5. *Coal's Effects on the Nervous System*

It is easy to understand that burning coal is likely to have an adverse impact on respiratory health: we inhale the products of combustion. It is less obvious that burning coal has important effects on the nervous system, particularly the brain. Cerebral vascular disease, i.e., stroke, and loss of intellectual capacity due to mercury are the two most important neurological consequences of burning coal.

THE BRAIN AND POLLUTION

The human brain is the organ that most clearly distinguishes us from other species. Our abilities to think abstractly, produce and enjoy music, art and literature, inquire about the nature of the universe, and a host of similar activities related to brain function are what makes us human. This uniquely human organ is also highly susceptible to disruption by what may appear to be relatively trivial acute or chronic abnormalities. Although the normal brain weighs 1,300–1,400 grams (about three pounds), the extremely high metabolic rate of the brain and the absence of significant energy stores within the brain mandate a high constant rate of blood flow in order to insure normal function and survival. When the body is at rest, between 15 and 20% of the cardiac output goes to the brain. Thus, even transient interruptions of the blood, oxygen, or glucose supplies to the brain may result in severe, permanent brain injury or brain death.

The complexity of the brain, coupled with its susceptibility to the effects of metabolic or physiological derangements or both, frequently leads to abnormalities of brain function that may be undetectable in an individual, but may have an enormous impact on the population as a whole. This, in turn, has public health consequences. This is illustrated in Figures 5.1 and 5.2, where the impact of a five-point decrement in IQ is depicted. The average IQ score is 100 and 95% of all individuals have IQ scores that fall between 70, the score below which one is considered to be retarded, and 130, the score above which one is considered to have superior intelligence. This is shown in Figure 5.1. Figure 5.2 demonstrates the effect of an across-the-board five-point decrement in IQ. For an individual, this

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Figure 5.1: Normal IQ distribution

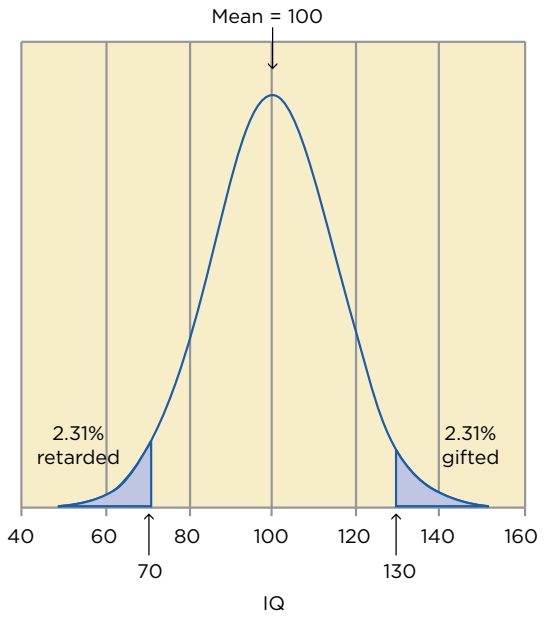
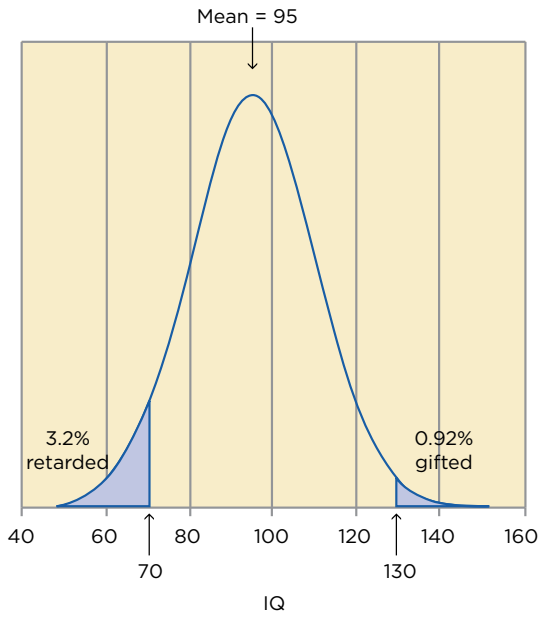


Figure 5.2: Change in IQ distribution with 5 point decrement



relatively small change would hardly be noticed. However, in a large population, substantial numbers of individuals are removed from the superior intelligence category and others are pushed down into the retarded category. The result is a smaller pool of individuals with outstanding intellects and a larger pool of individuals who require special resources to be able to function. It is this reality that makes it important to protect and preserve the brain's full potential.

