain the exceptions and anomalies. The germ theory has become a dogma because it neglects the many other factors which have a part to play in deciding whether the host/germ/ environment complex is to lead to infection. Among these are susceptibility, generic constitution, behaviour, and socioeconomic determinants. (*The Lancet*, May 18, 1968, 1077).

Another way of making roughly the same point is to say that a model of causality to be adequate to explain any disease/illness, but especially in an epidemic or pandemic such as COVID-19 must include both necessary and sufficient conditions. This is to remind the lay person that citing SARS-CoV-2 as the cause of COVID-19 is only to cite a necessary condition and not both its necessary and sufficient conditions.[8] However, sometimes, the medical

[8] For readers who are not over-familiar with causal discourse, an example to illustrate the distinction between necessary and sufficient conditions may be

professionals forget to say explicitly that when they say that the coronavirus is "the cause" of COVID-19, they are really talking about the understanding of or referring to cause only as necessary condition, not as both necessary and sufficient conditions. Examples may be found in the recent literature about the epidemic or pandemic of this oversight, some of which are cited below:

WHO. (April 2023). [9] Overview: "Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus".
CDC (USA): COVID-19. (Updated Nov. 4, 2021). [10] "COVID-19 is caused by a virus called SARS-CoV-2".

Nature: nature reviews microbiology. 19, 141-154 (2021). (06 October 2020).[11] "At the end of 2019, a novel coronavirus designated as SARS-CoV-2 emerged in the city of Wuhan, China, and caused an outbreak of unusual viral pneumonia"; "…the causative agent of this emerging disease is a betacoronavirus that had never been seen before".

Johns Hopkins Medicine. (Updated July 29, 2022).[12] "A coronavirus identified in 2019, SARS-CoV-2, has caused a pandemic of respiratory illness, called COVID-19." "COVID-19 is the disease caused by SARS-CoV-2, the coronavirus that emerged in December 2019."

---

appropriately invoked here. Take a fire. For a fire to take place, oxygen must be present in the air. This is to say that oxygen is a necessary condition of the occurrence of a fire – in the absence of oxygen, no fire can take place. However, the presence of oxygen in the atmosphere is not sufficient to bring about a fire – other conditions must also exist at the same time which are sufficient to generate fire as the outcome, such as the presence of inflammable material (say a wooden hut containing wood shavings, a stroke of lightening hitting the shed or some vandal passing by who throws his lighted cigarette onto the wood shavings. The oxygen (a necessary condition) plus the wooden hut containing the wood shavings plus the carelessly abandoned cigarette (the sufficient conditions) together would or could account for the fire as the causal outcome.

[9] "Coronavirus disease (COVID-19)". Accessed April 4, 2023, https://www. who. int/health-topics/coronavirus#tab=tab_1 .

[10] "Basics of COVID-19". Accessed April 4, 2023. https://www.cdc.gov /coronavirus/ 2019-ncov/your-health/about-covid-19/basics-covid-19.html .

[11] "Characteristics of SARS-CoV-2 and COVID-19" (by Ben Hu, Hua Gao, Peng Zhou & Zheng-Li Shi). (uploaded on 06/10/2020). Accessed April 4, 2023. https://www.nature.com/articles/s41579-020-00459-7 .

[12] "What Is Coronavirus?" Accessed April 4, 2023.
https://www. hopkinsmedicine.org/health/conditions-and-diseases/coronavirus .

Conclusion

1 To say simplistically that "the cause" of COVID-19 is the coronavirus, SARS-CoV-2 may be misleading, especially to the lay person, as it masks the complexity of the causal scene. It is inappropriate to pose the **W**hat question and then to answer it in terms of the coronavirus.

2 In part, the "instinct" to pronounce in such a simplistic manner may be traced to the highly prestigious conception of disease called the Monogenic Conception of Disease which is considered to have ushered in the modern age of scientific medicine in Clinical Medicine, with Pasteur and Koch as the giants leading the field. This prestigious conception may be called the Classical Version and may be lauded as the non-dogmatic version as it can be understood to articulate a new paradigm of scientificity in Medical Thinking for the Modern Age which in the case of infectious diseases explain disease/illness in terms of pathogenic micro-organisms which have invaded the patient's body.

