Severe Acute Hepatitis in Children: An Analysis from Philosophy of Science Using the Concept of Reduction

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Abstract
The present paper uses Carnap's reduction concept to address the problem of new severe acute hepatitis in children. First, it tries to show how that concept can help understand why some previous hypotheses of causality on the new hepatitis in children should be rejected. Second, Carnap's reduction concept is used to explain a complex hypothesis about the causes of that disease proposed in The Lancet in 2022. The latter hypothesis combines several factors: infection by SARS-CoV-2, a build-up of this virus in the bowel that comes in contact with blood circulation, and another infection by adenovirus. One of the points of the paper is to argue that a hypothesis can be described by means of a bilateral reduction sentence, which in turn would allow empirically comparison of the hypothesis in an easy way. Finally, the author considers a current cognitive framework, namely, the theory of mental models, to propose that bilateral reduction sentences should not be hard to handle for physicians or scientists.

Keywords: adenovirus; reduction; SARS-CoV-2; severe acute hepatitis in children; theory of mental models

Introduction

Several cases of a new 'severe acute hepatitis in children were reported around the world in 2022 (e.g., Brodin & Arditi, 2022). Physicians and researchers tried to find, by all means, an explanation and the causes of those cases (see also, e.g., Cañelles, 2022). In the process, some hypotheses were ruled out. Some of them were, for example, to deem the new hepatitis as a disease equivalent to one of the five kinds of hepatitis already known, or an adenovirus (Brodin & Artidi, 2022; Cañelles, 2022).

After rejecting other hypotheses as well, one more hypothesis was proposed. This new hypothesis, in principle, seemed difficult to verify. It claimed that several elements acting at the same time cause the severe acute hepatitis in children. The new hepatitis would appear when there is a SARS-CoV-2 infection and, as a result, the virus accumulates in the intestine. Then, the virus would enter the blood and flow throughout the body. At once, the liver would be inflamed because of an adenovirus infection (Brodin & Artidi, 2022; Cañelles, 2022).

This hypothesis appears to be hard to contrast. However, the main goal of the present paper is to show otherwise. If the procedure Carnap (1936, 1937) offered to relate properties or predicates, that is, his reduction process, is assumed, the task of empirical confirmation may not be so difficult. The literature reveals that, if it is accepted that the human mind follows, in its inferential processes, what the theory of mental models (e.g., Khemlani, Byrne, & Johnson-Laird, 2018) indicates, that procedure is not difficult at all (e.g., López-Astorga, 2021).

To achieve that goal, the present paper will have three sections. In the first section, some of the previous hypotheses about the causes of the new hepatitis in children will be taken as examples. The aim will be to explain how Carnap's reduction processes can help reveal the reasons why those hypotheses are not admissible. The second section will describe the complex hypothesis pointed out above. It will be argued that, despite what may be thought, Carnap's concept of reduction can lead to simple confirmations of that hypothesis. Based on the literature, the final section will show that to apply Carnap's reduction procedure to that hypothesis is not hard for people, at least, if the theses of the theory of mental models are right.

The new severe acute hepatitis in children: some previous hypotheses

Different previous hypotheses about the causes of the new hepatitis were proposed. This section will deal with some of them. The aim is to explain how Carnap's (1936, 1937) reduction processes can help check their falsity. In particular, the hypotheses that will be considered are: the severe acute hepatitis is one of the types of hepatitis already existing, the severe acute hepatitis is an adenovirus, and the enclosures because of COVID-19 pandemic caused children to be weaker against adenoviruses (Brodin & Arditi, 2022; Cañelles, 2022).

