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Fluid Drugs: Revisiting the Anthropology of Pharmaceuticals

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Abstract

This review discusses a growing body of scholarship at the intersection of anthropology and science and technology studies (STS) that examines how drugs are rendered efficacious in laboratories, therapeutic settings, and everyday lives. This literature foregrounds insights into how commercial interests and societal concerns shape the kinds of pharmaceutical effects that are actualized and how some efficacies are blocked in response to moral concerns. The work brought together here reveals how regulatory institutions and health policy makers seek to stabilize pharmaceutical actions while, on the front lines of care, pharmacists, health workers, and users tinker with dosages and indications to tailor pharmaceutical actions to specific circumstances. We show that there is no pure (pharmaceutical) object that precedes its socialization. Pharmaceuticals are not "discovered"; they are made and remade in relation to shifting contexts. This review outlines five key areas of ethnographic and STS research that examines such fluid drugs.

INTRODUCTION

This review discusses a growing body of scholarship at the intersection of anthropology and science and technology studies (STS) that examines how drugs are rendered efficacious in laboratories, therapeutic settings, drug outlets, and everyday lives across regulatory settings in the Global North and South. It is a sequel to the 1996 *Annual Review of Anthropology* article, "The Anthropology of Pharmaceuticals: A Biographical Approach" (van der Geest et al. 1996), which, inspired by Kopytoff (1986), focused on the social lives of pharmaceuticals (see also Whyte et al. 2002).[1] Since the mid-1990s, attention to pharmaceuticals has surged within both anthropology and STS. This article asks what can be gained by breaking open the pharmaceutical object and examining efficacy as a processual, relational, and situated event, as well as a pharmacological one.

As a discipline, anthropology has been marked by a tendency to read other people's engagements with the material world through the Western distinction between a thing and its representation (Henare et al. 2007, Kohn 2013, Latour 1993). Earlier medical anthropological analyses of pharmaceuticals somewhat fell prey to such dichotomizations, differentiating between the chemical properties of pharmaceuticals and their sociocultural interpretation. In an effort to highlight the extra-pharmacological efficacy of drugs, anthropologists showed how ritual, symbolic, and culturally structured responses shape how people use, experience, and generate healing with pharmaceutical substances (Etkin 1992, Granado et al. 2011, Helman 1978, Nichter & Vuckovic 1994, Prince & Geissler 2001, van der Geest & Whyte 1989). Our review of recent theoretical and empirical work suggests that there is no pure (pharmaceutical) object that precedes its socialization and interpretation. We argue that molecules are not "discovered" but made and remade; they are fluid, ever evolving in relation to their context. Our analysis is inspired by Barry (2005), who argues that chemistry is a science of associations in which molecules are "informed." In laboratories, researchers extract, isolate, purify, and modify such informed pharmaceutical material. This material then comes to act not in controlled laboratory settings, but "in living labyrinths whose topology varies in time, where partial and circumstantial causalities are so intertwined that they escape any a priori intelligibility" (Bensaude-Vincent & Stengers 1996, p. 263).

We discuss five key areas of ethnographic and STS research on pharmaceuticals that meticulously probe and examine these "living labyrinths." The first focuses on how pharmaceuticals are made into "informed materials" (Barry 2005, p. 52), looking specifically at the situated knowledge practices and techniques used to measure pharmaceutical action in clinical experiments. The second unpacks how differently constituted state–market nexuses and regulatory environments shape pharmaceutical action. The third theme examines the downstream informing of pharmaceutical materials that takes place through marketing and rescripting (Akrich 1992, 1995; Hardon 2006; Walsh & Goodman 2002). The fourth group of texts investigates how care practices (such as doctor–patient interactions and those that take place over the pharmacy counter) deactualize or reactualize pharmaceutical actions that may align with or disrupt the efficacies crafted in clinical trials. The final group of texts dissolves the boundaries between pharmaceuticals, bodies, and their environments. The literature presented here examines what lies beneath the pharmaceutical object's surface, unpacking the thing and attending to the evanescent nature of pharmaceuticals (Sanabria 2009), as objects destined to be digested, absorbed, and excreted.

