

A Human Genetics Parable

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Human genetics research appears to be approaching a period of re-examination due to the decades-long failure of molecular genetic research to uncover the genes presumed to underlie psychiatric disorders, psychological traits, and some common medical conditions. As currently dominant theories of genetic causation come more into question, we will see a renewed interest in reassessing the potential roles of genes and environment in these areas. To illustrate the potentially harmful and diversionary impact of emphasizing genetics over the environment, the author tells a story in the form of a parable. In this parable, the citizens of a medium-size city are confronted with the task of dealing with a group of arsonists who are systematically burning down several houses each week. The Mayor argues that the best way to prevent arson is to analyze the types of wood used to build the city's houses, with an accompanying lack of interest in arresting the arsonists. Her opponents argue that regardless of the type of wood used, the city and its citizens should prevent arson attacks by focusing attention on identifying and arresting the arsonists. The Mayor's position prevails, and the arson attacks continue for years to come at the same time as researchers continue to study and analyze the wood used to construct the houses. Informed readers will recognize the analogous ideas, research strategies, interest groups, publications, and historical controversies related to "nature–nurture" issues, which encompass every aspect of the parable.

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Despite high hopes from the 1980s onward, apart from a few rare Mendelian disorders, gene finding attempts in medicine, psychiatry, and psychology have produced few important results (Crow, 2011; Joseph, in press; Latham and Wilson, 2010; Wade, 2010). Although some genes appear to play a role in causing some medical disorders, decades of investigations, including the recent widespread use of genome-wide association (GWA) studies, have largely failed to uncover the genes presumed to underlie the major psychiatric disorders (Gershon, Alliey–Rodriguez, and Liu, 2011), and variation in normal psychological traits

such as IQ (Deary, Penke, and Johnson, 2010) and personality (Munafo and Flint, 2011; Verweij et al., 2010).

Rather than face the sobering yet distinct possibility that genes for the major psychiatric disorders and variation in psychological traits are either non-existent or irrelevant, and that the case for the importance of genes as a cause of common medical disorders such as cancer, type 2 diabetes, and heart disease has been greatly overstated, the leaders of these fields have adopted the position of “missing heritability” (Flint, Greenspan, and Kendler, 2010; Gershon et al., 2011; Maher, 2008; Manolio et al., 2009; Plomin, 2011). Proponents of the “missing heritability” position argue that the negative results of genome-wide association studies are due to genes having found “hiding” places in the human genome (Maher, 2008, p. 18). Therefore, they argue, researchers must develop better methods and obtain larger samples to find them. Teri Manolio and a prestigious group of researcher-coauthors, whose 2009 *Nature* publication “Finding the Missing Heritability of Complex Diseases” has served as the primary missing heritability reference point, saw “missing heritability” as the “‘dark matter’ of genome-wide association in the sense that one is sure it exists, can detect its influence, but simply cannot ‘see’ it (yet)” (Manolio et al., 2009, p. 748). The reason that these investigators were certain that genes exist and await discovery is their belief that previous studies of families, twins, and adoptees have conclusively proven that psychiatric disorders, psychological traits, and many common medical conditions are strongly influenced by genetic factors.

Other commentators, however, have interpreted years of molecular genetic failures very differently. “Instead of invoking missing genes,” wrote Latham and Wilson, if “we take the GWA [genome-wide association] studies at face value, then apart from the exceptions . . . genetic predispositions as significant factors in the prevalence of common diseases are refuted.” They concluded, “The dearth of disease-causing genes is without question a scientific discovery of tremendous significance” (Latham and Wilson, 2010).

Critics have argued that family, twin, and adoption studies in the behavioral sciences have been plagued by poor methodology, and that environmental confounds, such as the fact that reared-together identical (MZ or monozygotic) and fraternal (DZ or dizygotic) twin pairs experience very different environments, have rendered the results of these studies completely explainable by non-genetic factors (Joseph, 1998, 2004, 2006, 2010). Thus, genes that researchers now view as “missing” may well be non-existent (Joseph, 2011, in press).