3 However, subjecting Koch's postulates (sometimes also called the Henle-Koch postulates) to critical scrutiny by testing them against available medical data in the SARS-CoV-2/COVID-19 context shows that Postulate 1, in particular, which is key to the Monogenic Conception of Disease (held as dogma) is methodologically flawed.

4 Re-testing them but this time using the case of peptic ulcer disease and *H. pylori* as the causative agent, a hundred or more years after Koch, also throws up the same flaws in the Monogenic Conception of Disease.

5 The logic of that conception of disease which has since its appearance taken on the status of a dogma (until of late, say, post 1968) is so restrictive that it cannot cope with what Mackie called "inus conditions", a set of relevant factors which together in combination generates the disease/illness in question, although each of these relevant conditions, on its own, separate from the others, is neither necessary nor sufficient for the occurrence of the disease/illness.

6 The reader should always bear in mind that any adequate model of causality should include both the necessary and the sufficient conditions for the generation of a disease/illness, including a highly infectious one such as COVID-19 in an epidemic or pandemic. To say that SARS-CoV-2 is "the cause" of COVID-19 is just to say that it is a necessary condition for the generation of the disease and not that it is both necessary and sufficient. The set of necessary and sufficient conditions include many other factors such as "susceptibility, generic constitution, behaviour, and socioeconomic determinants" as aptly observed by Stewart 1968.

7 One ought to point out an ironical turn of events in Marshall's and Warren's discovery of the *H. pylori* as the cause of peptic ulcer disease. They spent up to twenty years to get the thesis first accepted and then to obtain the Nobel Prize in Medicine in 2005. This was because the medical community, for a considerable period of time, could not accept that bacteria could live and survive under acidic conditions in the stomach of a patient. So, they stuck to the view current at the time, that peptic ulcers were caused by stress and other lifestyle factors, not by a micro-organism. Marshall and Warren had difficulty getting medical journals, such as *The Lancet* from accepting their submission. Finally, in desperation, Marshall resorted to swallowing the pathogenic bacteria after first making sure that he was free from peptic ulcer disease at the beginning of the experiment, and that he became infected with it through the experiment. (See *The Lancet* 2005.) In other words, Marshall invoked (though not consciously) Collingwood's understanding of cause via manipulation and control (see Chapter 5). In this way, Marshall carried out Koch's Postulate 3. Marshall's heroic act paid off, as he was successful in pulling off the experiment on himself. He was lucky, but he need not have been. Remember Koch's experiment with cholera on animals? Those animals remained steadfastly asymptomatic. In any case, Marshall could, in principle, belong to that 90% of people in the world known to have *H. pylori* infection but who do not develop gastritis or peptic ulcers. Only 10% do. Statistics show that 80% of the world's population harbour *H. pylori* of which only 10% have the disease. In other words, large numbers are asymptomatic. His experiment of a single participant, that is himself, in any case, is not compatible with the normal guidelines for scientificity in conducting experiments. In other words, methodologically, Marshall was not standing on firm ground.

CHAPTER 3

WHO MANIFESTS A DISEASE? A CUT-AND-DRY MATTER?

This chapter continues the critique of the Monogenic Conception of Disease held as dogma by scrutinising in some detail the question: **W**ho manifests a disease/illness? Chapter 2 has examined the related **W**hat question and found the conception wanting when applied in the context of either a pathogenic virus (SARS-CoV-2 in the case of COVID-19) or a pathogenic bacterium (*H. pylori* in the case of peptic ulcer disease). These two cases involve infectious diseases. However, the Monogenic Conception of Disease claims a wider remit than viral and bacterial infection. In its widest understanding, it simply reads: one pathogenic cause, one effect. Pathogenic viruses and bacteria fit nicely into this formula which, however, is not limited to them only. For instance, defective genes could count as a pathogenic factor for disease-generation. Hence, this chapter focuses on phenylketonuria, a disease attributed to a defective gene, to see if the same criticism about the Monogenic Conception of Disease also obtains in this context, namely, that it cannot do justice to all the relevant data which constitute the complexity of disease-generation. This **W**ho question, like the **W**hat question, can only be adequately addressed by abandoning that conception of disease (held as dogma) and opting for a multifactorial model of relationships between two and/or more relevant variables, namely, the bi-directional, multifactorial mode of causation/BMC and not the unidirectional, monofactorial mode of causation/UMC.