Our analysis owes much to Ingold's (2011, 2012) critical engagement with material culture studies, in that we approach pharmaceuticals as never finished and as "always on the way to becoming something else" (Ingold 2011, p. 3). Ingold (2012) proposes a shift from studying objects

[1]This review excludes anthropological studies of addiction because these were covered in a recent review in this journal (Garriott & Raikhel 2015).

to knowing materials, which requires that we follow "matter-flow" (p. 433). Matter is always in movement, being molded and transformed by human and nonhuman processes and practices. We adopt this approach to shift the focus from an object-centered one, which dominated the anthropology of drugs in the 1990s and 2000s, to a process-centered approach that examines the articulations, dearticulations, and rearticulations of pharma-matter.

MAKING PHARMACEUTICALS WORK IN CLINICAL EXPERIMENTS

Prior to the emergence of randomized controlled trials (RCTs), therapeutic experiments with pharmaceuticals were conducted by chemists and doctors, at times on their own bodies. To overcome the limitations of case reports and isolated experiments, clinicians pooled their insights in cooperative investigations, which led to the consolidation of the RCT model of demonstrating safety and efficacy (Gaudillière 2007, 2008; Marks 2000). In the aftermath of the thalidomide disaster of the 1960s, regulatory agencies demanded proof of safety and efficacy before allowing pharmaceuticals on the market. Safety was thought to be guaranteed through the inclusion of a sufficiently large population that would give statistical power to the analysis and enable a comparison between the placebo and active arms of a trial (Gaudillière & Hess 2013). Anthropologists have critiqued such trials for taking a universal biological body as their point of departure, ignoring the social and infrastructural conditions that impinge on how technologies work and insufficiently attending to the benefits of placebo effects (Adams 2016; Biehl & Petryna 2013; Epstein 1998, 2004; Saethre & Stadler 2010). They call for new conceptual approaches that acknowledge how efficacy is mediated by context and influenced by expectations and user practices (Brives et al. 2016, Hardon & Pool 2016).

In her comparison of an American and French methadone clinical trial, Gomart (2002) develops a framework for understanding how efficacy is constructed. Arguing that substances do not have essential properties that are discovered in RCTs, she describes how the different effects of methadone must be understood with reference to the *dispositifs*[2] engaged in the trials. Her analysis points to a striking difference in the effects identified by the two methadone experiments: American researchers found that methadone blocks drug cravings and returns the user to a useful social life; French researchers found that the drug is "rarely therapeutic; it does not cure but is very instrumental in 'revealing the psychopathology' of the drug user" (Gomart 2002, p. 94). These differences are not related merely to different interpretations of the researchers nor to underlying differences in the kind of methadone tested. Rather, Gomart argues, to understand the different effects, we need to examine the techniques used in trial *dispositifs* to measure and generate effects and link them back to substances. Similarly, Laplante (2015) shows how the therapeutic efficacy of *Artemisia afra* in traditional South African settings is mediated by the practices of *isangoma* healers. Mapping the labor of translating this highly contextual efficacy to one that can be measured in the preclinical trial, she shows how the purified plantation-produced herbs are not the same thing when they are brought into the controlled setting of clinical trials.

These studies reveal how the *dispositifs* of the RCT and the techniques used to evaluate drug action deeply shape not just what is known of the molecule, but also how it acts and what it does. The influence of *dispositifs* is particularly clear in studies of innovative trial designs in the field of "psychedelic" psychiatry. Clinical trials designed to study the effects of psychotropic substances such as MDMA (3,4-methylenedioxy-methamphetamine) and LSD (lysergic acid diethylamide) acknowledge the profound influence of the setting on effects, including the pivotal role of the

[2]Gomart (2002) translates this term as "set-up," or one could also say "apparatus."

therapist who administers the drug (Dyke 2008; Langlitz 2012, 2016; Winkelman & Roberts 2007). Oram (2014) describes the experiment of the Spring Grove Group, in which LSD was used to help alcoholic patients overcome their addictions. Dosing sessions in this trial took place in a room made up like a comfortable living room, with a sofa and rugs, pictures and flowers, and a high-quality sound system. Eyeshades and music were used throughout the session, heightening emotionality and drawing the patients into their inner world. The setting and therapist directed the experience and helped patients feel safe and comfortable, encouraging them to let go and delve deeply into their minds. After the session, follow-up psychotherapy helped cement positive insights and experiences, ensuring lasting changes in patients' behavior and attitudes (Oram 2014, pp. 243–44).

