Is artificial blood safe for vampires to eat?

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What are the daily recommended nutritional requirements for a vampire? What does artificial blood taste like? Would you rather be a vampire or a zombie? These are not questions I ever thought I would be asked as a young scientist, but both have featured when I have been communicating my science to the general public. When I was growing up, vampires were evil and to be feared. Yet in recent years it appears that they were, in fact, much maligned and misunderstood; they really just want to live their lives in peace with their mortal compatriots. It is not reported what the late – and recently much lamented – Sir Christopher Lee thought of this transformation, although I strongly suspect that, like myself, he prefers his vampires raw in tooth and claw (or rather fang).

Historical perspective

There have been more films about vampires than any other fictional character. Most draw on the Bram Stoker 1897 novel *Dracula*; the vampire is frequently portrayed as a sexually alluring man, presumably as a way of drawing the audience into the film. Female versions of the myth have drawn on the novel *Carmilla* by Sheridan Le Fanu, which actually pre-dates Bram Stoker's novel by 26 years. Perhaps not surprisingly, the female vampires themselves are portrayed as sexual predators. Who can forget the 1970s Hammer Horror trilogy of *Vampire Lovers*, *Lust for a Vampire* and *Twins of Evil*? Not all films, however, feature such attractive vampires. A subgenre portrays the vampire as the hideous beast of Central European folklore; I fondly remember the 1979 Werner Herzog West German art-house movie *Nosferatu the Vampyre* starring Klaus Kinski.

Bram Stoker researched his famous book *Dracula* during a trip to Whitby in 1890. There is very little evidence that Stoker based his Count on a specific historical figure[1]. Yet vampire movie mythology is largely based on such characters, the male of the species being the eponymous Vlad Dracula, or rather Vlad III, Prince of Wallachia, a member of the House of Drăculești. Now immortalized as 'Vlad the Impaler', he lived in 15th Century Transylvania. This is in modern day Romania, although my Hungarian blood (and certainly my mother) might still wish to dispute sovereignty. Vlad was a Christian ruler and fought against the Ottoman Empire. His reputation is rather better in Eastern Europe than the West, although stories of wartime cruelty – including the famous impaling of his victims – exist in both cultures.

The female most closely associated with vampirism was definitely Hungarian – the princess and serial killer Countess Elizabeth of Bathory. Elizabeth was alleged to have drained the blood from over 600 young girls to feed her restorative blood baths. Again history cautions us from being too judgmental. Blood baths were not mentioned at the Countess's trial; the King at the time owed the Countess a lot of money, and the evidence against her was probably obtained under torture. Still this has not stopped her being named in the Guinness Book of Records as the most prolific murderer in the western world.

Another victim of the vampire myths is the poor vampire bat. Named after the novel, rather than the other way around, there are three species that all hail from the American continent: *Desmodus rotundus*, *Diphylla ecaudata* and *Diaemus youngi*. They do indeed feed entirely on blood. Although they hunt at night, their mode of attack is somewhat less dramatic than that of the eponymous Count. When they spot a sleeping mammal (including humans), they make a tiny incision with their sharp teeth. The victim remains asleep while the bat laps up their blood – real vampires don't suck! The blood continues to flow, rather than coagulating, because the saliva of the bat contains a glycoprotein that acts as an anticoagulant by inhibiting specific plasma coagulation factors. Let no one claim that biochemists lack a sense of humour, for this protein goes by the name of draculin. The effect of a vampire bat attack is rather less dramatic than that of a fictional vampire – the animal, after all, strives to avoid detection to carry on its meal. There is no chance of dying from blood loss or turning into a vampire; the only concern is transmission of rabies

Common vampire bat (*Desmodus rotundus*)

Tru:Blood (Part of a viral advertising campaign for *True Blood* TV *series)* © HBO

with over 70% of the (admittedly very low) incidences of rabies in the USA being traceable to the bite of a vampire bat.