Who is the Individual Person with the Disease?

Chapter 2 has already drawn attention to an important aspect of infection in an epidemic/pandemic, namely, that not all those who have been exposed to the germ in question and become infected by it will automatically exhibit symptoms of the disease. The data in the case of SARS-CoV-2/COVID-19 (published in May 2021) appear to show that at least one third of infected

cases are asymptomatic.[1] However, asymptomatic infection occurs not only with infection from a virus but also from pathogenic bacteria, such as *H. pylori* which is said to be "the cause" of peptic ulcer disease. Just to remind the reader, it turns out that although 80% of the world's population are bearers of *H. pylori* only 10% of them develop peptic ulcer disease. [2] This observation does not simply serve to undermine the validity of the Monogenic Conception of Disease (held as dogma) but is also a compelling signal for much needed research and investigation why this is so. No-body to date would and could claim to know as much as is desired, but a fair number of medical scientists may be prepared to argue that they must look beyond the simplistic Reductionist temptation offered by genetics (in its triumphalist phase following the discovery of the double helix structure of the DNA molecule by Crick and Watson in 1953) to answer the question – see Noble, 2006.

That early triumphalism was finally knocked on its head when the Human Genome Project, upon its completion, made known its findings in 2003. Contrary to expectation, the number of genes uncovered were relatively few, only probably about 20,500 genes when estimates had ranged from 50,000 to as many as 140,000. Science had to do some serious re-thinking. That is why Noble confessed that although he had spent the greater part of his career doing Reductionist science, he felt the need to change tack, to abandon Reductionism and to opt for a "systems"/Wholist approach. [3]

Although no rational person would doubt that genetic endowment plays a role in the individual's appearance and behaviour, no well-informed

---

[1] See Oran and Topol 2021; Ma, Liu, Liu, *et al*. 2021 for systematic reviews of available data.

[2] Peptic ulcer disease is not considered to be a pandemic minimally for three reasons: (a) infection though extensive and widespread throughout the globe is not considered to be alarming as only a minority of the infected shows symptoms of the disease; (b) those infected live mainly in the developing economies and (c) given that the mode of transmission of peptic ulcer disease does not affect people in the developed economies, there is little or no incentive to do anything about the matter. In contrast, SARS-CoV-2 is alarming as given its mode of transmission, developed economies could readily fall prey to it as, indeed, they have and continue to do so (in late August 2022, at the time of writing this chapter), grappling with BA.4 and BA.5 which are variants of the original Omicron virus, with the number of cases world-wide standing at just below 600 million and deaths world-wide at roughly 6 and a half million – see some figures, dated 10/07/2022, in Table 4.1 in chapter which follows, Chapter 4.

[3] See Chapter 1 for a clarification about the use of the terms "Wholist" and "Wholism". See Chapter 7 which explores Wholism via the concept of ecosystem-nesting.

person today would hold the view that the genotype determines the phenotype. We now know enough about the science of genetics to know that the genes in the human genome are themselves complexly related. See Figure 3.1 below:

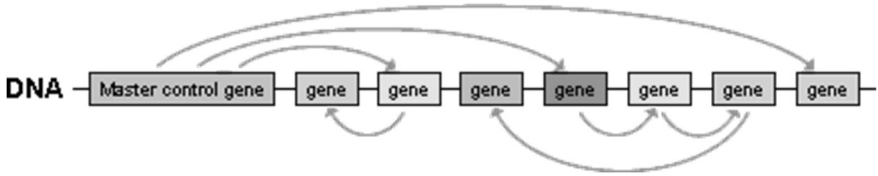

Figure 3.1. Complex relationships between genes [4]