Likewise, recent clinically oriented literature on the benefits of the placebo response points to the importance of the therapeutic relationship as a key mechanism for enhancing patients' responses to pharmaceutical treatment and optimizing care outcomes (Chaput de Saintonge & Herxheimer 1994, Kaptchuk & Miller 2015, Kirmayer 2011, Miller et al. 2009, Moerman 2013, Moerman & Jonas 2002). Such studies show that pharmaceutical efficacy is not just in the drug, but also synergistically potentialized by spaces, relationships, expectations, and ritual practices. These insights, and the novel trial designs that are emerging to account for such synergistic effects, challenge reductionist-materialist approaches that assume that symbolic significance or emotional and interpersonal dynamics do not affect pharmacological response (Thompson et al. 2009).

Furthermore, Nelson et al. (2014) show how the genomic turn in cancer clinical trials is changing how trials are carried out, linking patient data across clinics and generating evidence in a more open-ended way, allowing for unforeseen effects and incremental knowledge. The acknowledgment of heterogeneity in these more open-ended trials provides an opportunity to produce novel biological and clinical insights into pharmaceutical action (Hardon & Pool 2016, Montoya 2007, Nelson et al. 2014). In a fascinating ethnography on the development of a drug for heart failure, Pollock (2012) describes how BiDil was initially abandoned because it was found to be ineffective in the general population. Although clinical researchers had found that BiDil did work for African Americans, the company concluded that a drug for heart failure in blacks could never reach the scale of blockbuster drugs (see also Kahn 2013). However, given that existing remedies for heart failure [ACE (angiotensin-converting enzyme) inhibitors] were found to be less effective in blacks, a methods patent was granted for BiDil for its race-specific benefit, and a small biotech firm together with the Association of Black Cardiologists agreed to support a trial for this specific indication. In 2001, the trial started with a cohort of 1,050 self-identified black patients with heart failure, and the drug proved to be effective. Two years later, 43% fewer patients in the standard+BiDil group had died than in the placebo arm of the study (Pollock 2012). Pollock describes how, in this case, stakeholders aligned themselves in a practical project of making a specific pharmaceutical work. Alas, the drug has not, in practice, saved many lives because the target population in the United States fails to access health care, through which they could benefit from the treatment.

THE MARKET–STATE NEXUS

A substantial anthropological literature has examined the political economy of pharmaceutical drug development, raising concerns over the fact that trials are funded by pharmaceutical corporations and investment banks, who are motivated more by maximizing profit margins than by promoting health (Doshi et al. 2013; Dumit 2012; Healy 2006; Sismondo 2010, 2015; Sunder Rajan 2017). In such commercially driven research, academic and commercial interests are intertwined, leading to an emphasis on desirable pharmaceutical effects and to the downplaying of risks (Applbaum 2009, McGoey 2012). Driven by capitalist logics, companies focus on developing drugs for big

markets and chronic conditions, such as hypertension. Patients with these conditions are not cured nor do they die; rather they take "drugs for life" (Dumit 2012). Sunder Rajan (2017) discusses the globalization of harmonization strategies that enable local markets to produce drugs for the international market. He reminds us that such regulatory maneuvers are political acts heavily influenced by the interests of multinational corporations. Just as Biehl (2007) shows how health is increasingly pharmaceuticalized, Sunder Rajan (2017) unpacks the progressive capture of health by capital, a process by which health functions as an index whose value can be evaluated in terms set by the market. The transnational regulations involved include intellectual property and trade agreements, which regulate how long patent holders can retain monopoly rights over new chemical entities, and complex demands on how clinical research is to be done ('t Hoen 2002, Davis & Abraham 2013, Banerjee 2016).

Research into the political economy and symbolic regimes that surround the production and circulation of generic drugs has generated important conceptual insights for the anthropology of pharmaceuticals (Sunder Rajan 2017; Greene 2014; Hayden 2007, 2012; Sanabria 2014). A broad range of institutional rationalities underpin the management of therapeutic agents, and these differ across national contexts. Gaudillière & Hess (2013) propose that pharmaceuticals are regulated by the tightly coupled activities of physicians and pharmacists, drug companies themselves, the public, and judicial actors, in addition to administrative and state actors. These regulatory instances govern the development, marketing, and use of pharmaceuticals, as well as the creation of new molecules. Cassier & Corrêa (2009) present a fascinating study of resistance to these global regimes, showing how government-sponsored laboratories in Brazil made use of a loophole in international trade laws to permit them to work on reproducing several antiretroviral drugs before their patents expired. The chemical engineers did much more than copy the drugs; through reverse engineering, they improved the drugs and decreased their side effects. The Brazilian government now uses these cheaper and safer drugs for its national HIV prevention program, and Brazil was the first in the world to include in its constitution access to AIDS medicines as a human right (Cassier & Correa 2014).