CEREBRAL VASCULAR DISEASE

The same pathophysiological mechanisms that affect the coronary arteries and cause myocardial infarcts also apply to the arteries that nourish the brain, as shown in Figure 5.3. These common mechanisms include: stimulation of the inflammatory response in cerebral vessels leading to atherosclerotic plaque formation, rupture, and arterial occlusion; oxidative stress; and alterations in blood viscosity. In addition, arrhythmias may cause transient reductions of the cardiac output and cause hypoperfusion of the brain. The effects of reductions in the cardiac output are most prominent at the boundaries between major arteries (so-called watershed areas of the brain), and distal to sites of severe arterial stenosis.

The term stroke refers to a variety of acute cerebrovascular events including ischemic stroke, caused by occlusion of a cerebral artery by an atherosclerotic plaque or an embolus; cerebral hemorrhage, usually caused by rupture of a small artery in the brain; subarachnoid hemorrhage, often due to rupture of an aneurysm; or some other acute event due to a vascular cause. In the narrative that follows, unless otherwise stated, we will use the term stroke to mean an ischemic stroke caused by occlusion of a cerebral artery by an atherosclerotic plaque, the most common cause of stroke.

Although there have been major improvements in primary and secondary prevention of strokes in the past several decades, due to better care of

patients with hypertension and diabetes as well as improvements in smoking cessation efforts, stroke is still an important cause of death in the U.S. Current estimates indicate that the stroke death rate for men is 33.1 per 100,000 and 26.1 per 100,000 for women.[1]

Three large studies and several smaller studies have shown a correlation between air pollutants and acute strokes.

In their study of the relationship between fine particles ($PM_{2.5}$ or less) and hospital admission rates in the Medicare population, Domenici, et al., reported a 0.81% increase in the hospitalization rate for cerebrovascular disease (ICD 9 codes 430–438, 95% CI = 0.31–1.32%) for a 10 μg/m^3 increase.[2] This relationship was significant only on lag day zero (no lag between a peak and the admission) and not evident on lag days one and two. As with many of the other outcomes they considered in addition to cerebrovascular disease, this association was strongest in eastern parts of the U.S. when compared to western regions. This may be related to differences in the composition of PM due to the large number of coal-fired power plants in the east compared to the west.

In a second study of the Medicare population, Wellenius, et al., sought relationships between hospital admissions from 1986 to 1993 for ischemic and hemorrhagic strokes and increases in various air pollutants in nine major U.S. cities.[3] Admissions data were obtained from the Centers for Medicare and Medicaid Services and pollutant levels were obtained from the EPA. Pollutant levels are shown in Table 5.1. Note that PM_{10} levels were measured and not $PM_{2.5}$ levels as would be the case for more contemporary studies. They report that for an interquartile percentile increase in the PM_{10} concentration, there was a corresponding 1.03% increase in the admissions for ischemic stroke (95% CI = 0.04–2.04%) on the day of the increase. Similar results were observed for CO, NO_2, and SO_2 for ischemic strokes only. They did not find significant associations between pollutant levels and hemorrhagic strokes.

Figure 5.3: Pathophysiological mechanisms by which air pollution causes neurological disease