Developmental biology invokes the concept of a master gene, that is, a single gene whose expression constitutes the appropriate conditions for activating many other genes in a co-ordinated manner, ultimately leading to a specific tissue or organ being developed. Pax-6 is said to be such a gene which triggers development of the eye. However, what needs emphasising is that development of any cell, tissue, organ, or whole organism depends on more than the existence of genes, as the environment, both internal and external plays a critical role in human biology in particular and in biology in general. See Figure 3.2 below:

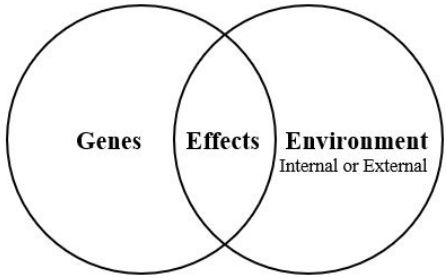

Figure 3.2 Genes interacting with environmental factors, internal and/or external.

Genes, we know, are embedded in cells; we also know that the internal as well as the external environment of a cell can affect which genes are "turned on", so to speak. For instance, hormones can "tell" a cell to activate

[4] Accessed and downloaded July 14, 2022.
https://evolution.berkeley.edu/ evo library/images/evo/control_gene.gif.

a specific gene (internal environmental factor). [5] Experimental data exist which confirm that outside temperature can affect the expression of the gene controlling the colour of fur in rabbits (external environmental factor). An ice pack was strapped to the back of a rabbit with white body fur. At the end of the experiment, when the ice pack was removed, one would find that the rabbit had a patch of much darker fur on its back in exactly the place where the ice pack was – see "Role of Environmental Factors in Gene Expression" 2012.

To clarify further what Figure 3.2 above means, take the case of the disease called phenylketonuria. Although disorders may involve single faulty genes, it does not mean that the disease would necessarily manifest itself. Phenylketonuria is one such instance. [6] In many countries, infants when born are tested to see if they have inherited this condition and in the rare cases where they have, their parents are immediately advised to put the child on a diet (probably lasting a lifetime) to avoid foods which are rich in phenylalanine, as the inherited defective gene means that the body cannot make an enzyme called phenylalanine hydroxylase (PAH), an enzyme necessary for converting the amino acid phenylalanine into other substances the body needs. Most forms of phenylketonuria are caused by mutations in the PAH gene on chromosome 12q23.2. The defective PAH gene then leads to the accumulation of the amino acid in the blood, causing a whole range of conditions (intellectual disability, delayed development, behavioural and social problems, psychiatric disorders and so forth), from mild to severe. In other words, the disease will manifest itself or the gene would only be "activated"/expressed in the presence of certain adverse environmental factors.

The external environment of the individual would naturally include other people and their behaviour/attitude, whether these others are aware of the person's dietary needs or are conscientious in implementing such a dietary regime or helping them to implement such a regime. If the external environment is not hospital to meeting the person's dietary needs, they would likely ingest foods rich in phenylalanine which then become part of their internal environment, wreaking havoc upon it.

The above complex interacting relationships are hardly amenable to the Monogenic Conception of Disease model of disease (held as dogma) and its implied UMC; rather they appear to go hand in hand with what may be

[5] See Ing 2005 for a review of the literature on how steroid hormones regulate gene expression.

[6] PKU is what is called an autosomal recessive metabolic genetic disorder. As such it requires two PKU alleles (one from each parent) to be present in individuals before they would experience symptoms of the disease.

called multifactorial inheritance (or polygenic) disorders, such as heart disease, diabetes, obesity and most cancers. These are caused by a combination of small inherited variations in genes but acting in conjunction with certain adverse environmental factors (namely, Mackie's "inus conditions").