As far as the first is concerned, it is known that there are five kinds of hepatitis: hepatitis A, hepatitis B, hepatitis C, hepatitis D, and hepatitis E. To check whether or not the new hepatitis is actually one of those kinds is easy if formulae of first-order predicate logic are built. In those formulae, the predicates can be these:

$C =_{df}$ to be a child

$H^a =_{df}$ to have hepatitis A

$H^b =_{df}$ to have hepatitis B

$H^c =_{df}$ to have hepatitis C

$H^d =_{df}$ to have hepatitis D

$H^e =_{df}$ to have hepatitis E

$N =_{df}$ to have the new severe acute hepatitis

Given these equivalences, the following five formulae can be formed:

(1) $\forall x\ [Cx \rightarrow (H^a x \rightarrow Nx)]$

(2) $\forall x\ [Cx \rightarrow (H^b x \rightarrow Nx)]$

(3) $\forall x\ [Cx \rightarrow (H^c x \rightarrow Nx)]$

(4) $\forall x\ [Cx \rightarrow (H^d x \rightarrow Nx)]$

(5) $\forall x\ [Cx \rightarrow (H^e x \rightarrow Nx)]$

Where '$\forall$' is the universal quantifier and ´$\rightarrow$' stands for the material conditional in classical logic.

According to Carnap (1936), formulae (1) to (5) are reduction sentences for N if they fulfill a requirement: cases of their two first predicates have to exist. Therefore, the requirements for formulae (1) to (5) are, respectively, (6) to (10).

(6) $\exists x\ (Cx \wedge H^a x)$

(7) $\exists x\ (Cx \wedge H^b x)$

(8) $\exists x\ (Cx \wedge H^c x)$

(9) $\exists x\ (Cx \wedge H^d x)$

(10) $\exists x\ (Cx \wedge H^e x)$

Where '∃' represents the existential quantifier and '∧' denotes logical conjunction.

These requirements are not a problem, since there are people thar are children and can develop the different types of hepatitis. Furthermore, to build reduction sentences to try to confirm theories is not absolutely unusual nowadays. There are some cases (e.g., López-Astorga, 2022).

Carnap (1936) thinks that absolute verification cannot be achieved. Nevertheless, formulae such as (1) to (5) can help progressively confirm the hypothesis that the new hepatitis in children is one of the kinds of hepatitis already identified. For the case of (1), it would be confirmed provided that cases of (11) were not found.

(11) $\exists x\ (Cx \wedge H^a x \wedge \neg Nx)$

Where '¬' indicates negation.

Cases of (12) would eliminate (2).

(12) $\exists x\ (Cx \wedge H^b x \wedge \neg Nx)$

What would be unacceptable for (3) is the existence of cases of (13).

(13) $\exists x\ (Cx \wedge H^c x \wedge \neg Nx)$

Formula (4) would be incompatible with (14).

(14) $\exists x\ (Cx \wedge H^d x \wedge \neg Nx)$

And the hypothesis corresponding to (5) could not be assumed if there were cases of (15).

(15) $\exists x\ (Cx \wedge H^e x \wedge \neg Nx)$

Nonetheless, one might suppose that the pieces of evidence the physicians found were not cases such as those indicated in (11) to (15), but, for example, cases such as those described in (16) to (20).

(16) $\exists x\ (Cx \wedge \neg H^a x \wedge Nx)$

(17) $\exists x\ (Cx \wedge \neg H^b x \wedge Nx)$

(18) $\exists x\ (Cx \wedge \neg H^c x \wedge Nx)$

(19) $\exists x\ (Cx \wedge \neg H^d x \wedge Nx)$

(20) $\exists x\ (Cx \wedge \neg H^e x \wedge Nx)$

That is, cases of children that had the severe acute hepatitis and not one of the types of hepatitis known (A, B, C, D, or E). The problem with (16) to (20) is that they do not make, respectively, (1) to

(5) false. In classical logic, whenever the antecedent of a conditional is false, that very conditional is true. In addition, (16) to (20) do not fulfill, respectively, requirements (6) to (10).

But this difficulty can be overcome. If what is researched is whether or not the new hepatitis in children is one of the kinds of hepatitis already discovered, what is wanted to do is to determine whether or not the new hepatitis in children is equivalent to one of the kinds of hepatitis already discovered. Thereby, the best formulae to express the equivalence relation are not (1) to (5), but (21) to (25).