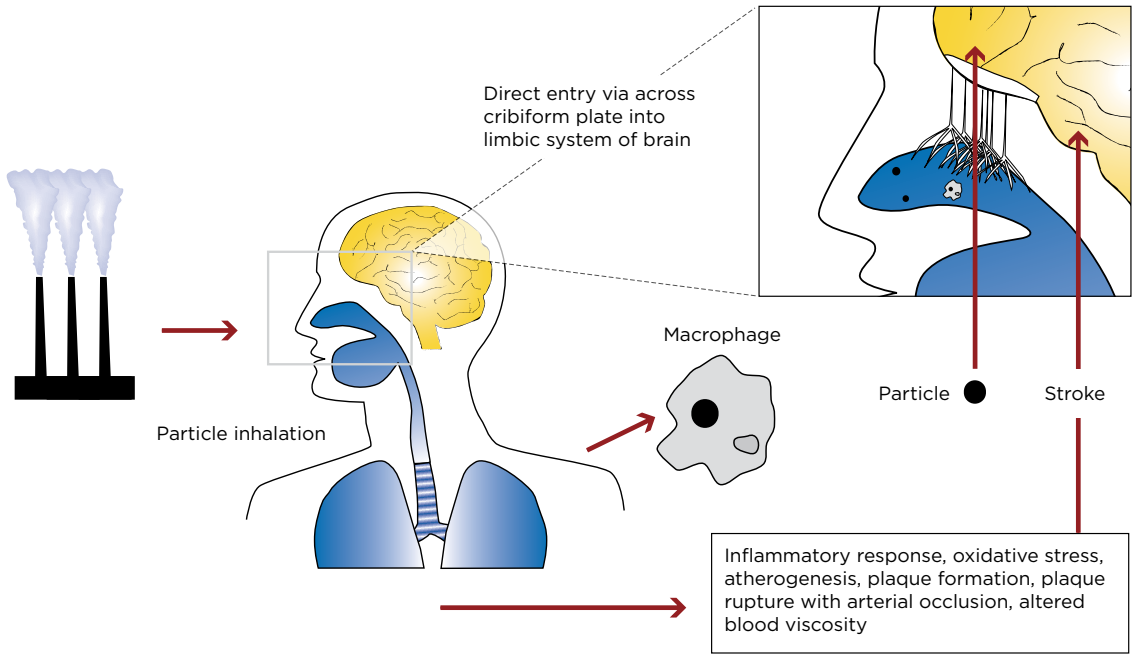


Table 5.1: Concentrations of various air pollutants in 9 U.S. cities

Pollutant	Percentile 25th	50th	75th
PM_{10} µg/m^3	18.88	28.36	41.84
CO ppm	0.73	1.02	1.44
NO_2 ppb	18.05	23.54	29.98
SO_2 ppb	3.57	6.22	10.26

Source: Wellenius GA, Schwartz J, Mittleman MA. Air pollution and hospital admissions for ischemic and hemorrhagic stroke among medicare beneficiaries. Stroke 2005; 36(12):2549–2553.

Finally, data from post-menopausal women enrolled in the Women's Health Initiative and collected in 2000 show that for each increase of 10 µg/m^3 in the $PM_{2.5}$ concentration, there was a 35% increase in the risk of a cerebrovascular event and an 83% increase in the risk of death from a cerebrovascular event.[4] The hazard ratio for the time to an acute cerebrovascular event, an indicator of relative risk, was reported as 1.35 (95% CI = 1.08–1.68). This observational study of post-menopausal women without a prior history of cardiovascular disease gains strength from the fact that the authors reviewed actual medical records, rather than relying on data from central databases. The restriction to this cohort of women loses some strength because the results may not be generalizable to men or younger women. They did not find any association between stroke and other air pollutants, including SO_2, NO_2, CO and O_3.

Two other studies conducted under more restricted circumstances have shown direct relationships between air pollutants and stroke. In a 2002 study of stroke mortality in Korea, Hong, et al., reported significant and increasing risk for death due to ischemic but not hemorrhagic stroke as same-day PM concentrations increased through four quartiles.[5] These authors also found significant temporal relationships between pollutants and stroke: same-day sulfur dioxide concentrations and ischemic stroke, a one-day lag between carbon monoxide and stroke, and a three-day lag between an ozone peak and stroke. In a more complex study of over 23,000 stroke admissions in Taiwan, Tsai, et al., reported significant positive associations between PM_{10}, NO_2, SO_2, CO, and O_3 when considered singly, and primary intracerebral hemorrhage and ischemic stroke admissions on days when the temperature was 20°C or greater.[6] On cooler days, the correlation between CO and ischemic stroke was the only factor that persisted. When they considered two pollutants together, there was a significant correlation between PM_{10} and NO_2 and both types of stroke.

In summary, even though a relatively small portion of all strokes appear to be related to concentration of PM, the fact that nearly 800,000 people in the U.S. have a stroke each year[7,8] makes the number of strokes attributable to PM a risk factor of importance. These studies emphasize the importance of measures designed to minimize PM concentrations in the air, including preventing the construction of new coal-fired power plants and developing and utilizing more effective technologies to reduce emissions from existing plants.

