Will medicine ever be able to halt the process of ageing?

Geoff Watts reports on the elusive search for ways to keep us young

Anti-ageing medicine may not be the most well developed branch of healthcare and medical research, but one thing it doesn’t lack is self confidence. “Anti-ageing medicine is the pinnacle of biotechnology joined with advanced clinical preventive medicine,” according to the website of the American Academy of Anti-Aging Medicine (A4M), one of the leading organisations in this endeavour.1 “It is scientific . . . It is evidence-based . . . It is well-documented in peer-reviewed journals.” The advances on offer to patients are the “most potent emerging biomedical technologies today.”

Some manifesto. And while A4M members and most other anti-ageists limit their ambitions to minimising age related disease and achieving a modest increase in longevity, a minority of true believers foresee much more: the indefinite postponement of death. Orthodox science may be irritated by what can be seen as ill founded over-optimism, but the notion of fending off the decrepitude of old age has always captured the public imagination. By 2015, according to one estimate, the global market in anti-ageing products will be worth nearly $300bn (£190bn; €210bn) annually.2

What, precisely, is encompassed by the term “anti-ageing”? A great deal of ordinary everyday medicine, be it the prevention of strokes or the removal of malignant tumours, is about prolonging life. But the full blooded anti-ageing prospectus goes beyond this; it focuses not only on the diseases associated with age but on the process of ageing. Evidence of the benefits of disease interventions is overwhelming; those aimed at the ageing process are still characterised less by achievement than by theory, by extrapolation and clinical promissory notes on the unlikely promise of a better human lifetime.

For example, radical theories of ageing predict that the human body will reach a certain point, where the repair and maintenance at the cellular and molecular level will slow, stop, or reverse the aging process. It is this challenge which is the life work of Dr Aubrey de Grey, founder of the SENS Foundation and one of the most influential anti-ageists. He concedes that some of his fellow researchers do find him exasperating, though he has a different explanation. “The challenge I’m facing with the biological community . . . is that I’m proposing the application of regenerative medicine to the problems of ageing. But regenerative medicine has been developed for purposes such as treating acute damage like spinal cord injury, not repair and maintenance at the cellular and molecular level.”

Free radicals are atoms or molecules with a single unpaired electron—which makes them chemically very reactive. First suggested as a cause of ageing in the 1950s, some people see them as the predominant factor whereas others view them as no more than a contributing factor to degenerative disorders such as Alzheimer’s disease. As in any field of research where there is uncertainty, theories move into and out of fashion. Although he was once committed to a free radical explanation, Dr de Magalhães is no longer so sure. Not all studies, he says, support it.

One man wholly untroubled by hand wringing uncertainty is Aubrey de Grey, chief science officer of the SENS Foundation, a non-profit organisation based in the US. He lists seven broad categories of primary damage that underlie the ageing process, ranging from mutant mitochondria to the accumulation of intracellular junk comprising defective molecules that can’t easily be broken down and eliminated. He’s confident that his list of categories is complete, even though he can’t say which are most influential.

No matter. Let’s suppose that at least some of the contending explanations really do account for ageing; can we delay or even halt it? SENS is an acronym of Strategies for Engineered Negligible Senescence, and, as its name implies, the organisation claims to have the answers, at least in principle. According to its website, “we know how to fix all of this damage today. For each major aging lesion, a SENS solution for its removal or repair either already exists in prototype form, or is foreseeable from existing scientific developments.”

When I suggested to Dr de Grey that many scientists working in ageing found his breezy confidence rather exasperating, he bristled at the use of the word “breezy,” citing his book as evidence that he’s well versed in the complexity of the problem. He concedes that some of his fellow researchers do find him exasperating, though he has a different explanation. “The challenge I’m facing with the biological community . . . is that I’m proposing the application of regenerative medicine to the problems of ageing. But regenerative medicine has been developed for purposes such as treating acute damage like spinal cord injury, not repair and maintenance at the cellular and molecular level.” He sees a gap between geriatric medicine and the science of gerontology, which he says he’s trying to plug.