(21) $\forall x\ [Cx \rightarrow (H^a x \leftrightarrow Nx)]$

(22) $\forall x\ [Cx \rightarrow (H^b x \leftrightarrow Nx)]$

(23) $\forall x\ [Cx \rightarrow (H^c x \leftrightarrow Nx)]$

(24) $\forall x\ [Cx \rightarrow (H^d x \leftrightarrow Nx)]$

(25) $\forall x\ [Cx \rightarrow (H^e x \leftrightarrow Nx)]$

Where '$\leftrightarrow$' is the symbol for biconditional relation.

Following Carnap (1936), (21) to (25) can be bilateral reduction sentences for N if they fulfill requirement (26).

(26) $\exists x\ Cx$

Requirement (26) being fulfilled, both (11) to (15) and (16) to (20) are inconsistent with, respectively, (21) to (25). This is what can explain, within Carnap's (1936, 1937) framework, the rejection of the hypothesis that the new severe acute hepatitis in children is one of the kinds of hepatitis already identified.

The second hypothesis is that the new hepatitis is an adenovirus. Given that, again, the hypothesis provides an equivalence (it considers the severe acute hepatitis in children to be equivalent to an adenovirus), a bilateral reduction sentence can be better than a reduction sentence here, too. To build that bilateral reduction sentence, a new predicate is necessary:

A $=_{df}$ to have a particular adenovirus; it can be adenovirus 41F (Brodin & Arditi, 2022).

Thus, the bilateral reduction sentence for the second hypothesis would be (27).

(27) $\forall x\ [Cx \rightarrow (Ax \leftrightarrow Nx)]$

Formula (27) also has to be coherent with requirement (26).

In principle, (27) seemed to be confirmed in most cases. But this hypothesis presents a difficulty: beyond the fact that adenovirus was not found in the patients' livers, adenovirus 41F is not related to hepatitis in medical literature (Brodin & Arditi, 2022; Cañelles, 2022). This can also be expressed from Carnap's approach. Given this predicate:

H $=_{df}$ to have a hepatitis of any kind

Formula (28) has a very low confirmation.

(28) $\forall x\ [Cx \rightarrow (Ax \rightarrow Hx)]$

To be a reduction sentence, (28) needs to be coherent with requirement (29).

(29) $\exists x\ (Cx \wedge Ax)$

The literature appears to report that (29) is the case, but (28) is not confirmed, since (30) holds.

(30) $\exists x\ (Cx \wedge Ax \wedge \neg Hx)$

The point is that, given that the new hepatitis in children is a hepatitis, (31) is also true.

(31) $\forall x\ (Nx \rightarrow Hx)$

And (30) and (31) together make (27) false.

The last hypothesis is linked to the confinements in pandemic. The idea is that isolation makes children less resistant to adenovirus. However, beyond the arguments above, which do not allow relating the new severe acute hepatitis to an adenovirus, many of the children with the disease were old enough to have gone to school before COVID-19 pandemic. So, those children should be, to a greater or lesser extent, strong against adenoviruses (e.g., Cañelles, 2022). This can also be expressed within Carnap's (1936, 1937) framework. One more new predicate can help.

$E =_{df}$ to have been exposed to adenoviruses

A reduction sentence for E could be (32).

(32) $\forall x\ [Cx \rightarrow (Nx \rightarrow \neg Ex)]$

Many children that tested the severe acute hepatitis positive were exposed to adenoviruses. So, (33) is true.

(33) $\exists x\ (Cx \wedge Nx \wedge Ex)$

In (33), Cx and Nx enables (32) to fulfill the requirement to be a reduction sentence (there are cases of its two first predicates). But Ex shows that (32) cannot be accepted.

Hence, Carnap's (1936, 1937) theses allow understanding the reasons why some previous hypotheses were discarded. The next section tries to show that the complex hypothesis subsequently proposed can also be submitted for confirmation processes such as those Carnap (1936) raises.

SARS-CoV-2 and superantigens

Basically, the complex hypothesis is as follows:

> "We hypothesise that the recently reported cases of severe acute hepatitis in children could be a consequence of adenovirus infection with intestinal trophism in children previously infected by SARS-CoV-2 and carrying viral reservoirs (appendix). In mice, adenovirus infection sensitises to subsequent Staphylococcal-enterotoxin-B-mediated toxic shock, leading to liver failure and death" (Brodin & Arditi, 2022, p. 1).