MERCURY

Coal contains trace amounts of mercury. When burned, this mercury evaporates and is emitted into the environment unless stringent control technologies are used to reduce those emissions. Coal-fired power plants are responsible for approximately one third of all emissions of mercury attributable to human activity, as shown in Table 5.2, making them the largest single source of mercury emissions. The 2007 Toxics Release Inventory listed point source releases of 7,935 pounds of mercury and 117,243 pounds of mercury compounds.[9] Point sources are stationary, single-site sources of a pollutant, such as a smoke stack at a power plant.

The mercury cycle is shown in Figure 5.4. Once mercury enters the atmosphere, it returns to the earth via rainfall, entering waterways. Mercury and other persistent toxicants in lakes and streams led various states, tribes, and territories to issue 3,221 advisories in 2004 urging caution when consuming fish from specific bodies of water, up from 3,089

Table 5.2: Anthropogenic sources of mercury

Source	Tons per year	Percent of total
Combustion	137.9	86.9
Electrical utilities	52.0	32.8
Municipal incinerators	29.6	18.7
Industrial boilers	28.4	17.9
Medical waste incinerators*	16.0	10.1
Other manufacturing	15.8	10.0

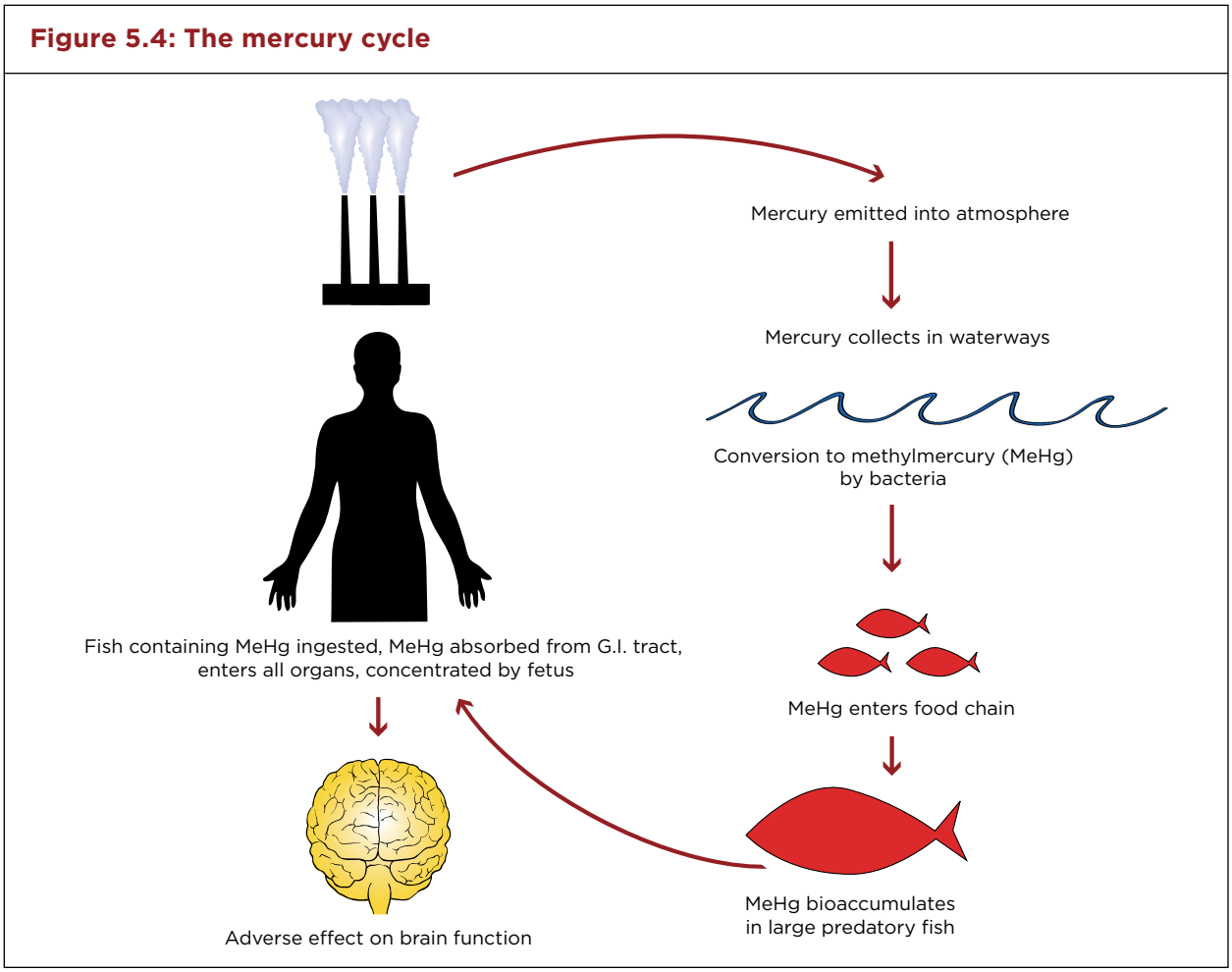
* Mercury emissions from medical waste incinerators are almost certainly lower at present due to regulations that have altered medical waste disposal methods.

