

NEIGHBOURHOODS THAT CAN KILL

The strain of inner-city life may send tumours into overdrive, reports **Peter Aldhous**. And cancer is just one disease fuelling US health inequalities



SARAH HOSKINS FOR NEWS SCIENTIST



Diana Garmon-Spears knows breast cancer is more deadly for black women living in Chicago

DEEP down, Diana Garmon-Spears knew something was seriously wrong when she noticed a lump in her right breast, about the size of a peanut. “I ignored it, but then my breast started to deform. I started to form a mass of lumps all around,” she recalls.

Two years later, she doesn’t expect doctors to cure her cancer, and has been forced to give up her office work. “I don’t think there’s any employer who’s going to understand you having chemo or radiation for 2 hours a day.”

As an African American woman living in Chicago, the dice are loaded against Garmon-Spears. Across the US, death rates among black women diagnosed with breast cancer are 37 per cent higher than for whites, but in Chicago the difference is an astonishing 68 per cent (*Cancer Causes & Control*, vol 18, p 323). Something about this heaving metropolis is sending black women to an early grave.

Poor access to screening and therapy is clearly an important factor. But according to a novel collaboration between sociologists and biologists, the strain of living in some of the toughest neighbourhoods in the US may cause biological changes that lead directly to earlier deaths.

Results from the collaboration indicate that social isolation and a fear of crime cause an overload of stress hormones that can change cell biology, sending tumours into overdrive. “We’re showing that your social environment can affect your health directly,” says Suzanne Conzen of the University of Chicago. “It goes into gene expression. That concept is really new.”

Crucially, this insidious influence is felt most by Chicago’s African American women, who are far more likely to live in the city’s deprived areas than their white counterparts.

The provocative hypothesis highlights the need for new ways of fighting breast cancer in black women in Chicago specifically, including via social interventions. More broadly, other health researchers are hailing the union of biology and sociology as a model for future studies into a whole range of health disparities. “It’s a great example of the kind of direction in which I can see us heading,” says Tim Rebbeck, an epidemiologist at the University of

Pennsylvania in Philadelphia. There are already hints that stress and social deprivation could have similar effects on diabetes and cardiovascular disease.

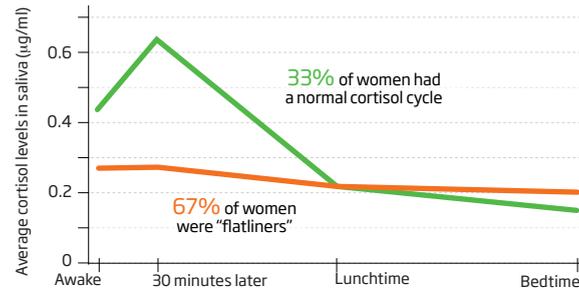
To get a handle on how tough life in Chicago can get, a good place to start is the neighbourhood of Englewood in the city's South Side (see diagram, opposite page). Poverty in Englewood is grinding, crime is endemic and amenities that the mostly white residents of comfortable suburbs like Clearing take for granted are long gone. "Even churches have moved out," says Sarah Gehlert of Washington University in St Louis, Missouri, lead sociologist on the project.

New Scientist got a taste of conditions on a tour of the South Side with members of Gehlert's research team. At vacant lots strewn with beer bottles and other debris, I'm told to watch my step. A previous visitor stumbled on a bag of urine and other medical waste. Along one Englewood street, we pass three burnt-out houses. On this winter morning, the gang activity that blights the area has yet to ramp up for the day. But the grilles on the windows of the Simon Guggenheim Elementary School are a testament to the crime that stalks these streets. You wouldn't want to be here after dark, says Charles Mininger, a graduate student on the project.

Other sociologists have documented the struggle to survive in this grim environment. But in 2003 Gehlert, then at the University of Chicago, took a novel approach when she teamed up with some of the university's

Stress hormone watch

Of 230 African American women with breast cancer in Chicago, the more socially isolated were "flatliners". This may be a sign of earlier overproduction of the stress hormone cortisol, which may have sent the women's tumours into overdrive



SOURCE: SARAH GEHLERT/MARTHA MCCLINTOCK

"Women with 'flatline' cortisol cycles tended to live in areas with more homicides and robberies"

leading oncologists and biologists to investigate how social circumstances might influence prospects for women with breast cancer.