However, even in the unlikely event that molecular genetic researchers are able to transform “missing heritability” into robust gene discoveries, it still wouldn’t mean that research attention should continue to focus on genetics. Even if important predisposing genes were eventually found, society and science could still choose to emphasize the importance of identifying and ameliorating the environmental causes of psychiatric disorders and medical conditions — not

the least of which is the status of living in poverty. Many common medical conditions have well known environmental causes, and despite frequent claims that the environmental causes of psychiatric disorders are not well understood, several researchers have shown that there is in fact a great deal of evidence linking psychiatric disorders to adverse life events (Bentall, 2003; Kessler et al., 2010; Read, Bentall, and Fosse, 2009; Read, Mosher, and Bentall, 2004). In addition, psychotherapists bear witness to the impact of psychologically harmful childhood and adult environments every day in their clinical practices. Apart from relatively rare single-gene medical disorders such as Huntington's disease, in many cases effective environmental interventions can prevent the appearance of disorders even if genetic factors also play a role (Jacobs, 1994). Environments can be changed; genes (at least for now) cannot be.

In contemporary U.S. society, corporations and politicians have an interest in emphasizing genes and de-emphasizing environmental causes of psychiatric and medical conditions (Chase, 1977/1980). Emphasizing the environment would cut into corporate profits by forcing companies, for example, to reduce the emission of known environmental toxins. It would greatly reduce the profits of the pharmaceutical industry, and would compel the U.S. government to divert the large sums of money it now spends on war ("national defense") towards a dramatic improvement in social, health, and educational conditions, the elimination of poverty, the creation of jobs, investment in community programs, and so on. Emphasizing genetics, despite the paucity of evidence, reduces the chances that these events will occur. It is therefore not surprising that groups with political and economic interests in promoting genetic theories would attempt to steer public thinking, and research agendas, in the genetic direction.

That current research attention remains focused on genetics, despite decades of fruitless gene efforts for conditions and traits such as schizophrenia, bipolar disorder, autism, attention-deficit/hyperactivity disorder, cognitive ability (IQ), and personality, is based on the ideology of genetic determinism (sometimes referred to as hereditarianism). According to the evolutionary biologist Richard Lewontin (2009), genetic determinism is the "assumption that all-important variations in basic physiological and developmental processes are the direct result of genetic variation"

An extreme form of genetic determinism holds that psychological traits are hereditarily set for us at birth. According to genetic researcher Dean Hamer, "People are different because they have different genes that created different brains that formed different personalities" (Hamer and Copeland, 1998, p. 25). Some have even argued that heredity is the main factor in medical conditions with known environmental causes. As the leading American eugenicist Charles Davenport wrote 100 years ago in relation to diseases such as syphilitic paresis, delirium tremens, and tuberculosis, "in general, the causes of disease as given in the pathologies are not the real causes. They are due to inciting conditions

acting on a susceptible protoplasm. The real cause of death of any person is his inability to cope with the disease germ, or other untoward conditions" (Davenport, 1911, pp. 253–254).

Most contemporary genetic researchers, however, believe that both genetic and environmental factors are necessary for the development of psychiatric disorders and common medical conditions, and many believe that environmental factors are important. Nevertheless, they continue to frame the causes of these conditions in terms of genetics and help direct research dollars in the genetic direction. Even in the case of medical disorders such as type 2 diabetes, for which social and dietary causes are well known, a great deal of research attention continues to be focused on genetics (Chaufan, 2007).

Psychologist Nicholas Pastore described his field's diverging environmentalist and hereditarian approaches in a 1949 publication. Although the value of eugenic programs is rarely debated openly in science anymore, much of his description remains relevant today:

Hereditarian — A hereditarian is one who accepts statements of the following type: heredity is more important than environment; individual and group differences are the result of innate factors (either in totality or predominantly); innate characteristics are not easily modified. Where a choice of interpretation is possible, the explanation in genetic terms is the one advanced and favored. To the hereditarian way of thinking, the problem of differential fecundity looms as a most significant one for society.

Environmentalist — An environmentalist is one who accepts statements of the following type: environment is more important than heredity; existing individual and group differences reflect (much more than commonly thought) differences in opportunity; innate characteristics are easily modified. Furthermore, the "plasticity" of the child is emphasized. Of possible alternative interpretations, he chooses one emphasizing environment. In addition, the environmentalist minimizes the importance of natural inequalities in the attainment of success and rejects the eugenic program (as usually conceived). (Pastore, 1949, p. 14)

Despite frequent claims that the "nature–nurture" debate is a thing of the past — a claim sometimes made by those suggesting that "nature" has won — the heredity–environment debate continues in full force. Indeed, as the historian of science Diane Paul once observed, "Perhaps the most striking feature of the nature–nurture debate is the number of times it has ostensibly ended" (Paul, 1998, p. 82).