Hayden's (2007, 2012) seminal work on generic pharmaceuticals unpacks the self-evident perception of chemistry as a stable material anchor out of which socially mediated effects can be read. Her study of generic substitution in Mexico describes the effects of international regulatory contests over how evaluations of the "same" are made. Mexico's adoption in the late 1990s of the standard of "bioequivalence"—a threshold used by the US Food and Drug Administration and favored by pharmaceutical multinationals—required that a generic molecule should not only look structurally the same as the original, tested molecule but also be metabolized in a sufficiently similar manner. Her ethnography questions not only the entanglement of regulatory standards and market interests but also, at a more conceptual level, whether the efficacy or even the identity of a drug can ever be reduced to its active chemical ingredients (Hayden 2012, p. 276). In this extraordinary scenario, the transnational pharmaceutical industry ends up insisting that pharmaceutical efficacy cannot be (entirely) reducible to chemical composition. In the face of generic competition, the pharmaceutical industry has repeatedly embraced a position that effectively multiplies the constitutive "givenness" of chemical matter, making it fluid. This tactic gave tremendous importance to small variations in molecular structure and revealed that individual metabolism, brand loyalty, and inactive chemical components used in drug delivery all affect a drug's action.

In a very different context, in Nigeria, Peterson (2014) describes how multinational pharmaceutical companies did not seek to protect their regional market interests but abandoned the country when an economic crisis and subsequent structural adjustment policies had reduced their purchasing power. Peterson describes how consumers turned to local traders, many of them involved in international narcotics trade, who import relatively cheap generic drugs from India and sell them

in local markets as well as through pharmacies. Peterson (2014) introduces the concept of "chemical arbitrage" to describe how chemical content and resulting efficacies change in response to market and regulatory dynamics. The generic suppliers make pills with the least possible amount of active component to meet regulatory demands, allowing them to cut costs. In this context, consumers ingest brand-name drugs in suboptimal dosages. For example, due to suboptimal dosages of antibiotics, antimicrobial resistance is on the rise, impacting not only the health outcomes of individual patients but also the future health of the whole Nigerian population.

Market–state dynamics are different for other categories of pharmaceuticals, such as vitamins, supplements, and commodified herbal medicines. Here, regulatory processes are less stringent. Anthropologists who study Asian medicines, for example, point to the way in which nation-states in Africa and Asia seek to facilitate the market entry and export of commodified herbal drugs through subsidies and relatively loose regulatory mechanisms (Blaikie 2015, Hardon & Idrus 2015, Lai & Farquhar 2015, Langwick 2015, Pordié & Hardon 2015, Wahlberg 2014). Pordié (2015), for example, shows how in India Ayurvedic medicines are reformulated for both local use and export. As long as preparations are referred to in ancient texts, they do not need to be tested in clinical trials in India, making market entry much faster. Indeed, as is the case with modern pharmaceuticals, there is an increasingly global market for Asian medicines. Langwick (2015) describes how, with Chinese financial and technical support, the Tanzanian state commoditized local traditional medicines, whereas Hsu (2015) shows how the country became a market for Chinese drugs, including purified artemisinin for the treatment of malaria.

DOWNSTREAM INFORMING

Once on the market, pharmaceuticals are often reinscribed with new information about their efficacy. This reinscription process often happens when companies face generic competition as patents run out. In addition to seeking to disqualify generics on the basis of a lack of bioequivalence, companies may seek to evergreen their products by linking them to new indications. An elucidating example is that given by Greenslit (2005), who describes how Pfizer successfully remarketed fluoxetine (the active principle of Prozac) as a treatment for premenstrual dysphoric disorder. The company gave the drug a new name (Sarafem), color (pink), and indication (premenstrual dysphoric disorder) and encouraged women to experience their menstrual cycle symptoms as worthy of treatment while avoiding a negative association with depression. Similar rescripting strategies have been described by Conrad (2006) and Lakoff (2000), who depict how Ritalin led to the change in diagnostic categories for attention deficit hyperactivity disorder (ADHD). Healy (2006) points to the emergence of social anxiety disorder to boost the sales of the antidepressant Paxil, and Hartley (2006) describes the "pinking" of Viagra to expand the market to female sexual dysfunction when the patent for erectile dysfunction was expiring.

