INTERVIEW WITH TOINE PIETERS

Rafaela Zorzanelli

This is the third interview in the journal's new "Conversations" section. Drawn from my broader project *Interviews with Researchers from the Anthropology, History, and Sociology of Pharmaceuticals: Mapping Out the Area*,[1] the following discussion features Professor Toine Pieters. From his early years of lab work in the Netherlands, to his move into social sciences and history, Pieters followed a path that stretched from studying molecules to analyzing their historicization. In the course of our discussion, he adopted a didactic approach, while not losing any analytical profundity, and he addressed several topics that will certainly interest drugs studies scholars. The conversation covers such subjects as the forgotten pasts of certain pharmaceuticals; the social appeal and promises embedded in "wonder drugs"; the agency of therapeutic drugs; the co-construction of drugs, diseases, and their handlers; the social interaction between doctors and patients; and the role of promise, hope, faith, and fashion in medicine and, particularly, in pharmaceuticals.

Pieters, who has written broadly about the history of pharmacy, medicines, and diseases, pervasively argues that a rational understanding of substances cannot fully account for their agency and cyclical trajectory. Put another way,

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1. Drug Trajectories: Interviews with Researchers, https://drugtrajectories.org. For more information about the project, see Rafaela Zorzanelli, "Drug Trajectories: Interviews with Researchers," *Pharmacy in History* 62, no. 1-2 (2020): 47–48, https://doi.org/10.26506/pharmhist.62.1-2.0047.

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given the impossibility of finding the exact points at which to "carve nature at its joints"—as in the Platonic metaphor—different fields of medicine require more sophisticated analytical techniques. In the study of substances, Pieters suggests, scholars must address the tension between realism and constructivism to better understand their complexity. He offers a methodological strategy to question the inflection points or dogmas in a field of scholarship. By debunking myths and contextualizing evidence in the contexts of drug development and of drug use, his approach—like that of other scholars in the field—addresses and analyzes substances as co-constructed with their set and setting. Countering blind faith in science and its processes, Pieters warns that all solutions achieved through drugs bring new problems in their wake. For an unabridged video version of the interview, visit the project website. I hope that readers of *History of Pharmacy and Pharmaceuticals* enjoy this thought-provoking and fruitful discussion.

Rafaela Zorzanelli: *As a pharmacist by training with a later education in history and philosophy of science, could you tell us a bit more about the path that brought you from molecules to social sciences?*

Toine Pieters: I was trained in the 1980s in the Pharmaceutical Sciences Department. At the end of my masters, I had to do a thesis, and I started to look around for people who were then in the field of social studies of science like Wiebe Bijker and Nelly Oudshoorn. I really got interested in the social construction of pharmaceuticals and especially of the new generation of recombinant-DNA produced biologicals like the interferons. It was interesting to learn more about the anthropology and sociology of "laboratory life" (inspired by Bruno Latour and Steve Woolgar[2]) and the social lives of pharmaceuticals. I started raising questions about why people use medicines in certain ways, how doctors prescribe in the consulting room, and what was the role of pharmacists. It really came to me as a surprise in the mid-80s during a conference that a pharmacist started complaining about non-compliance. What struck me is that quite a number of people with a serious disease like diabetes do not comply. Why would people not comply? And what role did promises play in the trajectories of medicines?

I decided to change course and move into social studies of science. I was lucky that Wiebe Bijker was willing to hire PhD students with only a science background. In the late 1980s and early 1990s, Maastricht University had an ambitious and expanding constructivist research group. So, I started in 1989 with my PhD

2. Bruno Latour and Steve Woolgar, *Laboratory Life: The Social Construction of Scientific Facts* (Beverly Hills, CA: Sage Publications, 1979).

about the trajectory of this new promising family of biologicals, the interferons. It was quite a challenging period. It was a bit like going native in an unfamiliar tribe. I did not understand their vocabulary, rituals, or values. I came straight from the laboratory. In a way, I had to start from scratch and started reading about the social studies of science.

Early on, I realized that, in order to study archival material about the history of interferon research, I would have to visit archives. Archival work in itself requires specific skills and I was lucky that I met Harmke Kamminga and Andrew Cunningham in Cambridge. They taught me how to do straightforward archival research and introduced me to other scholars working in the field of history of medicine. This enabled me to integrate medical history and social studies of science approaches in my thesis. I learned that therapeutic drugs have agency and that there is an ongoing co-construction between a drug, a disease, and its handlers. So, the moment a new drug compound appears on the scene, a trajectory evolves with particular dynamics. This now sounds like a truism, but back then I really struggled to get a grip on these conceptual notions.