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The following story illustrates the differing approaches and roles of hereditarians and environmentalists in the context of medical conditions, psychiatric disorders, and behavioral traits. I am confident that informed readers will recognize the analogous ideas, research strategies, interest groups, publications, and historical controversies which encompass every aspect of this story.

There was once a city of 500,000 inhabitants named Genomia. The city had been victimized by a group of arsonists, calling themselves the "House Burning Crew," who had begun a campaign of setting fire to five of Genomia's 50,000 single family homes each week. Before these attacks began, it was a rare occurrence for a house to burn down in Genomia.

The citizens became incensed and fearful, and decided to dedicate a portion of the city finances to stop the arson attacks. A group led by Mayor Ellen Geewas argued that, although everyone recognized that people were involved in setting the fires, the main problem was the variation among Genomia's houses in their ability to withstand arson attacks. She pointed out that some houses did not burn down when the arsonists attacked, whereas other houses did. Although all of Genomia's houses had been built of wood, various types were used in their construction. These included the less flammable hardwoods such as oak, mahogany, teak, walnut, and maple, and the more flammable softwoods such as cedar, Douglas fir, and pine. It was known that each type of wood burned at different rates and varied in its degree of flammability.

Mayor Geewas therefore proposed allocating a portion of Genomia's budget to hire a company to scan the city's 50,000 houses and to determine which were most likely to burn. She argued that after the company completed its work, citizens would finally be able to understand and prevent arson in their city. Genomia's newspapers and Internet sites spoke in a virtually unanimous voice that, while it was still necessary to keep an eye out for the people setting the fires, this scan was the best way to prevent further arson from occurring. Meanwhile, houses continued to burn down at the rate of five per week.

Although there was some grumbling about the Mayor's approach, she repeatedly justified her strategy on, as she called it, a "splendid natural experiment" that had occurred in the community. It seemed that around 3% of Genomia's houses had been built in *pairs* at the same time. These houses, which were built on adjacent lots, were popularly known as "The Twin House-Pairs of Genomia." Moreover, two types of house-pairs had been built. The first type was built with the identical type of wood and with identical plans, and was known as a "monomaterial house-pair" (usually referred to as "MM"). The second type of

pair consisted of houses that had been built with somewhat differing plans and types of wood. These pairs were known as “dimaterial house-pairs” (usually referred to as “DM”). The method used to compare them was known as the “house-pair method.” Meanwhile, houses continued to burn down at the rate of five per week.

Mayor Geewas believed that by applying the house-pair method of comparing the flammability of MM house-pairs versus that of the DM house-pairs in the cause of arson prevention, the city would be able to assess how much of the variation of arson was due to the materials used to build the houses, and how much was due to arsonists. She believed that it was important to quantify this variation, and she cited the concept of “arsonability,” which was presented as a number ranging from 0.0 to 1.0. Zero arsonability meant that the type of wood used to build the houses played no role in the arson attacks and that people are the main culprits; an arsonability approaching 1.0 meant that the variation of wood-type explained virtually all of the arson variability among the city’s 50,000 houses, and that arsonists played little if any role. (Although most people knew that the House Burning Crew was involved in the arson attacks, the Mayor and her allies continued to argue that the people involved could not be easily identified, and were therefore “mysterious.”)

The Mayor hired a team of “house-pair researchers” to study the flammability of each pair of houses. They started with house-pairs in which one house was burned by arsonists. Then they assessed whether the second house also burned in the attack. (The House Burning Crew usually attempted to burn down both houses in a house-pair.) The researchers obtained the following results. Among the MM pairs, which had been built identically, when one house burned, the second house also burned roughly 85% of the time. Among the DM pairs, which were built differently, the second house burned only 40% of the time. The arsonability statistic is calculated by doubling the difference between the MM versus DM pair burn rate, which meant that among the population of Genomia’s houses, the arsonability coefficient was .9 (or 90%). Meanwhile, houses continued to burn down at the rate of five per week.

