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Editorial

From the Zoo to the Clinic; New Ideas about Cancer

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Illustration

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Text: Peto's Paradox [1], named after the great epidemiologist and statistician Sir Richard Peto, is well known in cancer circles. If every cell has a similar chance of becoming cancerous (due to random DNA hits/mutations), then larger animals with longer life-spans and more cells in their bodies should have higher rates of cancer. The fact that they don't, is the paradox.

Larger and longer-lived animals must have developed highly effective chemo-protective machinery, because animals with 1000 times our number of cells do not have more cancer than us. In fact, some of the largest animals such as Great White sharks and elephants have significantly less cancer than we sickly humans do.

Given the difficulty of studying cancer epidemiology in the wild, Peto's Paradox remained in the 'probable but not quite proven' bin for almost half a century. A few months ago, a rather beautiful study [2] presented the results of a very large survey of autopsy data in 191 species of mammals that had lived and died in zoos, and had been minutely recorded. The researchers found that cancer mortality risk was largely independent of body size and life expectancy. Peto was right.

They found something else too, relating to diet (my obsession). Mammalian carnivores had significantly more cancer than herbivores and omnivores. The team cited three possible reasons for this including the acquisition of oncogenic pathogens from prey, the bio-accumulation of environmental toxins and a high-fat, low-fibre diet. I'll swallow the first two, but I am not convinced by the third.

Although the high-fat low-fibre diet certainly increases cancer risk in omnivores like us, I doubt that animals specialised in such diets are vulnerable in quite the same way; evolutionary theory runs counter to that idea. I think that increased cancer risk in carnivores may reflect their substantially lower intakes of chemo-protective phytonutrients such as polyphenols and carotenoids; and that if we could persuade carnivores to eat more of these, their cancer risk would fall.

I don't recommend force-feeding legumes to lions, but *Felis catus* (the domestic cat) is a different kettle of fish, and marginally easier to manipulate. While we think of cats as obligate carnivores, Hills pet food technologists were able to conceal plant foods in their kibble; and it turns out, perhaps counter-intuitively, that they can consume polyphenols and prebiotic fibres with impunity [3].

Hiding a polyphenol- and fibre-rich blend of inter alia ground pecan shells, flaxseed, beet pulp, citrus pulp, oats, chicory and crushed cranberries in the cats' diet resulted in a predictable shift in moggy's microbiome towards saccharolytic species and the formation of anti-inflammatory post-biotic compounds [4]. Less predictably, this created a series of gastrointestinal benefits [5,6].

The studies ran for only 6 to 8 weeks, so it is impossible to say if the polyphenol-rich fibres were chemo-protective. But given the fact that these phytonutrients have significant anti-cancer effects against cancer cell lines from primates, rodents and dogs [7,8] and exert anti-inflammatory effects in fish [9] and avian [10] species, I wager they would reduce cancer risk in cats and carnivores in general.

From an evolutionary perspective, the increased risk of cancer incurred by felids and other carnivores is presumably neutralised by the energetic advantages gained from this food source/ecological niche, and the fact that cancer in these creatures generally arrives well after breeding age. If Smilodons had learned to browse on blueberries, things might have been different.

Returning to Peto's Paradox, several of the chemo-protective mechanisms that have developed in larger animals have been elucidated. For example, elephants carry multiple copies of tumour suppressor genes TP53 and LIF. The pachyderms generate correspondingly higher levels of their respective gene products, leading to enhanced culling of potentially cancerous cells [11-13].

If we could utilise or mimic these and other defence mechanisms, which must have emerged via natural selection, we might theoretically reduce our own cancer risk to a thousandth of what it is today. But that way lies transhumanism, and the unfolding disaster of the Covid gene therapies will close that door for some time unless the Emperor Palpatine (né Klaus Schwab) wins the final battle.

Far safer to focus on chemo-prevention through diet and lifestyle. And there is another lesson we can learn from the animal kingdom which may relevant to our pets, and to us.