If Dr de Grey occupies one end of a spectrum, Leonard Hayflick—who determined the maximum number of divisions that a human embryonic cell can undergo before it succumbs to senescence (the Hayflick limit)—occupies the other. “No intervention will slow, stop, or reverse the aging process in humans,” he has written.5 “When it becomes
possible to slow, stop, or reverse the aging process in the simpler molecules that compose inanimate objects, such as machines, then that prospect may become tenable for the complex molecules that compose life forms.” But not until.

Biological approaches
Most gerontologists occupy neither extreme. Dr de Magalhães compares the problem of ageing with that of cancer. “Cancer’s a simple problem. You have over proliferating cells and you have to get rid of them. And yet with huge amounts of money and decades of research there’s a lot of cancer we still can’t cure.” But as he adds, “There’s no law of physics that says we can’t alter the process of ageing.”

The best known ploy to slow ageing is a calorie restricted diet, effective under certain circumstances in some animals. Linda Partridge, director of UCL’s Institute of Healthy Ageing, has taken a close interest in what may be the underlying mechanism of the phenomenon: the insulin/insulin-like growth factor signalling pathway. This responds to an animal’s nutritional intake, matching growth and reproduction to food availability—and also, it seems, affecting health and longevity.

She sees no reasons in principle why this mechanism couldn’t be manipulated pharmacologically. “A lot in the end will depend on the attitudes of the pharmaceutical companies. These nutrient sensing pathways have been the subject of scrutiny for a long time. What’s novel is the realisation that interfering with them can simultaneously affect many aspects of the ageing process.” But a high safety hurdle will have to be crossed before licensing bodies could consent to healthy people receiving a drug for a substantial part of their lives.

Professor Finch also sees no reason in principle why the mechanisms that underlie ageing cannot be thwarted. In the case of free radicals he is certain that their production can’t be halted. “You cannot have a cell operating in an aerobic environment without suffering free radical damage. And in the animals that have been studied there’s been no way of repairing it.” But could we eventually develop a repair process? Not impossible, he says. “In broad Utopist terms, any aspect of a living system which depends on chemistry cannot be thwarted. In the case of free radicals they wholly disreputable. “This is an area where the potential for contemporary medical discoveries and applications of biomedical technology to retard or reverse the otherwise inevitable process of senescence.” But the BMJ has learnt that A4M has had a periodically strained relationship with the American Academy of Anti-Aging Medicine (A4M). Its prospectus is uncontroversial: “There are no ‘magic bullet’ medicines. As we age, a series of biological changes take place in the body. Anti-ageing physicians seek to understand these age-related declines in order to enable a better grasp of the potential for contemporary medical discoveries and applications of biomedical technology to retard or reverse the otherwise inevitable process of senescence.” But the BMJ has learnt that A4M has had a periodically strained relationship with what it calls the gerontological “elite” or “establishment”—by which it seems to mean some of the leading academics working in gerontology.

Is it worth it?
More generally, the term anti-ageing is used to cover all sorts of products and practices, some of them wholly disreputable. “This is an area where the potential for snake oil is huge,” says Professor Partridge. “You only have to look at the face cream shelves in any drug store. There’s all sorts of stuff that does no good at all.” By contrast, other components of what is labelled anti-ageing medicine are really no more than a repackaging of sensible lifestyle advice and good preventive medical practice.

The questions most often prompted by talk of novel interventions to extend life, never mind postpone death, are usually social: the effect it would have on the structure and stability of society and on matters ranging from employment to overpopulation. But let us assume that effective methods to control ageing do become available: stem cell implants, gene therapy, whatever. How many of us would be prepared to bear the cost in time as well as money? The battery of interventions envisaged by Dr de Grey conjures up an image of life dominated by a never ending round of medical appointments, check-ups, discomfiting procedures, and Lord knows what else. Would the extra years be worth much if mostly taken up with the getting of them?

