CSF is produced deep within the structure of the brain and is drained via a complex and less than optimum arrangement of ventricles and aqueducts. CSF occupies and circulates throughout the subarachnoid space and is finally absorbed into the systemic venous circulation outwith the substance of the brain via the superior sagittal sinus. This arrangement predisposes to blockage with a consequent increase in ICP.

The meninges surround the brain and in several places, for example the dural midline falx cerebrei extend for a considerable distance into the substance of the brain. The function usually attributed to these structures is that they protect and stabilise the brain [9].

Using the simile of the Necker cube, an alternative is to view the meninges as a set of exquisitely designed structures which function to control intracranial pressure. The Dura is innervated by the trigeminal and vagus nerves in a similar manner to the eye and it is attractive to consider similar mechanisms protecting both the brain and the eye from excess pressure increases.

The Monro–Kellie hypothesis states that the cranial cavity is incompressible and the volume inside the cavity is fixed [10]. The cranium and its constituents, the nervous tissue, blood and CSF are in equilibrium, any increase in the volume of one must be compensated for by a decrease in another.

An uncompensated increase in ICP due to an increase in any of the constituents of the cranial cavity is potentially dangerous.

This rise in ICP stimulates the trigeminal and vagus nerves innervating the dural folds, this dural irritation is sufficient to excite an oculo-trigemino-vago-abdominal reflex resulting in vomiting [7]. Vomiting also causes stimulation of the sympathetic nervous system resulting in decreased CSF production [11].

It is interesting to note that the dural venous sinuses are equipped with structures which are resistant to pressure changes [12].

Vomiting results in profound changes to the body's biochemistry. It causes a loss of gastric fluid, containing Na^+, Cl^-, K^+ and water. It causes depletion of extra-cellular fluid volume and hypokalaemia. These gastric losses also result in the formation and excretion of excess HCO_3^- Na^+, and K^+ via the urine. Worsening volume depletion leads to aldosterone secretion which results in increased K^+ excretion, further exacerbating hypokalaemia [13]. In addition vomiting causes loss of H^+ and a metabolic alkalosis, resulting in cerebral vasoconstriction and a decrease in ICP. This acts to decrease the production of CFS compensating for the increases in ICP [10].

Vomiting should not be seen as a symptom of increased ICP but should be seen as a complex beneficial adaptation in cases of increased intracranial pressure.

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On the origin of cancer: Evolution and a mutation paradox

Nothing in biology makes sense except in the light of evolution.
Dobzhansky, 1937 [1]

In a recent contribution to Medical Hypotheses, Dr. Garcia-Garcia [2] developed the question whether cancer is a genetic program with an unknown function. In this personal view, I would like to emphasize a different rationalization and provide an answer on the basis of evolutionary considerations.

Indeed, as succinctly suggested by Dr. Greaves [3], when we try to understand cancer, we are actually looking at evolution and its very principles. According to Darwinian rationale, we are dealing here with crucial facets of and necessary conditions for evolution, namely changes in genes. In our short-term judgement some of the effects are certainly not appreciable (after all, cancer kills) but, ultimately, mutations are keys to our – and other species' – long-term adaptation to and survival under changing environmental conditions. Clearly, without the change of genes, there would be no evolution and thus, no us. And yet, if there were no changes in genes we would neither observe nor suffer from cancer [3].

Now, in analogy to Rose's prevention paradox (a preventive measure which brings much benefit to the population offers little to each participating individual; [4,5]), we are actually looking at a *mutation paradox* here [6]. Indeed, on the one hand, in individuals, mutations may have adverse health effects, including cancers. But on the other, populations as a whole are likely to benefit on the long run from changes of genes.

In conclusion, here is my answer to Dr. Garcia's question "Is cancer a genetic program with an unknown function?" [2]: in evolutionary terms, with no place for the "teological heresy of goal or purpose" [7], cancer is not a "program", neither specific nor unspecific, and it does not have a "function".

So what is cancer then and what should we do to better control it? More generally, cancer, as explained lucidly by Greaves in his authoritative views on the origin of cancer [3], is an "evolutionary

legacy". More specifically, cancer is a consequence of changes in genes which are conditiones sine qua non for evolution. Overall, in view of the additional fact that no two cancers are the same and that exogenous factors and not inherited genetic factors are the dominant determinants of cancers [8], rather than focussing too much on reductionist expectations in the functional role of one or more genes or mutations, it seems promising to identify factors in the environment which are manipulable for populations rather than for few individuals to battle the burden of cancer.

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