To bolster her case, the Mayor pointed to a few rare cases where house-pairs had been built identically on adjacent lots, but where one of the houses had been removed within the first few years of construction and had been relocated to a different (yet very similar) part of the city. Because research showed that both of these “separated MM” house-pairs were similarly disposed to burn with the same effort, she claimed that this finding supported her argument in favor of the high arsonability of Genomia’s houses, and that identifying and arresting the arsonists would do little to prevent houses from burning. Meanwhile, houses continued to burn down at the rate of five per week.

Several of Genomia’s journalists and scientists published widely distributed and influential books in which they wrote that house-pair research had estab-

lished (1) the primary importance of the houses' differing flammability, which was based on the type of wood cells the houses were made of; (2) that the house-pair method, and especially studies of separated MM houses, had forever changed the way we understand and approach arson; and (3) the obsolescence of the idea that arsonists were the main factor in intentional fire setting.

In one of these books, entitled *The Blank House*, the author argued that house-pair research showed that arson susceptibility is built into houses from the first day of construction, which refuted previous theorists who, he claimed, argued that all houses had been built identically and that all arson susceptibility variation was caused by events that took place after the houses had been completed. Other books supporting the Mayor's arson prevention strategy included *The Agile Wood Cell*, *The Arsonist Assumption*, *Built Like That*, *Entwined Houses*, *House Pairs: And What They Tell Us about What Houses Are*, *The Limits of Arresting Arsonists*, *Living With Our Wood Cells*, *Mean Wood Cells*, *No Two Houses Alike*, *The Selfish Wood Cell*, and *Wood Cells and Destiny*.

By far the most controversial of these books was entitled *The Wooden Curve*. In it, the authors argued that houses made out of darker color wood were inherently more flammable than houses made out of lighter wood, and that no amount of wood treatment or arson prevention measures could eliminate the gap. Meanwhile, houses continued to burn down at the rate of five per week.

One laboratory-based wood scientist at Genomia State University came out with a provocative tract called *The Wood Cell Bomb*, whose cover featured a photograph of an entire city set aflame by arsonists. In it, she attempted to revive the long-discredited doctrine of "woodgenics," which warned of the dangers that the most flammable houses posed to all other houses in the community. Early woodgenists had theorized that construction company foremen would see less-expensively built flammable houses and would be encouraged to reproduce many more of their kind, which eventually would lead to fire destroying the entire community and its people unless society intervened with "woodgenetic foresight."

The father of the discipline, Sir Welbourne Francis, had coined the term "woodgenics" and was the first to propose using house-pairs to assess for arson-ability. Francis initiated the field with his 19th century classic work *Hereditary Arson-Resistant Houses*, where he made the seminal discovery that the houses of the offspring of wealthy British aristocrats were as well-constructed and arson resistant as those of their parents, and were much more arson resistant than the houses of the offspring of working class parents. Sir Welbourne proposed two main strategies. The first was "positive woodgenics," which advocated paying bonuses to construction companies to build houses of less flammable wood. The second strategy was "negative woodgenics," which called on society to develop a deadly enzyme that would be injected into the wood of houses under construction. Some of his German and American followers even called for the

immediate destruction of what they believed were the most flammable houses as the fastest and most efficient way to create an arson-free society in the future.

Although the arson attacks continued just as before, the Mayor and the press continued to urge citizens to have faith that their strategy would soon pay dividends. They frequently stated that the arsonability of Genomia's homes was 90%, which meant that attention needed to be focused on the types of wood used to build the houses.

One day, a Genomia State University professor by the name of Samuel Eugene "Gene" Skeptic stepped up to the podium of a Genomia city council meeting. Although he recognized that in a few rare cases houses were built so poorly that they burned down even without House Burning Crew attacks, he openly disagreed with the Mayor's position. Dr. Skeptic reasoned as follows: "While it may or may not be true that some of Genomia's houses burn more easily than others, the best strategy to stop the arson attacks would be to devote most of the city's resources and funds toward tracking down and arresting the House Burning Crew. By concentrating on the houses, we are allowing the arsonists to continue to commit their crimes. If we catch them, the houses would be safe regardless of what type of wood was used to build them." He pointed out that the identity of the House Burning Crew membership was not mysterious at all, since when committing their crimes they proudly wore Crew tee-shirts with their last names emblazoned on the back. They even had their own website and a three-story building out of which they operated.