Source: EPA Office of Air Quality Planning & Standards and Office of Research and Development. Mercury study report to Congress. Volume II: an inventory of anthropogenic mercury emissions in the United States; Dec 1997: EPA-452/R-97-004.

the year before.[10] In the water, bacteria convert elemental mercury into methylmercury (MeHg), a form that is persistent and bioaccumulates. The concentration of MeHg increases as it passes up the food chain, reaching high levels in large predatory fish. The fish with the highest mercury concentrations are large tuna, swordfish, king mackerel, and tile fish. Marine mammals that eat fish also may have a large mercury burden. Humans are exposed to coal-related mercury primarily through fish consumption.

Since mercury is recycled in the environment and substantial amounts are released during volcanic eruptions, opponents of stricter mercury controls attempt to downplay the importance of coal-related emissions. Nevertheless, minimizing or eliminating coal-related mercury emissions is an important and concrete action that can be taken

Figure 5.4: The mercury cycle



to prevent additional amounts of mercury from entering the environment and affecting health.

In the 1950s, outbreaks of mercury poisoning in Minamata and Niigata, Japan, were caused by eating fish contaminated with mercury from industrial discharges. As a result, there were 3,000 confirmed cases and 600 deaths. A second outbreak occurred in Iraq, caused by eating seed-grain that had been treated with a fungicide containing MeHg.[11] This caused 649 deaths among 6,530 affected individuals. Until recently, a dose-response curve, derived from these exposures and interpolated to more typical blood mercury levels, served as the basis for determining the permissible daily intake of mercury.[12] Because of deficiencies in these data and their analysis, alternate populations were examined in great detail.

Based on three large-scale, prospective studies of cohorts children exposed *in utero* to MeHg in the Seychelles, the Faroe Islands, and New Zealand, the National Research Council recommended establishing a benchmark dose of 58 µg/L of mercury in the cord blood of newborns. The benchmark dose is the lower 95% confidence interval for an estimated dose that results in doubling the prevalence of children with neurodevelopmental test scores that are in the clinically impaired range.[13] This somewhat arbitrary choice is thought to provide an adequate margin of safety and to provide a rational basis for regulatory actions. Based on the National Research Council recommendations, the EPA applied a tenfold safety factor, which is typical for EPA regulatory actions, and set the reference dose (RfD), the maximum tolerable daily dose, at 0.1 microgram of mercury per kilogram of body weight per day, the amount believed to lead to a mercury concentration of 5.8 µg/L mercury in cord blood.[14] To translate this standard into a practical form, it is necessary to know the maternal mercury blood level and the maternal-fetal mercury ratio. Fetal mercury levels are approximately 1.7 times those in the mother.[15]

Between 316,588 and 631,233 children are born in the U.S. each year with blood mercury levels high enough to cause lifelong loss of intelligence.