Companies promote certain medical efficacies, but they also link their brand to a population of customers and lifestyle needs through attractive imaginaries, promising happiness, health, mood-swing-free menstruation, and more (Droney 2016, Ecks & Basu 2009, Jenkins 2011, Nakassis 2013, Quintero & Nichter 2011, Wolf-Meyer 2014). Martin (2006, p. 282) illuminates how marketing works by foregrounding carefully engineered images and concepts with sparse language designed to capture desires and hopes, while transposing in minuscule font the potential side effects that are not really meant to be read. These imageries, or placebo texts (Degrandpre 2006), deeply shape the way pharmaceuticals are experienced and work.

In linking drugs with attractive imaginaries, manufacturers have to navigate prevailing moralities, even if these moralities stand against their market interests. Wentzell (2011) describes how Pfizer, in advertising Viagra for men, chose to ignore its widespread use in gay communities as a

recreational drug. Rather, it stuck to the script that Viagra is a treatment for erectile dysfunction, a medical condition. Through advertisements showing married heterosexual couples embracing, Viagra was marketed as a couple's cure that would strengthen the social fabric through sex (Baglia 2005). Interesting in this regard is that the US Food and Drug Administration opposed the marketing of the drug for sexual pleasure, even for heterosexual men. It requested that Pfizer pull advertisements showing a man growing devil horns at the sight of lingerie, arguing that the advertisements sold "sex" rather than treatment for the medical condition (Wentzell 2011).

Such moral constraints shape the informing of pharmaceuticals, but they do not necessarily prevent them from being used in morally disapproved ways (Gezon 2012, Race 2009, Wynn & Trussell 2006). Anthropologists have shown that information on libido and pleasure-enhancing efficacies of pharmaceuticals travels quickly in our globalizing world, where virtually any chemical can be ordered online and over the counter in states with weak oversight of pharmaceutical supply chains (Ecks 2013, Ecks & Basu 2009, Hardon & Idrus 2014, Sanabria 2014). Alternatively, as is done by young people who want to access legal amphetamines such as Ritalin, they can look up the indications for drugs and seek to obtain them through their doctors by feigning symptoms (DeSantis et al. 2008).

The case of misoprostol is especially interesting in this regard. This drug, originally on the market for the treatment of ulcers, became known worldwide for its efficacy as an abortifacient. De Zordo (2016) describes how knowledge accumulated by women in Brazil circulated from the streets and women's homes to scientific laboratories and hospitals worldwide. Women's experience and subsequent publicly funded research led to the confirmation of misoprostol's abortifacient properties and to more detailed safe administration guidelines. This example shows how such information travels, especially in countries where women do not have access to safe abortion services.

The rescribing of pharmaceutical action that takes place after market entry, through advertisements and appropriation by consumers, points to the ever-emergent nature of pharmaceutical effects. These can be fully understood only by following pharmaceutical matter-flow through the trajectories of development, regulation, marketing, and use. The processes are anything but linear: Rescribing often informs new clinical research, whereas regulatory or national moral concerns may block certain drug indications from market entry. Whereas clinical trials are designed to inform about pharmaceuticals and convince regulators with evidence of the effects of pharmaceuticals, advertising and branding are designed to inform about pharmaceuticals using placebo and social efficacies.

MAKING PHARMACEUTICALS WORK IN CARE SETTINGS

In her study of Tibetan medicines, Craig (2012, p. 7) says, "[O]ne cannot really know whether a medicine or therapeutic approach is efficacious until a practitioner makes and/or prescribes it, a patient uses it, and then reacts to its use." Likewise, Hsu (2012, p. 35) advocates a practice-based understanding of efficacy in which "the-plant-materials-of-the-environment-in-interaction-with-human-beings form a continuum." Indeed, pharmaceutical actions continue to be actualized, modified, and reactualized in care settings. Guidelines made by medical associations, governments, and insurance companies aim to regulate and stabilize pharmaceutical action and to discipline patients, but ethnographic studies show that these sites of stabilization can simultaneously become sites of innovation in response to patients' health concerns and other desires.