Mayor Geewas vehemently objected. "We cannot understand or prevent these arson attacks," she thundered, "until we understand the wood cell architecture of the houses of this community." She again cited house-pair studies and the 90% arsonability figure. She accused Dr. Skeptic of being a politically-motivated ideologue who does not even reside in Genomia, knows little about wood science or the house-pair method, and repeats long-discredited "arrest the arsonists," "arsonogenic homeowner," "refrigerator-like homeowner," or even "spontaneous combustion" theories of arson prevention. Meanwhile, houses continued to burn down at the rate of five per week.

Dr. Skeptic argued that even if the 90% arsonability figure were correct, or even if it were 100%, it would still make much more sense to focus attention on arresting members of the House Burning Crew. Furthermore, he had uncovered a fatal flaw with the house-pair method of comparing MM versus DM house-pairs. It seemed that the house-pair method was based on a little-mentioned theoretical assumption that arsonists would attempt to burn both houses in a pair the same way. This was known as the "equal arson assumption." However, decades of research had shown that although arsonists usually approached the burning of an MM pair in the same way because they were constructed the same way, they approached DM house pairs somewhat differently. The researchers discovered that although the DM houses made of flammable wood burned easily,

the second house was sometimes more difficult to set ablaze because it was built of less flammable wood. The arsonists frequently left the scene of the crime rather than taking the extra time necessary to set the second house on fire, which would increase their chances of being caught.

Dr. Skeptic argued, therefore, that the equal arson assumption of the house-pair method was not valid, and that the House Burning Crew treated MM and DM house pairs differently. Thus, it was likely that the house-pair method recorded little more than differing ways that the House Burning Crew approached the burning of MM and DM house-pairs. In truth, it was obvious to Dr. Skeptic that focusing on the House Burning Crew was the best strategy to prevent arson even if the house-pair method were valid. But because the method was widely used by the Mayor and others to justify doing little-to-nothing to stop the Crew, he felt it was important to show that the house-pair method was based on false assumptions.

The Mayor responded by conceding that arsonists usually approach MM and DM house-pairs somewhat differently, but that in numerous studies house-pair researchers had tested and upheld the equal arson assumption, and that the house-pair method was therefore valid. She said that house-pair researchers had arrived at that conclusion because they had discovered that the houses themselves had "created" or "elicited" arsonists' differing house burning approaches. Most of the politicians and citizens attending the meeting agreed with the Mayor, and Dr. Skeptic was forced to leave by an angry mob of the Mayor's supporters. Meanwhile, houses continued to burn down at the rate of five per week.

Dr. Skeptic came out with a book entitled *Not in Their Wood Cells*, where he made a strong case that arsonability studies, which included the house-pair method, contained numerous flaws and implausible assumptions. In his concluding chapter he urged the community to pay less attention to wood and to make a concerted effort to arrest the House Burning Crew. Dr. Skeptic's book, however, was not widely discussed, and was rarely mentioned in the media or by the authors of the popular books that supported the Mayor's position. House-pair researchers usually ignored his arguments too, and when they did address his views they often presented them in a distorted way, or made *ad hominem* attacks. Meanwhile, houses continued to burn down at the rate of five per week.

Over at Genomia State University, arson prevention research focused mainly on arsonability studies and the flammability of differing wood types. The University had established an Arson Science Department to coordinate this research. The department was heavily funded by the giant "Profitsus Corporation," which had large holdings in lumber, roofing material, and an arson-resistant chemical used to treat wood, which the company marketed under the trade-name "Arzonax." In addition, the Profitsus Corporation was the parent company of Ignite-a-Fire LLC, which produced a very expensive fire starting kit that was frequently used

by the House Burning Crew. Although some of its other products helped Genomia's residents repair and prevent different (non fire-related) types of damage done to their houses, much of Profitsus's advertizing and promotion focused on Arzonax.

Dr. Skeptic issued frequent press releases pointing out the obvious conflict of interest that the Profitsus Corporation, which profited from arson and therefore had a financial interest in not preventing it, funded and played a major role in dictating the research agenda. He stressed that it was in the company's interest to divert attention from the House Burning Crew and to promote sales of its lumber and roofing material, and the use of its highly profitable Arzonax wood treatment product.