At the end of this cite, there is a reference to another work (Yarovinsky, Mohning, Bradford, Monick, & Hunninghake, 2005) to give further support to the hypothesis, which requires to take a new predicate into account. Most children with the new severe acute hepatitis sometime had

COVID-19. The medical circumstances associated to this last disease are different for children and adults. In the case of children, the virus can keep in the bowel, and that situation can cause MIS-C (Multisystem Inflammatory Syndrome in Children). On the other hand, protein spike present in SARS-CoV-2 and enterotoxin-B appear to have certain similar characteristics. Those characteristics are related to a superantigen to which the human body can overreacts, and that overreaction can cause inflammation. As indicated, enterotoxin-B has a significant influence on mice with adenovirus. Accordingly, adenovirus can be another important factor (see also Cañelles, 2022). To build a formula considering all of this, one more predicate is necessary:

M $=_{df}$ to develop MIS-C

This new predicate is needed but it suffices. A child with MIS-C is a child that has had COVID-19. COVID-19 in turn implies the presence of protein spike. This last protein is what, given an adenovirus infection, causes an overreaction. So, a bilateral reduction sentence for N could be, in this case, (34).

(34) $\forall x \{Cx \rightarrow [(Mx \wedge Ax) \leftrightarrow Nx]\}$

Formula (34) is a bilateral reduction sentence if (26) is the case. That is not a problem, since there are children. However, one might think that the empirical confirmation of (34) is hard. Contemporary cognitive science seems to indicate otherwise.

The theory of mental models, MIS-C, and adenovirus

The theory of mental models is a framework based on the general idea that sentential connectives such as the conditional, the biconditional, conjunction, or disjunction are processed as 'conjunctions of possibilities' (see also, e.g., Johnson-Laird & Ragni, 2019). Given that the main sentential connectives in (34) are the conditional and the biconditional, this section will essentially focus on the way the theory of mental models understands those two sentential connectives.

One important feature of the theory of mental models is that it is a dual-process theory (e.g., Reyna, 2004). Hence, it claims that two systems, System 1 and System 2, can work in the human mind. The two systems are as follows:

> "**Systems 1 and 2**: the two systems of reasoning postulated in dual-process theories of judgment and reasoning, in which system 1 yields rapid intuitions and system 2 yields slower deliberations. Many versions of the theory exist" (Johnson-Laird, Khemlani, & Goodwin, 2015, p. 202; bold in text).

This means that to use System 1 is easy because it is intuitive, and that to reason with System 2 is harder because it is deliberative and analytic (see also, e.g., Byrne & Johnson-Laird, 2009). The distinction between these two systems was applied to show that Carnap's (1936) reduction sentences and bilateral reduction sentences are not difficult to confirm, as they only need the use of the intuitive and easy system, that is, System 1 (e.g., López-Astorga, 2021). Then, this point is developed for the case of (34).

The theory of mental models provides the following correspondences (see also, e.g., Byrne & Johnson-Laird, 2020):

(35) $X \rightarrow Y =_{df} \Diamond(X \wedge Y) \wedge \Diamond(\neg X \wedge Y) \wedge \Diamond(\neg X \wedge \neg Y)$

(36) $X \leftrightarrow Y =_{df} \Diamond(X \wedge Y) \wedge \Diamond(\neg X \wedge \neg Y)$

Where '$\Diamond$' represents possibility.

Both in (35) and in (36), a conjunction of possibilities is assigned to a sentential connective. In the case of (35), the connective is the conditional. In the case of (36), it is the biconditional. But the theory of mental models is not a normal modal logic: the correspondences in (35) and (36) are not admissible in normal modal logics. Both of them allow coming to $\Diamond(X \wedge Y)$: this last possibility is the first conjunct both in (35) and in (36). This deduction is correct in no normal modal logic (e.g., Espino, Byrne, & Johnson-Laird, 2020).

Beyond this, what is important for this section is that people only consider the conjunctions of possibilities in (35) and (36) if they are reasoning with System 2. System 1 only enables to establish the definitions in (37) and (38).