After finishing my PhD thesis (published as *Interferon: The Science and Selling of a Miracle Drug*),[3] I became primarily interested in long-term mechanisms and patterns of drug development, production, and consumption. In studying the dynamics of subsequent generations of psychotropic drugs, I realized that the trajectories have a common feature: they run in cycles. Life cycles describe the market behavior of many products, and drug life cycles generally have four stages. First, there is a testing and approval trajectory. Second, after the drug is introduced, there is market expansion, and the product is accompanied by growing expectations and drug indication extension. Next, drug maturity with a high sales volume is accompanied by rising criticism and disappointment regarding drug effectiveness and side-effects. Finally, there is contracting use and limited drug application. In most cases, this is a gradual process that involves the documentation of less favorable experiences and reports of the drug's effectiveness and adverse reactions in everyday practice. Thus, a drug's benefit-risk assessment and the resulting safety profile is under constant revision. Over time, newer and presumably better alternatives gain attention. This is part of an evolutionary process of selection and adaptation.

But we have to realize that this is just a general pattern. To really understand what happens within the context of drug use, you also have to include the set and

3. Toine Pieters, *Interferon: The Science and Selling of a Miracle Drug* (London: Routledge, 2005), https://doi.org/10.4324/9780203481530.

setting concept. Not in the literal sense of how Norman Zinberg[4] in the 1970s proposed this concept, but in a looser way. You have to realize that in taking drugs—and not only psychoactive ones, but also other drugs—the user is important in terms of the mindset (including expectations, preparation, mood, and other psychological factors) in combination with the context (or the setting) of use.

Users can be understood individually but also on a collective level, and there is always a tension between the individual user and the collective. The drug trial industry implies that the greater part of testing drugs has become a statistical exercise, meaning that the average person is the person we treat. So, to translate, personalized medicine is a kind of fallacy. Personalized medicine is a problematic concept because it originates within the field of genetics and genomics, which is also dominated by statistics. So, they intend to be personal, but in essence are not.

For the sake of analysis, you have to simplify the complexity of drug dynamics. For that reason, I use these conceptual tools: drug trajectories, drug cycles, social lives of medicines and drug, set, and setting. Are they perfect? Of course not. For instance, the anthropological approach of social lives of medicines does not take on board the whole issue of agency in the way that the constructivists do. To understand agency is important in order to understand the deep sense in which medicines have invaded the capillaries of society. For instance, psychoactive drugs are being used in medical and non-medical contexts that are connected and in constant flux. This is an important feature for understanding the opioid crisis. But, before we apply any of these approaches, we first have to pay attention to the research question and see what conceptual tools are required to do the job.

RZ: *You have a very special position as a former pharmacist, because, as far as I understand, your work has a strong constructionist view. Substances are seen as a result of their pharmacological effect plus their set and setting. This means that your point of departure is, at least, that pharmaceuticals do not produce universal biological effects. Can you comment on this idea?*

TP: What I like about the social lives of medicines approach that started with Sjaak van der Geest[5] in the Netherlands is this whole idea of the social interaction between the person who prescribes a drug—the doctor—and the patient. The

4. Norman Zinberg, *Drug, Set, And Setting: The Basis for Controlled Intoxicant Use* (New Haven, CT: Yale University Press, 1986).
5. Susan Reynolds Whyte, Sjaak Van der Geest, and Anita Hardon, *Social Lives of Medicines* (New York: Cambridge University Press, 2002).

consulting room represents an anthropological encounter between the doctor and the patient. They both interact as part of this act of prescribing and being prescribed. And this is something that has been studied less within the constructivist perspective. So, that's why I really appreciate the anthropological approach. This social contract between the doctor and the patient, between the patient and the pharmacist, and between the patient and their relatives is an important part of the trajectories of drugs. It should be studied even more than it is and with mixed method approaches to further our understanding of issues like compliance and non-compliance. It is interesting to see, for instance, the influence of a charismatic doctor in the act of prescribing and being prescribed. Is it that patients will be more compliant with a charismatic doctor, or is it more likely that the faith in the social contract will be higher, and there will be a more effective treatment outcome? In this consulting context, the placebo and nocebo effects are also constructed. Promise, hope, faith, and disappointment are all part of this effectiveness construction during the treatment process.