From the work of Nigerian-born Funmi Olopade, the researchers knew that women of west African descent are more likely than their white counterparts to develop "triple-negative" tumours. These tumours, which usually strike before menopause, can be particularly deadly because they don't carry large amounts of a surface protein called HER2/neu and also lack receptors for the sex hormones oestrogen and progesterone. As a result, they fail to respond to either of the leading breast cancer drugs: tamoxifen, which blocks the stimulating effect of oestrogen; or Herceptin, which targets HER2/neu.

Tumour type can't fully explain the astonishingly high death rate from breast cancer among black Chicagoan

women, however. A clue that social factors might contribute to this tragic trend came from the lab of behavioural biologist Martha McClintock, also at the University of Chicago. When she housed normally gregarious rats alone, she noticed that they tended to die early from a variety of tumours. She has since investigated the phenomenon in detail, revealing last month that isolated female rats become edgy and vigilant, have high levels of the stress hormone cortisol, and are 3.3 times more likely to develop breast cancer than animals living in groups (*Proceedings of the National Academy of Sciences*, DOI: 10.1073/pnas.0910753106).

Gehlert was struck by the parallels between McClintock's rats and the vigilant, stressed women she knew from the scariest South Side neighbourhoods. She decided to find out if the stress and isolation these women experience has direct biological effects on their health too. Over the past five years, Gehlert's team has recruited some 230 black Chicagoan women, newly diagnosed with breast cancer, for a survey that combines interviews, analyses of crime statistics and other conditions in their neighbourhoods, plus hormonal measurements and molecular studies of biopsies from tumours. Garmon-Spears is one of the volunteers.

In a seminar last month at the National Institutes of Health in Bethesda, Maryland, Gehlert described her team's findings. Most striking is the fact that the women fall into two groups based on the daily patterns of cortisol in their saliva (see graph, above). One-third of the women had a normal daily cycle, with a peak about 30 minutes after waking up. But the other two-thirds, dubbed "flatliners", had no cortisol cycle at all.

It turned out that the flatliners lived in areas with more homicides and robberies, and scored higher for depression. Women who felt they had strong social networks, and scored low on a psychometric test for loneliness, were more likely to have a normal cycle.

Gehlert suggests that the fear that comes with living in high-crime areas combined with scant social support causes overproduction of cortisol,

FROM CITY STREETS TO COUNTRY ROADS

At first glance, the rural backwaters of south-east Missouri have little in common with the South Side of Chicago. But they are both examples of social environments that may be causing biological changes in people's bodies that can send them to an early grave.

Sarah Gehlert of the University of Chicago is looking at how the strain

and isolation of life in tough neighbourhoods in Chicago might explain the high death rates from breast cancer in black women (see main story).

In Missouri, she is teaming up with Graham Colditz at the University of Washington in St Louis to recruit about 300 black and white women with breast cancer. Here, crime is lower than in Chicago,

but the poverty is similar. A sparse population means social isolation is also a serious problem.

Meanwhile, Gehlert's collaborator Electra Paskett of Ohio State University in Columbus is exploring whether social isolation in poor white women in the Appalachian mountains depresses immunity, allowing papillomaviruses

to trigger cervical cancer.

And in Philadelphia, Tim Rebbeck of the University of Pennsylvania is looking at the social and biological factors behind the black-white disparity for prostate cancer. He has found that the prognosis is worst for black men in deprived areas who lack a supportive social network through family or church.

similar to that seen in McClintock's isolated rats. This eventually erodes the body's ability to release the stress hormone, creating the flatline effect. Similar "burnout" patterns have been seen in patients with post-traumatic stress disorder.

In this respect, Garmon-Spears's prospects may be better than many. While she grew up in a tough South Side housing project, and lost her husband to an overdose of crack cocaine over a decade ago, she feels comfortable in her present home, just north of the city centre. "I'm watchful; I'm careful, but I'm not scared," she says. Between caring for her mother, chatting with her sisters, and attending Jehovah's Witnesses meetings, she has a busy social life.

But among the flatliners, fear of crime and lack of amenities creates severe social isolation. "When they list their five closest ties, it's unlikely they'll be in the vicinity," Gehlert says. "In the worst neighbourhoods, they have no casual ties, because businesses have moved out."