Dr de Grey is predictably upbeat. The treatments will overwhelmingly be provided by injection. “Initially, when they’re still experimental, there will be a great deal of monitoring involved, and one might have to spend a while in hospital. But that won’t be an issue for long.” Many people, he’s sure, would welcome the gain.

I wonder. In a recent session on ageing at the Cheltenham Science Festival, a clear majority in an audience of all ages favoured dying in their 80s. The 90s were notably less popular, and only one might have to spend a while in hospital. But that won’t be an issue for long.” Many people, he’s sure, would welcome the gain.

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OLD AGE AND THE CITY

How can cities, which have been designed for youth, be encouraged to accommodate an ageing population and keep the over 60s healthier for longer? Edwin Heathcote reports on projects from Berlin to New York

We can all imagine a picturesque evening street scene in the intimate piazzas of a Mediterranean city. The old folk have taken out plastic chairs and are sitting outside their houses and apartment blocks. Or they might be sitting on benches while the grandchildren play in the street or stroll up and down with their parents enjoying the passeggiata. Or perhaps a street scene from old Brooklyn in which the seniors sit chatting on the stoop outside their homes, complaining about how the world has gone downhill.

These may be idealised scenes, snapshots that exist more in our collective memories of holidays and movies, but they do illustrate how the city streets can be a place in which elderly people play the pivotal role. They are the guardians of the street: watching, listening, shopping at the corner store, occasionally scolding, gossiping, perhaps interfering, but always aware, making the street a conduit of conversation rather than transportation.

Modernism, as Jane Jacobs pointed out in her 1961 book, *The Death and Life of American Cities*, nearly did away with all that. Jacobs highlighted how the idea of “zoning” was killing the city street. The separating out of retail, living, and working into distinct and separate zones was creating enclaves of ennui, zones where only one thing happened and then only at certain times of the day. The vibrancy which was the whole point of city life was fading away as nations suburbanised, increasing distances between dwellings and people, relying ever more on cars and the depersonalised non-spaces of the supermarket and shopping centre. Old people were shipped out to retirement homes, soporific waiting rooms for death built in a twee, suburban genre. They were, in effect, removed from city life.

What do older people want?
The question, in an ageing world—in which the proportion of the population over 60 is predicted to almost double over the next decade—is how can they be brought back? How can cities, which have been predicated on youth, be encouraged to accommodate an ageing population and so ensure their survival as heterogeneous, lively places? And, as if that wasn’t a big enough question it is compounded by an even bigger consideration. What are old people like? I once spoke to a man with terminal cancer who had been put in a hospice and spent his days looking out at lawns and trees. He told me it reminded him of the bland, soporific landscape of a crematorium and all he longed for was to see a bit of city life, to watch girls go by, and have a pint.

If there has been an assumption in architecture and planning it has been that elderly people are infirm and need level spaces, ramps, and a lack of obstacles. They need big bold signs and disabled toilets, benches and lots of green space. Yet the huge majority of people over 60 are hardly invalids—in fact, most of them will be working for a long time to come. As healthcare and outcomes continue to improve elderly people will continue to get fitter, will live longer—more of them will be active. There is no average over 60, which makes planning a city sympathetic to their needs a particularly complex yet singularly fascinating problem.

The issue of ageing in cities is finally reaching a kind of maturity. The World Health Organization has launched an ambitious programme to develop age friendly cities. An age friendly city, it says in WHO’s brochure “encourages active ageing by optimising opportunities for health, participation and security in order to enhance quality of life as people age.”

