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DOJ JOINS BILLING CASE VS. HOSPITAL GROUP

Prime Healthcare accused of inflated Medicare claims

BY PAUL SISSON

The U.S. Justice Department has joined a years-old whistleblower case against Prime Healthcare Services, adding substantial weight to allegations of widespread Medicare overbilling at 14 of the company's hospitals in California.

Federal court documents show that a judge granted the agency's request to join the case Tuesday, one day after the government declared in a court filing that its investigation of Prime has "yielded sufficient evidence" that the targeted facilities "submitted or caused the submission of claims to Medicare for unnecessary inpatient stays."

Anti-fraud statutes allow fines of $5,500 to $11,000 — plus triple damages under certain circumstances — for each false or inaccurate bill submitted by hospitals and other health care companies.

In 2012, for example, pharmaceutical giant GlaxoSmithKline agreed to pay $2 billion to the federal gov-

SEE PRIME • A8

U-T WATCHDOG

PUC GAVE EDISON HELP WITH SUBPOENA

Agency aided utility it would soon probe

BY JEFF MCDONALD

Even as it was preparing to review a $4.7 billion deal settling costs for the failed San Onofre nuclear plant, the California Public Utilities Commission was working behind the scenes to draft and send subpoenas on behalf of plant owner Southern California Edison.

The legal demands for reams of technical documents and information were sent to Mitsubishi Heavy Industries, the Japanese maker of replacement steam generators that brought down the twin reactors housed in domes on San Diego County's north coast.

The close cooperation came as the commission was investigating the role of the utility and its vendor in the failure at the plant, raising the question of whether it was truly impartial.

Records obtained by The San Diego Union-Tribune show commission lawyers started their process with subpoenas drafted by Edi-

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KEVIN LAMARQUE AP

Then-Secretary of State Hillary Clinton checks her Blackberry from a desk inside a C-17 military transport in 2009.

REPORT HITS CLINTON OVER EMAIL PRACTICES

Watchdog charges State Department rules were clearly broken

BY EVAN HALPER

WASHINGTON

A new finding by the State Department's internal watchdog that Hillary Clinton clearly broke department rules when she used private email for government business once again focuses the presidential race on an issue the Democratic frontrunner has worked for months to put behind her.

The highly critical report, issued by the department's inspector general and sent to Capitol Hill on Wednesday, concluded that Clinton created a security risk and violated transparency and disclosure policies.

The 79-page report faulted Clinton for not seeking permission to use a personal email account and server, noting the investigation found "no evidence that the Secretary requested or obtained guidance or approval to conduct official business via a personal email account on her private server." Department officials "did not — and would not — approve" of such a practice, the report added.

Clinton's failure to

SEE CLINTON • A6

JAE C. HONG AP

Orange County sheriff's deputies take a protester into custody Wednesday outside the Anaheim Convention Center while Republican presidential candidate Donald Trump conducts a rally. Trump will appear at the San Diego Convention Center at 2 p.m. Friday.

S.D. POLICE PREPARE FOR CLASHES AT TRUMP RALLY

GOP candidate's event Friday at convention center expected to draw hordes of supporters, protesters

BY JOSHUA STEWART

After clashes between supporters, protesters and police at campaign events across the country, anxiety has grown ahead of Donald Trump's rally scheduled for Friday afternoon in San Diego.

Thousands of the presumptive Republican nominee's supporters and protesters are expected to flood downtown near the convention center where Trump has a 2 p.m. event planned.

Recent confrontations have turned violent, notably in New Mexico on Tuesday where people lit fires and threw rocks at Albuquerque police officers. On Wednesday, protesters were arrested during clashes with police at a Trump rally in Anaheim.

San Diego Police Chief Shelley

TRUMP RALLY SPURS PROTESTS IN ANAHEIM

A4 • Candidate's supporters, protesters clash outside venue.

Zimmerman said law enforcement will be able to respond to any sort of incident. The department is familiar with creating plans for all kinds of large gatherings, from Comic-Con to political demonstrations.

"The contingency plan that we have in place here is going to allow for a safe environment, and if anyone chooses to do something otherwise, we're confident that our contingency plan can address those few individuals who don't choose to follow the law," she said.

Others are concerned whether law and order will be maintained.

SEE TRUMP • A6

HARVARD STUDY ASKS IF INFECTIONS ARE THE CULPRIT IN ALZHEIMER'S

BY GINA KOLATA

Could it be that Alzheimer's disease stems from the toxic remnants of the brain's attempt to fight off infection?

Provocative new research by a team of investigators at Harvard leads to this startling hypothesis, which could explain the origins of plaque, the mysterious hard little balls that pockmark the brains of people with Alzheimer's.

It is still early days, but Alzheimer's experts not associated with the work are captivated by the idea that infections, including ones that are too mild to elicit symptoms, may produce a fierce reaction that leaves debris in the brain, causing Alzheimer's. The idea is surprising, but it makes sense, and the Harvard group's data, published Wednesday in the journal Science Translational Medicine, supports it. If it holds up, the hypothesis has major implications for preventing and treating this degenerative brain disease.