Vampiric science

How does science fit into vampire mythology? Some films do appear more science fiction than horror. Several explore themes from the 1954 Richard Matheson novel *I Am Legend*. This depicts vampires as infected by a strain of bacteria. Vampire myths are explained in scientific terms: fear of garlic, mirrors and crosses is explained as a form of psychological conditioning or hysteria induced by the infection; direct sunlight kills the bacteria; infecting deep wounds (stake through the heart?) converts the bacteria from mild anaerobic symbionts into active aerobic parasites, resulting in the rapid consumption of the host. Vampire mythology has even made its way into a serious discussion of disease. In 1985, the biochemist David Dolphin made a speech suggesting that people suffering with the disease porphyria might have contributed to the historical vampire myth. The porphyrias are diseases associated with abnormal haem metabolism. Some versions cause extreme light-sensitivity and are treated with blood transfusions or injections of haem. Therefore a sufferer in medieval times might have the characteristics of a vampire, avoiding light and eating blood (haem is readily absorbed in the gut). However, this theory has been criticized[2]. The extreme form of the disease, congenital erythropoietic porphyria that is most associated with the 'vampiric' symptoms is extremely rare; fear of sunlight is a late introduction to the vampire myth probably originating from the 1922 film *Nosferatu*; and it stigmatizes patients suffering from an incurable disease. In fact Dolphin's 'theory' was probably intended to be no more than an interesting presentation at an American Association for the Advancement of Science meeting[3]; and neither was it particularly original as the idea of porphyria as a part of the mythology of vampires (and werewolves) had at least two historical antecedents[4,5]. Such is the power of the vampire myth, however, that this one speech has probably garnered more popular press than most of the rest of Dolphin's distinguished career in porphyrin chemistry.

It's all in the blood

The science in the vampire myths that most interest me, however, is that relating to what sustains the vampire diet? With vampire chic on the rise from the *Twilight* books and TV series such as *Being Human*, it is an interesting time to ask this question. In the old days, Hammer Horror would have us believe that Count Dracula could survive exclusively on the blood of comely wenches. But what if there isn't a single wench left? Or what if the Count had pangs of conscience? Clearly for the modern vampire wanting to integrate into human society, eating human blood is a no-no. A variety of methods are used to get around this problem. Vampires in the BBC series *Being Human* can survive without eating blood; blood lust is modelled more as a drug addiction than

Christopher Caruso (Vince Colosimo) and Edward Dalton (Ethan Hawke) inject a vampire patient with an artificial blood subsitute in *Daybreakers* © Lionsgate

Professor Chris Cooper show off the colours of haemoglobin. Oxyhaemoglobin (red), deoxyhaemglobin (claret), methaemoglobin (brown) and oxidatively modified haemoglobin (green)

a nutritional necessity. In the *Twilight* franchise, the Cullen vampire clan are able to survive on animal blood, thinking of themselves as vegetarian. However (and here I must apologize to my vegetarian wife), Edward likened drinking animal blood to eating tofu in that it keeps you strong, but it never fully satisfies you. As Edward says to Bella, "it wouldn't be like drinking your blood, for instance" – cue much teenage angst and soul searching.

The most interesting recent approaches to vampire nutrition are found in the HBO series *True Blood* and the film *Daybreakers* by the Spierig brothers. In *True Blood*, Japanese scientists have developed synthetic blood. This was designed to be a long-lasting and virus-free product to replace blood for medical emergencies. However, it has had the additional effect of being an ideal food source for vampires. No longer forced to live in secret and prey on humans, vampires are now able to live freely in society. The HBO series was accompanied by a viral marketing campaign including an American Vampire League promoting the 'Tru Blood' drink because "Friends don't let friends drink friends" and "Real blood is for suckers"[6]. You can even buy a Tru Blood drink in the real world; it is a pretty sickly and disgusting orange/red soda, but the bottles look great. In *Daybreakers*, the vampires are less assimilated. These vampires are weakened by drinking animal blood; they crave the 'real thing'. In this dystopian future, the vampire government hunts humans down and the pharmaceutical companies farm humans for blood. But an environmental catastrophe awaits. What happens when they run out of humans? The current human population is down to 5%, and blood supplies will not last more than a month. It is against this backdrop that the vampire haematologists research the development of an artificial blood substitute.