Phenylketonuria is a clear instance of what may be called synergism at work. The faulty gene on its own may not produce the brain damage; neither does a normal diet relatively high in phenylalanine (in the absence of the faulty gene). Each of the factors cited, on its own, does not bring about brain damage. Yet when the factors happen to combine, then and only then, does brain damage occur. The brain damage is the synergistic effect of all these causally relevant factors. Under synergism, the total effect is more than or is different from the sum of the effects of each of these factors when measured separately on its own. Synergism in certain contexts could lead even to death. Such as taking sleeping pills and alcohol, if an individual were to swallow more than the number of sleeping pills prescribed for their condition, this on its own would not necessarily kill the person, although they may cause some very unpleasant effects. Similarly, if the person were to drink half a bottle of whisky on its own, a very nasty hangover the next day would ensue. However, should the individual swallow the pills at the same time as consuming the alcohol, then death could, and would ensue in certain instances, if the attempt combining both was not discovered in time by others.

The case of phenylketonuria handily illustrates the complex relationship between the gene/host relationship when that relationship operates within a larger environment which itself can be broken up into three sub-environments, namely, the physical, the social as well as the chemical and biological – see the version here (Figure 3.3 below) of what is found in Bhopal, 2008, 135. The host/person possesses the gene defect which leads to an enzyme deficiency which, in turn, may lead to brain damage. The host/person operates within a larger (physical-social) environment which includes facilities for early diagnosis, as early diagnosis backed up by dietary control could help prevent/control the manifestation of the disease. The host/person also operates within a specific social environment which includes active support to make it possible to sustain on a long-term basis the special dietary regimen, if prevention/control were to be effective. Such special diet, if conscientiously sustained, would mean that the host's chemical and biological environment would be such that the disease would not manifest itself in the lifetime of the host. This enlarged wheel model of causal complexity shows very clearly that it would be distorting to regard phenylketonuria simplistically as a genetic disease in which its "cause" is a gene defect *tout court*. Phenylketonuria is also an environmental disease.

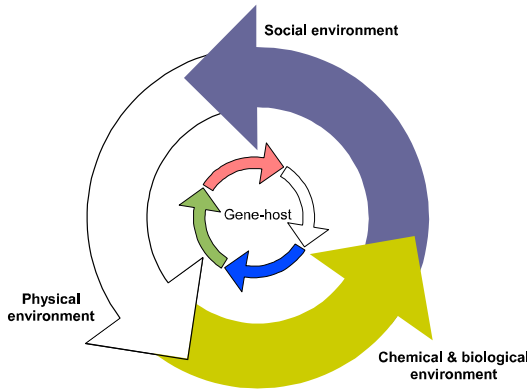

Figure 3.3 Three external environments acting upon the Gene-host with its own internally complex interactions in generating phenylketonuria.

In other words, whether the outcome is related to a defective gene as in the case of phenylketonuria or to pathogenic bacteria, *H. pylori* as in peptic ulcer disease, or to a virus, SARS-CoV-2 as in COVID-19, environmental (physical and social) factors play a critical role in disease-generation/illness when they act in tandem with a gene/bacteria/virus. From this, one may plausibly conclude that diseases do not conform to the Monogenic Conception of Disease model of disease-generation (held simplistically and as dogma) and its implied UMC.

Conclusion

1 This chapter subjects the Monogenic Conception of Disease-UMC to test by confronting it with data from yet another context of disease-generation, the case of phenylketonuria where a defective gene is said to play the definitive role and, hence, has been singled out as "the cause" of the disease called phenylketonuria.
2 However, a critical examination shows that the conclusion of the Monogenic Conception of Disease in this context (held simplistically and as dogma) is not justified. Phenylketonuria, just like peptic ulcer disease and COVID-19, does not conform to the Monogenic Conception of Disease account of disease-generation (held as dogma).
3 All three diseases would not, and could not be generated except when the problematic item (in phenylketonuria it is the PAH gene, in peptic ulcer disease, it is the pathogenic bacteria, *H. pylori* and in COVID-19,