The Harvard researchers report a scenario seemingly out of science fiction. A virus, fungus or bacterium gets into the brain, passing through a membrane — the blood-brain barrier — that becomes leaky as people age. The brain's defense system rushes in to stop the invader by making a sticky cage out of proteins, called beta amyloid. The microbe, like a fly in a spider web, becomes trapped in the cage and dies. What is left behind is the cage — a plaque that is the hallmark of Alzheimer's.

So far, the group has confirmed this hypothesis in neurons growing in petri dishes as well as in yeast,

SEE ALZHEIMER'S • A9

ALZHEIMER'S • Disease may stem from fighting infections

FROM A1

roundworms, fruit flies and mice. There is much more work to be done to determine if a similar sequence happens in humans, but plans — and funding — are in place to start those studies, involving a multicenter project that will examine human brains.

"It's interesting and provocative," said Dr. Michael Weiner, a radiology professor at the University of California, San Francisco, and a principal investigator of the Alzheimer's Disease Neuroimaging Initiative, a large national effort to track the progression of the disease and look for biomarkers like blood proteins and brain imaging to signal the disease's presence.

Dr. David Holtzman, a professor and the chairman of neurology at the Washington University School of Medicine in St. Louis, was also intrigued. "It is obviously outside the box," he said. "It really is an innovative and novel study."

The work began when Robert Moir, of Harvard Medical School and Massachusetts General Hospital, had an idea about the function of amyloid proteins, normal brain proteins whose role had long been a mystery.

The proteins were traditionally thought to be garbage that accumulates in the brain with age. But Moir noticed that they looked a lot like proteins of the innate immune system, a primitive system that is the body's first line of defense against infections.

Elsewhere in the body, such proteins trap microbes — viruses, fungi, yeast and bacteria. Then white blood cells come by and clear up the mess. Perhaps amyloid was part of this system, Moir thought.

He began collaborating with Rudolph Tanzi, also at Harvard Medical School and Massachusetts General Hospital, in a study funded by the National Institutes of Health and the Cure Alzheimer's Fund. The idea was to see if amyloid trapped microbes in living animals and if mice without amyloid proteins were quickly ravaged by infections that amyloid could have stopped.

The answers, they reported, were yes and yes.

In one study, the group injected Salmonella bacteria into the brains of young mice that did not have plaques.

"Overnight, the bacteria seeded plaques," Tanzi said. "The hippocampus was full of plaques, and each plaque had a single bacterium at its center."

In contrast, mice that did not make beta amyloid succumbed more quickly to the bacterial infection, and did not make plaques.

For years, researchers had been fixated on the idea of plaques as a sort of trash that gathered in the brain. Few had asked if there might be some other explanation.

As Dr. Samuel Gandy, a professor of neurology and psychiatry at the Icahn School of Medicine at Mount Sinai Hospital in New York, explained, there was a long and persuasive body of research laying out the Alzheimer's pathway: Plaques form and set off the formation of tangled threadlike tau proteins. Then, as tangles of tau kill nerve cells, the brain becomes inflamed, resulting in the killing of many more nerve cells.

There were a few puzzling clues that something else might be going on, but they did not make much sense.

For example, Weiner said, some investigators reported that people who had developed Alzheimer's had higher levels of antibodies to herpes, an indicator of a previous infection, than people who did not have the disease.

"The suggestion that herpes was causative seemed a bit far-fetched," he said.

The new paper, Gandy and Weiner said, provides a plausible explanation.

Dr. Berislav Zlokovic, director of the Zilkha Neurogenetic Institute at the University of Southern California, said his studies of the blood-brain barrier also fit well with the new hypothesis. When he discovered that the barrier started to break down with aging, he noticed that the leakiest part was the membrane that protects the hippocampus, the site of learning and memory. That is also where Alzheimer's plaques form.

Tanzi and Moir's hypothesis, he said, "is very hypothetical at this point, but it does make sense."

Of course, there must be more to Alzheimer's than the brain's innate immune system. What about people who have a mutated gene that guarantees they will develop the disease at an early age?

For them, Tanzi says, the problem is that they vastly overproduce beta amyloid. There is so much that it clumps on its own, without the presence of microbes.

Not everyone who has had a brain infection develops Alzheimer's, though. Why would some be more vulnerable than others? According to the new theory, it probably has to do with the brain's ability to clear out the balls of beta amyloid after they have killed microbes, Tanzi said. For example, it is known that people with a gene called ApoE2 have brains that are good at sweeping out plaque, and have a low risk of Alzheimer's in old age. Those with a different version, ApoE4, are inefficient in removing plaque, and have a high risk of Alzheimer's.

Recent data suggest that the incidence of dementia is decreasing. It could be because of better control of blood pressure and cholesterol levels, staving off ministrokes that can cause dementia. But could a decline in infections also be part of the picture?

"That's a possibility," Weiner said.

At this point, the Harvard researchers have what many say is an intriguing hypothesis, but they readily acknowledge that much work lies ahead.

The Cure Alzheimer's Fund is starting a collaborative project that will use gene sequencing technology to look for microbes in brains from people who had Alzheimer's and those who did not. Researchers will also look for microbes in plaques found in human brains.

That, though, "is a big, big second step," Tanzi said. "First we need to ask whether there are microbes that may sneak into the brain as we age and trigger amyloid deposition."

"Then," he said, "we can aim at stopping them."

Kolata writes for The New York Times.