Based on the 1999-2000 National Health and Nutrition Examination Survey data,[16] approximately 15.7% of all American women of childbearing age were found to have blood mercury levels that would cause them to give birth to children with cord blood mercury levels of 5.8 µg/L mercury or more, i.e., above the target concentration. (Subsequent modeling by Stern suggested that the maternal:fetal ratio was overestimated in the earlier study.[17] However, direct measurements in a Swedish cohort suggest that the original ratio may be correct.[18]) Using these data and conservative estimates of blood mercury levels and their effect on intellectual performance, Trasande, et al., estimated that between 316,588 and 631,233 children are born in the U.S. each year with blood mercury levels high enough to impair performance on neurodevelopmental tests.[19] These authors further concluded that this lifelong diminution in intelligence costs society $8.7 billion per year (range $2.2–$43.8 billion in 2000 dollars). These cost estimates contrast sharply with others as low as $10 million dollars attributed to U.S. power plants by Griffiths, et al.[20]

HEALTH EFFECTS ON THE HORIZON

In prior sections, we have reviewed the peer-reviewed evidence published in leading medical journals that links pollutants produced by coal-burning power plants to diseases of the pulmonary, cardiovascular, and nervous systems. Emerging data that are based on smaller samples, and are therefore more speculative, suggest that there may be links between coal-derived pollutants and other diseases, such as Alzheimer's disease (AD) and diabetes mellitus, two of the most prevalent, costly, and debilitating chronic diseases of adults. If these early observations are upheld by more rigorous studies of large populations using contemporary epidemiological and statistical methods, such as those we refer to in earlier sections,

the public health implications will be enormous. Therefore, because of their possible importance, we will consider these potential links briefly.

ALZHEIMER'S DISEASE

The evidence linking air pollution and AD comes from studies comparing brains of dogs and humans living in highly polluted versus non-polluted cities in Mexico.[21,22] Animal data suggest that $PM_{2.5}$ crosses the nasal mucosa and enters the limbic system of the brain via the olfactory nerve.[23,24] Once in the brain, these PM cause inflammation and appear to lead to the deposition of amyloid, a neuropathological feature characteristic of AD. The authors suggest that "exposure to urban air pollution may cause brain inflammation and accelerate the accumulation of β-amyloid42, a putative mediator of neurodegeneration and AD pathogenesis." Similar findings were reported in animal experiments in which several strains of transgenic mice were exposed to PM.[25] The possible link between airborne pollutants and neurodegenerative diseases has not been firmly established. However it is potentially important because of the large and growing number of patients with AD and the disease's financial and societal impact.

DIABETES MELLITUS

The prevalence of diabetes mellitus (DM), particularly Type II DM, is increasing. In 2002, Lockwood observed a statistically significant relationship between the by-state prevalence of diabetes and the by-state air emissions of pollutants reported in the Toxics Release Inventory.[26]

In 2005, Brook postulated several mechanisms by which the inhalation of particulates might lead to the development of insulin resistance, a condition in which the body produces insulin but does not use it properly, thereby increasing the risk for the development of DM.[27] Again, the process begins with the inhalation of small particles that stimulate pulmonary inflammation and the generation of reactive oxygen species and oxidative stress. Subsequent pathways that involve the autonomic nervous system, the adrenal gland, and others are thought to lead to the development of insulin resistance and subsequently, to DM. This hypothesis gained credence with the publication of a paper linking NO_2 exposure with DM in women.[28] A positive relationship was found between NO_2 exposure and DM after controlling for several potential confounding factors such as age and body mass index. The authors conclude that their results "suggest that common air pollutants are associated with DM." That report used NO_2 levels as a surrogate marker for traffic-related air pollutants, including PM. Since substantial amounts of NO_2 and PM are emitted when coal is burned, there may be a link between NO_2 and PM derived from coal and DM.

DIABETES MELLITUS AND ALZHEIMER'S DISEASE

Converging evidence suggests that insulin resistance is a risk factor for a number of dementia-related conditions including Type II DM and impaired glucose tolerance, obesity, inflammation, ischemia, hypertension, cardiovascular disease, and abnormal lipid metabolism including hypercholesterolemia. To some extent, these associations blur the distinction between vascular causes of dementia and AD.[29] The putative mechanisms linking AD and DM include inflammation and oxidative stress. As discussed throughout this report, these two mechanisms are intimately related to exposure to various air pollutants, particularly fine particles, including those produced by burning coal.

SUMMARY

It is possible that the protean adverse health effects of burning coal may extend beyond those that are well established to include other common and costly chronic diseases. This possibility warrants vigilance and further investigation.

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