That's why I came up with this drug cycle concept in the first place. We have to acknowledge the power of imagination and drug marketing. Imagery is as much part of the fabric of drugs as chemistry and pharmacology. The circulation of these drug images (which may turn into standard icons) succeed in bringing something immaterial to the drugs themselves: an aura of allure or fantasy, the mysterious fever of the benefit of the new, or the anxiety about doing good with no harm to body and mind. It filters out eventually. You can reduce it by focusing on certain aspects of this transaction between the healer and patient, between the patient and his/her relatives, or focusing on the over-the-counter transaction. So, you have to take subsets or focus on sub-contexts of drug use.

What I find amazing is that the economics and marketing of drugs have not yet received much attention by scholars as an integral part of drug trajectories. The economics of drug use is very much a part of what a patient perceives as an effective drug. Patients tend to think that expensive branded drugs are better than the cheap generic alternatives. The same is true for other consumer goods, and the marketers do everything they can to reinforce this belief. This is also something that is undervalued in discussions about these extremely costly new generations of medicines being introduced by the pharmaceutical industry. The more expensive, the more effective people think these drugs are. The psychology of taking expensive drugs interferes with the biological effects of these drugs. So, it is always about interrelatedness—about interfering with different spheres when it comes to pharmaceuticals and also other medical interventions.

I believe that with my constructivist historical approach I can contribute, for instance, to rethinking the opioid crisis or to rethinking the development of

drugs. This may sound a little bit overly optimistic—or maybe arrogant—to say that, yes, as a pharmaceutical humanities scholar, I can contribute to the development phase of a drug. What I see in the long run is that you have these dogmas in research, these fashions, so to speak. Time and again, everybody copies the same research perspectives and approaches in the pharmaceutical industry, producing endless series of me-too drug compounds. Whereas the complexity of diseases asks for interdisciplinary and creative approaches. You need intermediaries who both understand the biological and the social sides of the coin. Without taking both into account, you leave out essential elements in what constitutes or makes an effective medicine. Dogmas are there to deconstruct. And by deconstructing the dogmas, you can offer alternatives.

Go back into history. Take seriously how people in the nineteenth and early twentieth centuries used certain therapies that we have forgotten about. Take seriously past experiences and practices, whether it concerns plant medicines, serum therapies, or chemical pharmaceuticals that went out of fashion. We tend to forget about old therapies, a kind of selective amnesia that prefers new promises. But old drugs can reemerge in new dosage forms that are presented as new and promising. Exemplary in this respect is oxycodone, which was introduced in the 1920s, and then almost forgotten about until decades after World War Two. It was reintroduced as a new slow-release painkiller in the 1990s by Purdue Pharma. In the 1920s through the 1960s a lot of experience was built up coping with oxycodone-related addiction risks and harm reduction schedules. Unfortunately, amnesia prevented doctors from remembering the serious habit-forming qualities of oxycodone and the need for prescription monitoring. We should try to understand why we tend to forget. This may provide new inroads in innovation processes in drug development and drug use.

RZ: *A lot has been discussed, without any consensus being reached, about the concepts of addiction, tolerance, and non-compliance in the field of prescription drugs. Could you share some of your thoughts about how these concepts apply (or not) to the case of people who use prescription drugs regularly?*

TP: Addiction, of course, is related to the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*). You have definitions of addiction that tend to mostly serve the treatment protocols and insurance payment criteria. But addiction is far more. It is about the discomfort, and the breaking apart of a person's social situation and social network and living with a stigma. The disruptive qualities of addiction are almost never associated with habit formation in the case of prescription medicines. It can be a silent and creeping process with regular refills.

There is not an immediate problem, but, gradually, the dependence or addiction on prescription starts to manifest itself in disruptive ways. The moment you have to start buying drugs from illegal markets outside of the medical prescription context, it all changes. You are dependent on a particular drug, but there is no longer a refill that suits your needs. You have to go somewhere out there to buy or to steal it. It becomes quite a different thing.

It is quite amazing to see the lack of knowledge by doctors and pharmacists—as the historically self-proclaimed gatekeepers of opiates—about the addictive qualities of particular prescription drugs, about what it means to get addicted, and about what kinds of harm reduction treatments are available. They have a rule that when they stop prescribing a habit-forming drug, they should taper the patient. So, they slowly deprescribe the drug—for instance taking a forty-day period to taper. But to think then that each patient will have no further urge to use the drug after forty days is a misunderstanding of the whole concept of addiction. It disregards the need for expertise regarding substitution therapy. That really worries me.