A significant body of ethnographic research draws attention to the micropolitics of power in everyday care where doctors are expected to discipline patients into adhering to biomedical regimens (Applbaum & Oldani 2010, Crowley-Matoka & True 2012, Hunt & Arar 2001). Mattes (2011) shows how in Tanzania, HIV-positive patients seek traditional healing practices that seem easier

to handle, more appropriate, and less harmful than antiretroviral drugs. In Uganda, Kyakuwa & Hardon (2012) describe how nurses who are themselves HIV positive team up with their patients in resisting biomedical guidelines that advise against the use of traditional medicine by incorporating a traditional cream into the AIDS program to alleviate the side effects of antiretroviral treatment. Similarly, ethnographic studies of doctor–patient interactions around another chronic condition—asthma—describe how patients modify their use of drugs (Fortun et al. 2014, Willems 1992), evaluate the effects of inhalers alongside other traditional remedies (Whitmarsh 2008), and experiment with pharmaceutical regimes (Persson et al. 2016, Trnka 2014).

Medical anthropologists have focused more on the practices and experiences of patients than on those of medical doctors, though recent ethnographies show how doctors are also reflexive about their practices. Whitmarsh (2008) shows how doctors in Barbados are concerned about the influence of the pharmaceutical industry on asthma guidelines, which advise doctors to measure patients' lung function before and after the use of pharmaceutical bronchodilators. These doctors observe that with this new technique more adults and children who have not experienced asthma attacks or wheezing are being diagnosed as asthmatics, and they have expressed concern that they are overprescribing the drugs. Mol (2008) describes how doctors in diabetes care align themselves with patients by tinkering with pharmaceutical regimes to adapt the treatment protocol to the specific situation of each patient. Mol argues that, in the practice of doctoring, general practitioners know that evidence from RCTs and treatment guidelines based on these trials do not necessarily apply to all patients. They observe pharmaceutical action in practice, in a much larger and more diverse population than those included in clinical trials (see also Knaapen 2014).

Sanabria's (2016) ethnographic study of the prescription and consumption of sex hormones in Brazil maps the rescripting of side effects (such as menstrual suppression) into primary effects.[3] She examines how new efficacies are made for hormones, which are injected, implanted, or diffused transdermally or through the uterus in addition to being administered orally. In this loosely regulated context, where drugs are bought out of pocket and not subjected to national or private insurance approval, patients obtain hormones from doctors or pharmacists for an ever-widening array of purposes beyond contraception, for example, to relieve premenstrual tension, increase libido, lose weight, and build muscle during workouts (Edmonds & Sanabria 2014). This potential for downstream pharmaceutical informing in care settings is not lost on pharmaceutical corporations, who make use of their sales representatives to gather information from prescribers on how their patients experience drugs (Oldani 2004). Pharmacies are thus key sites where pharmaceutical action is negotiated and reactualized (Das & Das 2006, Kamat & Nichter 1998, Sanabria 2014). Kamat & Nichter (1998) point to the proliferation of pharmacies in Mumbai slums, where virtually any drug can be bought without a prescription. Pharmacies, they argue, are primary care providers. In industrialized settings, where sales are more regulated, pharmacists position themselves as first-line carers with pharmaceutical expertise, and they are increasingly being called on to monitor patients' use of drugs for chronic conditions such as asthma, hypertension, and diabetes. However, little anthropological work has been done on the rearticulating of pharmaceutical actions in pharmacies.

LEAKAGE: LUNGS, GUTS, AND METABOLISM

The studies that we have reviewed thus far take us only up to the moment at which pharmaceuticals are consumed, as in ingested, digested, and absorbed (Sanabria 2016). Such research focuses less

[3] See also Etkin (1992) and Kamat & Nichter (1998) on the reinterpretation of side effects.

on the dissolution or other metamorphosis of pharma-matter when it enters and leaks out of our bodies. Ingold (2012) makes this point when he argues that studies of materiality focus on the "materiality of objects" without giving sufficient consideration to materials and their properties. These change as they move not only through space and time but also through the body, which is "sustained thanks to the continual taking in of materials from its surroundings, and in turn, the discharge into them, in the processes of respiration and metabolism" (Ingold 2012, p. 438).

A new space for critical reflection has opened at the intersection between ecological understandings of pharmaceutical flows in, through, out of, and back into (human) bodies. We suggest that this space is an important area for future thinking about pharma-matter flows because, as Nading (2016) points out, pharmaceuticals are only one part of global health's chemical infrastructure, which includes insecticides, bleach, and other chemical agents that contaminate our environments and affect our health. As Murphy (2008, p. 696) observes, we are "altered by the pharmaceuticals imbibed at record-profit rates, which are then excreted half metabolized back into the sewer to flow back to local bodies of water, and then again redispersed to the populace en masse through the tap."