Age friendly design
But how will any of these noble (if slightly vague) intentions begin to physically change the cities we live in? Firstly, and arguably most importantly, the answer has to be “not much at all.” John Beard, the director of WHO’s department of ageing and life course, told me: “We brought out guidelines...
“Old people were shipped out to retirement homes, soporific waiting rooms for death built in a twee, suburban genre. They were, in effect, removed from city life”

on how to assess the age-friendliness of a city in 2007. Most of the recommendations were based on common sense about the physical environment, access, public transport, park benches, toilets, the kind of things that older people had told us make a difference. But they were not always about the concrete structure of the city, there were issues of social participation, of engagement for older people and ways in which older people can connect with each other, with society and participate in decision making. We were swamped by cities wanting to take part in a programme that didn’t exist yet, so in 2010 we set up the Age Friendly Cities Network.

That network now embraces cities including Geneva, Brussels, La Plata, Canberra, and Germany’s entire Ruhr region and others and, most notably perhaps, New York. The city’s mayor, Michael Bloomberg, has been an enthusiastic proponent, stressing that an age friendly city is a city friendly for all ages. I spoke to Dorian Block, of the New York Academy of Medicine and spokesperson for New York’s “Aging Improvement Districts” and she explained some of the measures that her city has undertaken: “What we’ve found is that it is fear that keeps older people at home. Their radius of travel reduces and they’re unwilling to travel more than five blocks.” That fear is often about security, but it is also, almost pathologically, of falling down or tripping, which can cause injuries that are devastating to older bodies. Busy streets and hazardous crossings are also a problem. “The city has selected more than a dozen intersections,” Ms Block continues, “adding medians [traffic islands] so people can stop safely in the middle of the road. We’re making sure there’s visibility around the edges and the corners of road surfaces and we’ve put bollards in so that cars can’t park on the sidewalks.” The programme also includes such deceptively simple things as a list of grocery stores which have toilets and moves to make store’s shelves lower and more accessible and labels easier to read.

The interesting thing about New York is that, fundamentally, it has always been a good city to “age in place.” One million of its residents are over 65. Its neighbourhood infrastructure of corner stores, laundromats, and diners, its extensive sidewalks and parks, its excellent public transit have made it a model city. But a combination of the elderly moving out (or being moved out) to residential homes (usually in the suburbs), or to the more pleasant climate of Miami and of the radically changing nature of neighbourhoods as they are gentrified and become “corporatised,” led to it becoming a less age friendly city than it could have been.

The question “Is the programme working?” is less easy to answer. Certainly, older people who have been involved have been enthusiastic, but Ms Block says, “It’s been difficult to evaluate and we struggle to identify evidence—the programme has only been running for three years and it’s still early.”

Ann-Sophie Parent, the director of AGE, a European platform for older people, talks of similar changes being instigated across Europe. “There are a number of cities that have started to adapt,” she says. “Some have looked at the problem from a broader perspective, looking at how to use these initiatives to regenerate city centres, places with deserted offices, where there are no shops, and old people have become isolated. Germany has been particularly innovative, and there are a number of subsidised programmes. Berlin has been looking at the mobility needs of old people but also of children and women, looking at how they can promote intergenerational accommodation, the sharing of services, the recreation of community support.”

One of the most ambitious initiatives is being undertaken in the Ruhr area, formerly the heart of Germany’s mighty industrial engine but now a pioneering place of post-industrial innovation. As the heavy industrial jobs in the Ruhr disappeared so did much of the younger population and the demographic changed radically. Town planner and architect Albert Speer Jr has been implementing plans for Duisburg, a city in the west of the Ruhr area, to become a model for intergenerational living. The idea is to create a “compact city” in which everything from culture and shopping, medical services, and leisure spaces is within walking distance, enabling older populations to keep active, to keep walking while they are able, and to keep engaged in civic life. Mr Speer also asks whether infrastructure currently used by the young—the city centre nurseries and schools—could, once it is no longer needed, be easily converted into social facilities or care homes. The needs of both groups can be surprisingly similar, and the sites are already there.