It is rather awkward that the gatekeepers of opiates have little expertise and knowledge about addiction and harm reduction substitution therapies. That amazes me. That is what I find most shocking about the opioid epidemic in general, and also about the fact that, for instance in the United States, you have these emergency packages with naloxone to treat overdoses. In itself that is ok, but there are no clean antagonists. There is always an agonistic effect. So, you should be aware of that. It is not like, yes this is the wonder drug. There are no wonder drugs.

That is something I keep being surprised about: the holy belief in miracle drugs, in magic bullets, in wonder drugs. We hope that they are there to provide us with a fountain of youth. But it's a complete misconception of the complexity of the body, the interaction between the drug and the body, and the set and setting of drug use. Still, we like to believe in wonder drugs, and periodically, twice a decade or sometimes even more frequently—depends on the "pressure" in the medical system—we blow off steam regarding disappointing oversold promises. We go into procession and pray collectively to the Lord for this new wonder drug. Whether it is Prozac, Viagra, or another new promising drug that comes along the line. You always end up with unfulfilled promises, and the whole cycle starts again. But these processions, collective forms of mass hysteria about a new wonder drug, are a repeating phenomenon. We collectively let out the pressure from the medical system and then things calm down. And we are waiting for the next procession that will be fueled by our rather childish disappointment that eternal life is further away than what we thought.

RZ: *The idea of a drug's life-cycle, or drug career and the Seige Cycle, is an analytical tool you use to describe and analyze the different drug trajectories (interferon, cannabis, choral-hydrate, methamphetamine, benzos, and so on). What sources inspired you to build up this concept and how does this idea differ from others focusing on the social lives of medicines?*

TP: The idea came from the hype cycle phenomenon, the Gartner Cycle, etc. from the fields of economics and sociology. It is also about life and product cycles, and it is interesting to see what kind of repeat mechanisms there are in the social lives of medicines. In talking about careers or biographies, there is the danger that you underestimate the influence of contingency. Because the moment you start talking about repeat mechanisms, then you run the risk of introducing predetermined drug trajectories. And of course, that is not the case. But on the other hand, it shows you certain common patterns in the lives of drugs, and it also enables you to include fashion research in your analysis. As pharmaceutical studies scholars, we should be open to what economic historians and fashion historians have to offer us.

Fashions are so important, not only in the context of drug development and drug use, but in medicine in general. And it is quite a thing, because we always would like to speak about evidence-based medicine as an important step forward, but there are fashions in evidence. The fashions are paradigmatic, and paradigms withhold us from innovation. At the same time, if we speak about fashion in evidence, it also shows us that science can, on the one hand, be an objective measure. But on the other hand, it can be a subjective way of looking at things. So, it is opening our eyes for certain developments but also closing our eyes for others. That's what I like about questioning evidence. It always makes sense to debunk evidence. Contextualizing evidence enables you to ask questions that have never been asked. So, it is more complicated than the more we know the better we can treat.

Every new solution produces a new problem. That is a general rule I encountered in most case studies. The moment you solve a problem in medicine with a drug, a new problem arises. One of the most telling examples of this phenomenon was in the 1990s with the development of a new generation of anti-TNF-alpha biological agents for the treatment of rheumatoid arthritis. Up to that time, this crippling disease was treated with corticosteroids used in combination with NSAIDs (Nonsteroidal anti-inflammatory drugs). In the waiting room of the rheumatologist, you would see people in wheelchairs, people with canes, disabled patients. With the arrival of the biologicals, the wheelchairs and canes almost disappeared overnight. So, it seemed a great step forward with impressive quality

of life gains. But, at the same time, you had a new phenomenon, of a higher drug-induced mortality in young patients. And it changed the conversation in the consulting room. It was:

> Am I going to take that risk? I am in my 30s, I have this really problematic early form of rheumatoid arthritis, but I still want to have children. Am I going to take the biologicals that will improve my quality of life significantly? What about the risk of dying due to that very same therapy?

So, the patient discourse and moral issues changed with the arrival of the new drugs with new health challenges.