Landecker (2015) provides an example of how we can follow pharmaceuticals across bodily boundaries. She describes how antibiotics, while targeted at individual bodies, produce large-scale evolutionary and ecological events far beyond these bodies. They sediment a history of biopolitical risk management in the body politic of bacteria, which is changed genetically, physiologically, and ecologically in this distributed, porous environment of widespread antibiotic use. Landecker's (2013) historical reading of metabolism provides critical insights to think about this border between the inside and outside of bodies, between bodies and environments, and about pharmaceutical activity as emergence. She suggests that the very concept of metabolism brings about the notion of there being an organism distinct from the environment, while showing that "exchange of matter with the environment is not a peripheral activity engaged in by a persistent core: it is the total mode of continuity (self-continuation) of the subject of life itself" (Landecker 2013, p. 218).

Chemical infrastructures bring together, though in disjointed ways, experts, disciplinary knowledges, and ways of knowing and assessing such infrastructures. The problem for ethnographers of such distributed chemical relations is that it is not possible to directly follow the "living labyrinth" of chemical effects into bodies or ecosystems. Although anthropologists can directly observe visible practices (such as manufacturing, marketing, and prescribing), they must rely on others—scientists, patients, activists—when seeking to describe distributed, microscopic, topographically inverted, or otherwise invisible practices. Thus they are caught in a reflexive loop, enfolding in their description a description of describing, or rendering, to adopt Myers's (2015) terminology, as well as an account of the politics and practices that make certain descriptions come to matter. The fruitful dialogue between medical anthropology and STS has led to a spate of new work that does not take biomedical facts for granted in anthropological analyses but rather critically engages with pharmacological, toxicological, and environmental facts as knowledge practices in and of themselves. These ethnographic works show how knowledges are constituted through practices of expertise and seek to develop ways of engaging with scientific evidence as historically situated, emergent, negotiated, strategically rendered, partial, and incomplete (Heimer 2012, McGoey 2012, Healy 2006, Sismondo 2015).

Bodies are not the passive site of pharmaceutical action but the "penultimate multisensory organ" (Thompson et al. 2009, p. 128). Wilson's (2015, p. 89) analysis is exemplary here, when she notes that more attention has been given to how "SSRIs are represented, marketed, and prescribed" than to how they are "physiologically absorbed, distributed, metabolized, and excreted." Her analysis of the pharmacokinetics of SSRIs does not attribute "all the pharmacological agency to the pill" (p. 99) but asks about the broader networks of alliances through which bodies and minds

exert their influences on the drugs. Her objective is to critique the brain-centeredness of critical theory and to mobilize biomedical data to show how the peripheral body (in particular, the gut) is involved in depression and its treatment. Wilson's (2015) analysis of how antidepressants become bioavailable in bodies highlights how the difference between a drug and its by-product, between primary effect and side effect, between distribution and elimination, is constantly made and remade. "These pills are not autocratic agents that operate unilaterally on body and mind; rather, they are substances that find their pharmaceutical efficacy by being trafficked, circulated, transformed and broken down" (Wilson 2015, p. 102). Wilson notes that she does not seek to build a seamless narrative, to reach consilience between pharmacology and critical theory, but rather to experiment with how these approaches can interrupt and reconfigure each other. Cousins's (2015a,b, 2016) ethnographic study of the entanglements of nutrition interventions and antiretroviral therapies in South Africa also leads him to examine the making of pharmaceutical efficacy in the gut. He tracks how expert attention to the gut intersects with local belly idioms of strength, depletion, and cosmological disorder, where magical snakes that occupy the belly, dispatched by unscrupulous kin, are treated with postcolonial emetics and purgatives. Likewise, Ecks (2013) traces the key importance of the belly and digestive metaphors in postcolonial reconfigurations of understanding of mental health, well-being, and kinship in Calcutta.

By calling attention to the inherent leakiness of pharmaceuticals (which must dissolve and be absorbed to be effective) and to their pharmacokinetics, bodies and their interstices also cease to appear so skin-bounded. The gut, lungs, skin, and metabolism function, instead, as zones of exchange between bodies and regulatory, postcolonial, and chemically saturated environments.

CONCLUSION

The work reviewed here demonstrates that pharmaceutical action is not reducible to the chemical properties of pharmaceuticals but is articulated, elicited, and informed within a meshwork of experimental, regulatory, and care settings. Brought together, these studies partake in a broader effort to attend to things-in-themselves without desuturing them from the practices and social dynamics within which objects come into being and through which they are made meaningful. Our analysis of the processes at stake draws inspiration from contemporary thinking that moves away from self-contained objects in structures to assemblages and processes of actualization, deactualization, and reactualization in fluid arrangements, characteristic of a broader turn toward Deleuze in social theory (Povinelli 2016). Attending to the movement and flow of pharmaceutical materials through research and development, regulatory regimes, advertising, and care practices, we point to the always-emergent nature of pharmaceutical action.