Dr. Skeptic showed that Arzonax was enormously successful not only because of Genomia's potential market of 50,000 houses, but also because Arzonax would need to be administered weekly for the entire life of the house. In their television and magazine advertisements, as well as in frequent ads appearing in building contractor journals, Profitsus stressed that flammability was a house characteristic just like any other house characteristic, and required lifelong wood treatment with Arzonax in the same way that lawns needed watering several times a week. Their television ads even attempted to convince the owners of the less flammable houses that they may be in danger, and therefore needed to use Arzonax to ease their worries. The treatments were expensive, and every ten years or so, after the patent ran out and the wood treatment formula became "generic" and inexpensive, the company came out with a "new and improved" expensive wood treatment product which it marketed by telling everyone that their old product was potentially dangerous, could cause wood rot, and might not be very good at preventing arson after all. Dr. Skeptic's press releases continued to criticize this state of affairs, but the media continued to ignore him. Around town, it was whispered that the Profitsus Corporation held a 70% stake in Genomia's main newspapers, Internet sites, and television and radio stations.

Genomia State University researchers friendly to Dr. Skeptic, who wanted to focus on the people who set fires as the main task of arson prevention, were also frustrated. It seemed that when they applied for grants from the Genomia Institute of House Health (GIHH) to investigate ways to arrest arsonists, they would frequently be turned down on the grounds that arsonability studies were the Institute's top priority. These researchers decided to channel their frustration into a bit of research into the GIHH itself. They discovered the existence of a "very cozy relationship" between the Profitsus Corporation and the GIHH, and that the company provided 63% of the GIHH's operating budget. Many of the GIHH directors and researchers had previously worked for Profitsus, and many others were given high paying positions in the company after they left the GIHH. Dr. Skeptic did his best to publicize these practices too, but few paid attention. Meanwhile, houses continued to burn down at the rate of five per week.

The city press was dominated by reports that great progress had been made in identifying the houses made of easily burning wood, and that a program would soon be undertaken to provide city-subsidized Arzonax treatments to the most "at risk" houses. Mayor Geewas also proposed the creation of a research program to develop a new cutting edge treatment: "wood cell therapy." However, she acknowledged that this type of therapy might be years or even decades away, despite the fact that the multi-billion dollar internationally conducted "House Wood Cell Project" (HWCP) had been completed nearly a decade earlier. The scientists leading and promoting the HWCP had promised at its inception that, once the DNA of wood cells had been sequenced and mapped, we would finally be able understand and prevent arson. The most well known of these scientists went so far as to state that for the first time in history, the HWCP would allow us to understand what a house really is. The Mayor continued to make regular announcements on progress, and had convinced the citizens that Genomia was witnessing the "dawn of a new era of arson prevention." Meanwhile, houses continued to burn down at the rate of five per week.

Later, an outside investigation uncovered the fact that Mayor Geewas had for years received lavish consulting fees and gifts from the Profitsus Corporation, as well as from other home building material and wood-treating companies. The city decided to pass a law requiring politicians to disclose this type of income in all subsequent official documents, which the Mayor reluctantly did. But she denied that there was any conflict of interest, and few of her colleagues seemed to pay much attention. A footnote in one of the newer city documents, printed in small type, read: "Mayor Geewas has served on the Advisory Board and receives consulting and speaking fees from the Profitsus Corporation. In addition, she has received support and consulting fees from Genomia Roofing Products Inc., The National Wood Treatment Association, Genomia Lumber, and the Genomia Institute of House Health." Meanwhile, houses continued to burn down at the rate of five per week.

A journalist visited Genomia eight years later. She reported that the House Burning Crew continued to burn five houses per week, and that Mayor Geewas was finding it difficult to develop an efficacious method of treating the wood of Genomia's most vulnerable houses. (It turned out that Arzonax did not work most of the time, even though sales and marketing remained strong. The Profitsus Corporation was in the process of patenting a new wood treatment product chemically similar to Arzonax, which it planned to market as "Burnzarest.") Still, the Mayor promised that better treatment methods were being developed, which would lead to the prevention of arson attacks in the near future. For Mayor Geewas, a major issue was the "missing arsonability" problem of identifying the houses that needed treatment. Once this problem was resolved, she said, better arson treatment could be developed. Meanwhile, houses continued to burn down at the rate of five per week.

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