No donors involved

My research area is the creation of an artificial blood substitute that is virus-free, needs no typing, is long-lasting and can be stored at room temperature[7]. How scientifically accurate are these films and how close are we to creating such a product in the real world? Well, my Japanese colleagues are probably irritated that *True Blood* predicted that a fictional Japanese company – the Yakonomo Corporation – would develop a blood substitute product, for at about the same time in the real world, the Japanese-based Terumo Corporation cut all the funding for its blood substitute programme. The fictional Tru Blood product comes in different blood types (A, B, O etc.). However, the intention of a real-world synthetic blood product is to have no blood type and be suitable for all recipients. How is this managed? Well, synthetic blood comes in two forms. The first blood substitutes were completely artificial. If you have watched the James Cameron movie *The Abyss*, you will have heard of "fluid breathing", using oxygen-rich perfluorocarbon molecules to breathe underwater. The same molecules were licensed for use as a blood substitute in the 1980s, but have since rather fallen out of favour. My work, and that of many others, has been based on modifying the natural iron-rich haemoglobin

molecule that transports oxygen in the red blood cell. The protein is purified from out-dated human blood from blood banks, umbilical cord blood, animal blood or via recombinant techniques. It is then modified to increase its lifetime in the vasculature via chemical or genetic cross-linking, polymerization, conjugation or encapsulation. Different products have been used in many clinical trials. Lacking any red cell membranes, these products do not have a blood type, unlike the Tru Blood product. However, recent attempts to make artificial red cells using stem cell technology do create a product with a definite blood type[8]. In fact, one of the advantages of stem cell technology is to grow blood ideally matched to a donor who needs multiple drug transfusions, such as a thalassaemic. Stem cell blood, like Tru Blood, does have a defined blood type.

In some areas, fiction hits perhaps a bit too close to home, particularly with regard to toxicity. Although the problem of replacing the volume and oxygen-carrying capacity of blood has been solved by a number of different techniques, the products suffer from adverse side effects[9]. There is now good evidence that these are caused by a combination of scavenging of the vasodilator nitric oxide, haemoglobin-induced free radical oxidative toxicity and inflammatory responses to free haem. The side effects have meant that no product is currently licensed for use in Europe or the USA, although there are ongoing clinical trials. Current trials focus on using modified haemoglobin oxygen carriers to enhance oxygen transport *in the presence of red blood cells*, i.e. the products are not blood substitutes as such, but are designed to deliver enhanced oxygen delivery where the patient's normal blood cells are failing such as in sickle cell disease.

Some of the earliest clinical trials of synthetic blood were halted as the product showed increased mortality compared with placebo. There is a tense scene in *Daybreakers* that echoes this. The chief vampire forces the haematologist hero to test a product early: "we must commence testing the blood substitute". Alas the patient undergoes a violent reaction on the operating table. Still there is a happy ending (of sorts). At the last minute, the hero's junior sidekick rushes in announcing that he has finally created a safe blood substitute. Like me, he is called Chris. I cherished this moment in the film, although not for long as, in the next frame, his head exploded. I took some comfort that at least this (very) adverse side effect was caused by the humans attacking him and not by his product!

So would you rather be a vampire or a zombie? I was asked this in an interview on Radio 4 (no dumbing down for the BBC there). I answered a vampire. Who wouldn't want to look like Tom Cruise or Christopher Lee, live forever and feast of the blood of young virgins (although I didn't quite put it like that!)? But this was the wrong answer. Like me, nearly everyone opted to be a vampire. So my contribution ended up on the cutting room floor. Now what do zombies eat again? ■

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