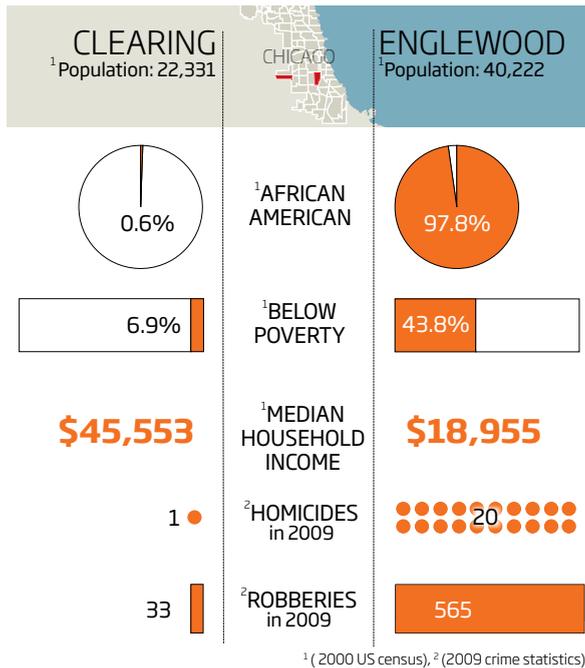
Meanwhile, Conzen and McClintock have come up with a biological mechanism that could explain how high levels of cortisol caused by social isolation might increase women's death rate from breast cancer. In mice that were genetically predisposed to breast cancer, the researchers found that the surge in cortisol caused by social isolation works through receptors on the surface of tumour cells to increase the activity of certain genes. This increase allows the tumour cells to use sugars and fats more efficiently. By 21 weeks of age, isolated mice had tumours that were on average more than 50 per cent larger than those in mice that were also prone to breast cancer, but housed in groups (*Cancer Prevention Research*, vol 2, p 850).

Health disparities

To complete the picture, Olopade is now studying biopsies of the women's tumours to see if the flatliners, in particular, have altered gene activity that is similar to patterns seen in the isolated mice – although she warns that a bigger sample of women may be needed to produce definitive results.

The wrong side of town

There are stark social differences between a comfortable Chicago suburb like Clearing and an inner-city area like Englewood. Are these contributing to high death rates from breast cancer among black women living in the city?



So far, the results from the collaboration have impressed other researchers interested in health disparities. "Loneliness is something that people might not think of immediately as an obvious factor on the pathway to aggressive breast cancer," says Marshall Chin, a diabetes specialist also at the University of Chicago. Other projects are examining whether a fusion of sociology and biology can shed light on why other disadvantaged US populations, both black and white, are disproportionately affected by cancer (see "From city streets to country roads", opposite).

The key test of the approach, however, will be whether or not it can improve survival rates. Gehlert is already planning trial interventions for the next phase of the Chicago project. Stress-control techniques are a non-starter. "If we taught a woman relaxation, we'd be helping her biologically but she'd probably be murdered," Gehlert says. "Where there are a lot of crimes and unsafe housing, they really do need to be vigilant."

Instead, she plans to recruit "neighbourhood coordinators" within

South Side communities who will help women to negotiate obstacles such as the bureaucracy that frustrates attempts to obtain housing, healthcare and other necessities. The coordinators will also work with free clinics and other community groups to find spaces where isolated women can meet one another and get the social support that is missing from their lives. "We need places where women can have some social interaction without fearing harm," Gehlert says.

Meanwhile, biologists on the team are thinking about affordable drugs that might help. Given the apparent involvement of genes that affect the metabolism of sugars, Conzen suggests that metformin, which decreases the amount of glucose absorbed from food and released from the liver, might starve the women's tumours of nutrients, making them less aggressive.

Metformin is already used to treat type 2 diabetes, and there is a possibility that similar stress-induced changes in gene activity could contribute to disparities in the incidence of this disease. "There's a lot of interest in cortisol burnout in diabetes," says Graham Colditz, an epidemiologist at Washington University in St Louis. Indeed, related mechanisms might help explain why disadvantaged populations suffer heavily from a whole range of major killers. "They have high cancer, high diabetes, high heart disease, and very high stroke," Colditz says.

Could a combination of social interventions and drug treatments give Gehlert's flatliners a fighting chance? Will it be necessary to intervene earlier to stave off cortisol burnout in younger women before the damage is done? For now, there are more questions than answers. But when answers come, they may resonate in the corridors of power. The young Barack Obama cut his teeth as a community organiser on Chicago's South Side. His wife, Michelle, was on the planning committee for Gehlert's project.

The women of the South Side urgently need a message of hope. But turning hope into improved health outcomes for disadvantaged populations across the US may require political action at the highest level. ■

"Relaxation might help a woman biologically but she'd probably be murdered"

SOURCE: US CENSUS BUREAU AND HTTP://GISCHICAGO.POLICE.ORG