RZ: *I've seen you a couple of times in your lectures or research meetings commenting on the usefulness of concepts such as medicalization and pharmaceuticalization. This kind of criticism has been increasing in recent decades. Could you comment a bit more about your own criticisms of these concepts?*

TP: What I find problematic about medicalization—but also pharmaceuticalization—is the political and ideological dimension. In the 1970s, medicalization was part of a democratization process to open up the stronghold of medicine and associated power structures. It was strongly influenced by Marxist ideologies. It really did a good job within this particular context. But once you have debunked medicine, you have to rethink the conditions for using the conceptual frame of medicalization to critically question the concept and its analytical power. So, I think it is still important to discuss medicalization and pharmaceuticalization but to do it in a smart way and not only in a kind of top-down, ideological way. Because if you closely look at medicine in action, it's bottom-up and top-down. It is both. They interact; it is supply and demand.

If we talk about drugs, for instance, we always talk about these waves of supply and the abundance of supply. We find it difficult to talk about consumption demand issues—that people demand certain drugs, that people don't like to change their lifestyles. Instead, it's dangerous to say: they like to take drugs to prevent lifestyle interventions. This is something we do not like to hear because doctors are instructed to intervene—more and earlier—into "unhealthy" lifestyles. But in medical school, I already taught the medical students: do not expect this to be an easy job, because it is so difficult to intervene into personal lifestyles. Maybe in the short run, you may produce some results. But in the long run, people love to embrace bad habits. They are so disciplined that they love to be undisciplined.

Medicalization is the result of both bottom-up and top-down processes and supply-and-demand interactions. The same holds for pharmaceuticalization. Our

longing for eternal life means that most people confronted with, for instance, cancer, chose to survive, of course, when given the option—and they are prepared to go for the utmost. The utmost means enduring horrible side effects, meaning all kinds of quality-of-life issues. So, it makes sense to interview people taking these new generations of so-called wonder drugs that can prolong life for three to five years despite having melanoma or having lung cancer. They perceive these drugs as miracle drugs, but, on the other hand, all kinds of new questions are raised within families. For example, they prepare for funerals twice, three times. It is a burden for a family to be confronted with a "living dead" person. So, pharmaceuticalization raises moral issues that go far beyond the supply-driven forces within the pharmaceutical industry and pharmaceutical marketing.

RZ: *I would like to pick out two passages from your paper "Cultural Enthusiasm, Resistance and the Societal Embedding of New Technologies: Psychotropic Drugs in the 20th Century,"[6] published in 2007 with Stephen Snelders and Frank Geels.*

The first one is: "Despite public debates and concerns over addictive and potentially harmful consequences, public demand for benzodiazepines continued to grow" (p. 158); and the second is: "Apparently, the quest for solutions to problems of stress, anxiety and nervousness was bigger than the fear for possible side effects" (p. 159).

If we think about drugs as biotechnologies, it seems that the wave of resistance and concerns about the long-term effects of benzodiazepines has not been enough to prevent the rise or maintenance of their use. Could you comment on this?

TP: What we actually see is that there is quite a disparity between the public discourse in the news media about certain drugs and the actual use and prescribing practices in the consulting room. This applies both to the Valium-Librium family or the Prozac-SSRI (Selective Serotonin Reuptake Inhibitor) family. Regardless of the negative media news, in the consulting room people are trying to look for solutions to their everyday problems, such as anxiety, stress, depressive moods, and mood swings. We can call them everyday problems, but still they are annoying, and they can be bothering and a burden. So, the doctors and the patients are searching for whatever solution there is at hand. Yes, we all like, in principle, the idea of going to the therapist, and talking about our problems, and we do so. But, at the same time, we keep taking drugs, regardless of all kinds of drug scandals.

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6. Frank W. Geels, Toine Pieters, and Stephen Snelders, "Cultural Enthusiasm, Resistance and the Societal Embedding of Psychotropic Drugs in the 20th Century," *Technology Analysis & Strategic Management* 19, no. 2 (2007): 145–65, https://doi.org/10.1080/09537320601168052.

This was the case in the 1980s with rather strong public sentiments towards the benzos, and the same happened in the 2000s with the SSRIs. So, it is interesting to see: the SSRIs are acknowledged as antidepressants, but in every day practice, they became replacements for benzos. What we see is that the greater number of prescriptions for SSRIs are for treating anxiety-related problems. Stress and anxiety are part and parcel of modernity and post-modernity—an existential problem we have to deal with. And people want to take drugs for it.

So, yes, in public discourses about what people say they do and what people really do, there is an enormous disparity in all contexts. What the doctor says he or she prescribes, and what the patient says he or she does, and, in reality, what he or she will do—or the pharmacists or any other person involved in the medical context—is a different thing.