While Peto's Paradox may be true in the artificial environment of the zoo, it is not entirely clear how far it extends beyond the bars. In the wild, animals that fall sick are culled very quickly. Furthermore, generally lower life expectancy means that their risk of acquiring diseases of old age such as cancer is correspondingly reduced.

Wild-life cancer stats must, therefore, be carefully parsed. In the largest data set of its kind, a series of over 100,000 animal autopsies reported by the National Wildlife Health Centre in Madison, Wisconsin, only 22 animals were reportedly found to have tumours [14]. This is one to two orders of magnitude below the incidence reported in the zoo study [2].

Anthropogenic environmental damage is undoubtedly changing this. When the carcinogen benzo(a)pyrene leached into the Puget Sound it bio-accumulated in the local population of Beluga whales, beautiful and intelligent animals which now have a cancer incidence

close to 30% [15]. There are reports that cancer may be increasing in many other wild-life species too [16] and if so, it is probably for similar reasons.

Are domesticated animals any better off? Well, the domesticated primates they live with currently have the highest cancer rates of any species known, with a 45-50% lifetime risk [17,18]. Why is Hom Sap such an outlier?

Some see this an inevitable consequence of our longevity, as per Bruce Ames' ahistoric theory of cumulative mutations. Medical historians and anthropologists take a more nuanced view, because they know that cancer rates are significantly lower in historically and/or geographically defined blue zones [19-22].

Blue zone data has its weaknesses, but the idea that a lifestyle more suited to our evolutionary requirements is far less likely to promote cancer is supported by the fact that modifiable factors related to the modern diet and lifestyle account for almost half of all cancer deaths today [23]. If these were removed and our diets were then optimized, our cancer rate would fall into line with that of carnivores (circa 10%). Perhaps even lower.

The problem is, we love those modifiable factors. These include alcohol and tobacco, together with low levels of physical activity and consumption of ultra-processed foods [23,24], which create obesity and metabolic skew. And interestingly, the only animals that have cancer rates anywhere near those of humans are those which most closely share our homes, diet and lifestyle.

Dogs currently have a 30% incidence of cancer [25-27], putting them in second equal place (with the environmentally-challenged Beluga) behind the post-transitional dog-owner. There is some evidence that canine cancer rates may even be increasing [28], but cancer is not a reportable disease in pets so accurate trend analysis is hard to find.

We do know, however, that dogs share their owners' lifestyle diseases [29] and acquire them for much the same reasons. Physical inactivity, ultra-processed foods and smoking (passive, except for beagles), are all in the mix. But there are two other factors that hit man's alleged best friend particularly hard.

Periodontal disease [30] and in-breeding [31-38] both increase the risk of a range of cancers in humans, and both of these factors are very prevalent in the canine world [39,40]. Periodontal disease is easy to counter by adding a pinch of algal fucoidans to your pet's meals [41]. In-breeding cannot easily be countered, but can be pre-empted.

Some breeds which are very cancer-prone would clearly benefit from out-breeding. The Bernese Mountain Dog, the Irish wolfhound and the Leonberger are among the most affected, with roughly 50% of them dying from cancer [42,43]. Shih Tzus are far less affected at 14% and beagles in the non-smoking section are almost immune [42,43].

If we cannot change their genes, could we at least offer our four-legged friends chemo-protection by improving their diet?

The food industry pays more attention to the nutritional qualities of pet food than it does to human fodder, and the better kibbles and wet foods are considerably healthier than many of the products we eat. But while ultra-processed dog foods are not bad (I have sampled a few of them, for science of course, and other brave souls have taken things further than I ever did [44]), they are far from optimal.

Adding raw offal, fresh vegetables and oily fish such as sardines to the menu can pay huge health dividends, including cancer risk reduction. If sardines aren't your thing, the standard dose of Balance oil (0,15 ml per kilo body weight) will provide the same benefits.

And maybe our dogs can repay the favor. Already proving their worth as cancer detectives [45], those breeds with ultra-low cancer rates are providing clues [46] to how we too might fetch, roll over and stay a little longer.

Next week: Bones of the saints; why I hate supplements.

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