Realisation is increasingly that the ideal interventions are those to existing, familiar infrastructures. The urban environment—both inside and out—becomes more critical during old age. Elderly people spend more time in their apartments or houses so the internal layout and convenience become more important to them. But then again, the time they do spend outside, on the streets, in the park, perhaps sitting in a square or at a market, often becomes their only engagement with the world outside because they have no workplace and their family is dispersed. “We’ve looked at ways of recreating public space so that it is better adapted to old people,” says Mrs Parent. “Basic things like more toilets, places where you can sit without...
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They’ve set up labs to train older people to use the internet for instance, and there are huge opportuni-

ties for life-long learning.”

Returning to the physical realm, a model scheme—though not aimed particularly at the old—in London highlights some of the problems in adapting cities. The Royal Borough of Kensington and Chelsea has for years been attempting to create a “shared space” scheme for Exhibition Road, the spine of London’s museums district, with architects Dixon Jones. The idea is that there is no distinction between pavement and road, no kerb, and a single, elegantly paved road surface. Drivers need to take extra care, and the street can accommodate changing levels of crowds. From an urban point of view the system has proved to be safe in pilot schemes in the Netherlands and Denmark. But there were immediately howls of protest from lobby groups for visually impaired people, who say they use the kerb to navigate and negotiate traffic. Nevertheless the scheme is going ahead.

If these proposals sound rather restrained, the almost imperceptible tweaking of existing urban fabric, there is also a striking vision of how an age friendly city might begin to look. Architect Matthias Hollwich of New York practice HWKN has specialised in a vision of how the city might be transformed to accommodate ageing populations. Working in his native Germany with the Bauhaus school he has developed the extraordinary, speculative plans for Geropolis. Although the visualisations may look a little extreme—the wackier end of avant-garde design—the points he makes are serious. Taking as its setting the typically defunct centre of a de-industrialised, depopulated eastern German city, the design looks at how to reinvigorate tower blocks, windswept plazas, and the familiar tropes of failed modernism. “We were trying to use architectural insertions to be able to update cities to accommodate ageing populations without them having to move into nursing homes,” Mr Hollwich tells me. “We wondered how we could visualise this kind of city. We tried to make it a little extreme and we stopped calling elderly people ‘elderly’ and started calling them ‘pioneers’ because no-one will have been to those stages of life before.” That re-casting of the

problem enabled them to construct an engaging vision of radical architecture in which monolithic blocks are hollowed out to create social spaces, churches, and the kind of small scale retail which keeps city blocks alive. If the usual approach is to regenerate a city centre by trying to attract young, creative, arty, and gay populations, this approach does the opposite—regeneration through re-imagination while the population stays the same. Yet more extraordinary is his plan for “Boom” a retirement village for a lesbian, gay, bisexual, and transgender population in Palm Springs, once an exotic getaway for the wealthy and celebrities. Building on the radical modernist architectural aesthetic of the modernist villas which litter the sandy landscape around the California city, it is a life enhancing vision of a town built to keep its inhabitants active and together. “It is the world’s most dangerous nursing home,” writes Mr Hollwich. “It defies all expectations. It isn’t lonely because it isn’t home. Rather it is designed to trigger curiosity and engagement and make them places we never want to leave.”

“A large part of society relies on corporate services,” says Mr Hollwich. “How can we re-engineer that structure where people can rely on each other, providing care which is more personal but also less expensive [he has coined a good phrase for this—‘stealth care’]. We need to build beautiful stairs so that people are encouraged to use them, to meet people coming the other way, until they absolutely can’t—when there are elevators. You don’t want people to get lazy but you don’t want them to have to move out.”

There is always an impression that adaptation of urban fabric for an older population will somehow create a medicalised environment, the city equivalent of the grim institutional aesthetic of the disabled toilet. “In fact,” says Mrs Parent, “measures that help old people also help the whole population.” Cities are going to have to accommodate older populations, it’ll be fascinating to see whether a shifting demographic can really do what it ought to, and improve cities for all of us and make them places we never want to leave.

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