(37) $X \rightarrow Y =_{df} \Diamond(X \wedge Y)$

(38) $X \leftrightarrow Y =_{df} \Diamond(X \wedge Y)$

The conjuncts that are missing in (37) and (38), but they are in (35) and (36), can only be identified by virtue of System 2. However, as said, the literature reveals that reduction sentences and bilateral reduction sentences need to be applied just System 1 (e.g., López-Astorga, 2021). This can be checked by means of (34). If, for explanation purposes, the universal quantifier is ignored, (37) shows that the conditional in (34) leads to (39).

(39) $\Diamond\{Cx \wedge [(Mx \wedge Ax) \leftrightarrow Nx]\}$

Likewise, (38) allows transforming (39) into (40).

(40) $\Diamond\{Cx \wedge \Diamond[(Mx \wedge Ax) \wedge Nx]\}$

And (40) is equivalent to (41).

(41) $\Diamond[Cx \wedge \Diamond(Mx \wedge Ax \wedge Nx)]$

Because (34) is a bilateral reduction sentence and, hence, it needs to fulfill (26), Cx can be ignored too. After all, (26) makes the researcher be aware that (34) requires a universe consisting of children to be applied. For this reason, one might think that, to try to confirm (41), physicians only need to take into account that universe and its three last predicates, that is, that universe and (42).

(42) $\Diamond(Mx \wedge Ax \wedge Nx)$

Besides, the tests would be made only in an even smaller universe, that is, in the universe of the children already diagnosed with the severe acute hepatitis. This means that Nx can be removed as well, the result being (43).

(43) $\Diamond(Mx \wedge Ax)$

In this way, the only task to do would be to confirm, for every case, (43), that is, that the child has MIS-C and adenovirus. Each case having these two predicates progressively would confirm the hypothesis.

Conclusions

The severe acute hepatitis in children was a challenge for medical science. Different hypotheses were proposed. For example: it is one of the types of hepatitis already known (A, B, C, D, or E), it is an adenovirus, or, because of isolations enacted by reason of COVID-19 pandemic, children do not have the necessary resistance against adenoviruses. These hypotheses can be analyzed from Carnap's (1936, 1937) perspective. In fact, Carnap's framework can explain why they should be rejected.

After those hypotheses, a much more complex idea was proposed. The new hepatitis in children was understood as a combination of several factors. The children with the disease acquired COVID-19. In some cases, that infection led them to MIS-C. These last children were those that get the severe acute hepatitis when, in addition, they were infected with an adenovirus.

It is possible to build a bilateral reduction sentence corresponding to this last hypothesis. Although it can seem a sentence difficult to check, that is not necessarily the case, at least, if the theory of mental models is right and the human inferential processes happen as this theory indicates. It is enough to confirm whether or not two circumstances occur at once: to have MIS-C and to have an adenovirus. If only one of these two situations is present in the case of a child with the severe acute hepatitis, then it is possible to doubt the hypothesis. However, every case with the two conditions is a confirmation of it.

To have just MIS-C with neither adenovirus nor the new hepatitis in children is not evidence against the hypothesis. To have adenovirus with neither MIS-C nor the severe acute hepatitis in children is not either. For these reasons, the hypothesis can appear to be hard to check, since it includes several variables. Nevertheless, it is not that difficult. According to the hypothesis, it is not possible to have the new hepatitis in children without the other two conditions. Thus, the only universe to consider would be that of the children with severe acute hepatitis. And what would have to be done is just to review whether or not the other two diseases (MIS-C and adenovirus), and not only one of them, are also present.

Science quickly moves forward. Thereby, it is possible that the main hypothesis dealt with here is reviewed enough when the arguments in the present paper are published. In any case, the proposal above, at a minimum, tries to show a way to work in accordance with Carnap's (1936, 1937) framework even in the case of complex hypotheses referring to several alternative circumstances.

Declaration of Conflict of Interests

The author(s) declared no potential conflicts of interest.

Funding

PIA Ciencias Cognitivas, Centro de Investigación en Ciencias Cognitivas, Instituto de Estudios Humanísticos, Universidad de Talca.

Fondo Fondecyt de Continuidad para Investigadores Senior, código FCSEN2102, Universidad de Talca.

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