Our processual analysis first reviews research practices in which molecular action is actualized or blocked through situated techniques and devices. We have then shown how innovative trials harness the influence of the experimental environment to enhance the efficacy of materials. Here, diverse commercial interests and societal concerns shape the kinds of pharmaceutical effects that are actualized and reactualized and guide the entry of pharmaceuticals into the market. We have also highlighted how efficacies are ignored or blocked in response to moral concerns, while noting how the global flow of both pharmaceuticals and information about their effects means that regulatory and moral blockages can be circumvented in the hands of users and health workers such as nurses and pharmacists. We have described how regulatory institutions and health policy makers seek to stabilize pharmaceutical actions through guidelines, whereas on the front lines of care, pharmacists, health workers, and users tinker with dosages and indications to tailor pharmaceutical actions to specific circumstances. Pharmaceutical companies have long known of these

rearticulation practices, which they capture through market research in order to rescribe materials with new potentials. Finally, we have turned to a range of authors who follow the matter-flow into bodies. Recent anthropological research into how guts metabolize pharmaceuticals and render them effective by making them bioavailable can be read alongside literature that examines the toxic flows of chemicals in postindustrial landscapes. After pharmaceuticals are absorbed into human metabolisms, they leak back out into water cycles, troubling and reconfiguring topologies and understandings of causality (Fortun 2012).

Our review points to a methodological horizon beyond multisited fieldwork (Marcus 1995), one that connects the synthetic chemicals at the heart of the pharmaceutical nexus (Petryna et al. 2006) with those that are only beginning to enter the scope of global health's concern with environmental health and toxicity. New work is emerging that attempts to think these "witting and unwitting efficacies" together (Sanabria 2016), linking the carcinogenic side effects of the massive global health rollout of antiretrovirals to toxic capital (Livingstone 2012) and explicitly tying the defense of national welfare infrastructure to reduced environmental regulation and tax breaks for petroleum-dependent industries, which saturate environments with toxic waste (Murphy 2011). A focus on pharmaceutical flows thus requires seeing the body as porous and in constant exchange with its multiply constituted environments. For anthropologists, the challenge remains being critically reflexive about how we mobilize biological, pharmacological, and ecological understandings and to what ends (Fraser 2003, Lock & Nguyen 2010). The task cannot be just to replace one biological metaphor or construct with another, such as a brain-centered account of depression for a gut-centered one. Rather, evoking other biological metaphors may reveal the multiplicity of medical and scientific practices (Berg & Mol 1998, Mol 2002).

This review aims to bring together a range of generally unrelated anthropological work on pharmaceuticals (on their political economy, practices of evidence and regulation, marketing, and use in care settings) with a focus on how materialities come into being locally. The anthropological literature on pharmaceuticals tends to focus separately on how pharma-matter is informed in regulatory and evidentiary practices or on how it is used in local, stratified practices that span the Global North and South. We bring these stories together to ask which efficacies are enabled or actualized out of the myriad possible local iterations of pharmaceutical action. We have suggested that there is no pure (pharmaceutical) object that precedes its socialization: Social practices, market interests, and experimental regimes may potentialize or agonize new pharmaceutical efficacies. In this sense, pharmaceuticals have open-ended propensities (Gomart & Hennion 1999). Anthropologists have done an excellent job unraveling the state-market dynamics that affect how pharmaceuticals are made to work. They have been less engaged in interdisciplinary endeavors to reconceptualize trial modalities or the so-called placebo effect. Yet anthropology surely has an important part to play not just in analyzing which propensities are enabled or blocked but in leveraging ethnography to recommend new ways of making pharma-matter. Barry (2005) argues that chemical matter is inherently relational, and Strathern (2005, 2014) has suggested that anthropology as a discipline uses relations to uncover relations. These suggestions point to uniquely fruitful avenues for collaborative endeavors that leverage the very specific form of knowing that is ethnographic knowing for the purpose of developing new insights into how pharmaceuticals could, perhaps, come to work better.

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Annual Review of Anthropology

Volume 46, 2017

Contents

Indexes

Errata

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