Efficient fish not faint-hearted

Elizabeth Brainerd

The blood circulation systems of certain air-breathing fishes and most reptiles appear to be primitive and inefficient. But there may well be good reason that they are designed the way they are, and the principles concerned could inform clinicians who treat heart disease.

A primary function of blood circulation is to provide oxygenated blood to the tissues of the body. Why, then, in some air-breathing fishes, does oxygenated blood flow from the lung to the heart and then to the gills, rather than flowing directly to oxygenate the body? And why do the hearts of most reptiles retain an only partially divided ventricle, given that mixing venous and arterial blood reduces oxygen delivery to the body? Writing in the August issue of *Paleobiology*, Colleen Farmer[1] proposes an intriguing function for these puzzling circulatory patterns — that they provide oxygenated blood to the heart muscle itself.

Gar and bowfin, two North American freshwater fishes, possess both gills and a lung, and are therefore able to extract oxygen from both water and air. In these fishes, oxygenated blood drains from the lung directly back to the heart, where it mixes with venous blood and is then pumped through the gills before flowing out to the body (Fig. 1a). Comparative physiologists have traditionally viewed such systems as primitive and inefficient because oxygenated blood from the lung is diluted with deoxygenated blood before being pumped to the body. Furthermore, some fishes that have this system could actually lose oxygen through the gills if the surrounding water is very deoxygenated. Farmer proposes, however, that this circulatory design serves the function of providing highly oxygenated blood to the heart muscle (myocardium) itself, which may help to explain the persistence of an apparently inefficient circulatory design through evolutionary time.

In most fishes, amphibians and reptiles, the ventricle of the heart lacks a dedicated coronary circulation. Much of the heart muscle is arranged in a loose, spongy matrix that receives oxygen directly from the blood as it is pumped through the heart chambers. The lung of an air-breathing fish provides a source of highly oxygenated blood that flows directly back to the heart (Fig. 1a). Oxygen supplied by the lung may be particularly important for the heart when an air-breathing fish exercises, during which the swimming muscles increase their oxygen extraction from the arterial blood. Thus the venous blood returning to the heart contains even less oxygen than it does when the fish is at rest, precisely at a time when the heart is working harder and needs more oxygen.

In birds and mammals, the systemic (body) circulation is completely divided from the pulmonary circulation (Fig. 1c). This division has traditionally been viewed as the most efficient circulatory design because venous and arterial blood do not mix, and so only maximally oxygenated blood is sent to the body. In turtles and squamate reptiles (lizards and snakes), however, the ventricle is only partially divided. Bloodflow patterns in the heart generally keep arterial and venous blood separate, but some mixing can occur (Fig. 1b). As with the air-breathing fishes, this incomplete division of the heart was historically seen as a primitive, intermediate system on its way to becoming the more efficient mammalian design.

More recently, physiologists have recognized that the partially divided circulation of turtles and squamates may be an adaptation for the intermittent breathing pattern of such animals[2–4]. These studies emphasize the shunting of blood from the right to the left ventricle, which diverts blood away from the lungs when they are not in use. But a perplexing left-to-right shunt of blood has also been measured during exercise in reptiles, in which part of the oxygenated blood from the lungs is sent from the left to the right ventricle and thence back to the lungs[5].

Farmer proposes that the left-to-right shunt provides oxygenated blood to the spongy myocardium of the right ventricle. Without this intracardiac shunt, the right side of the heart would receive only deoxygenated, venous blood, and could suffer from lack of oxygen during activity. In birds and mammals, this problem has been circumvented by the evolution of coronary circulation that feeds oxygenated blood from the aorta back to the left and right sides of the heart. Coronary circulation has also allowed the evolution of compact myocardium, further reducing the uptake of oxygen directly from the blood flowing through the lumen of the heart.

Medical researchers seeking treatments for blocked coronary arteries are now becoming interested in the spongy myocardium of fishes and reptiles[6]. Surgeons have begun using lasers to punch holes in the left ventricle to permit some oxygenation directly from the luminal blood, a technique known as transmyocardial revascularization[6,7]. Farmer's ideas about the oxygenation of fish hearts could inspire other treatments. Perhaps it would be feasible to implant a device, analogous to a fish lung, that would inject a small amount of a highly oxygenated solution directly into the coronary arteries, either as a temporary remedy during an acute heart

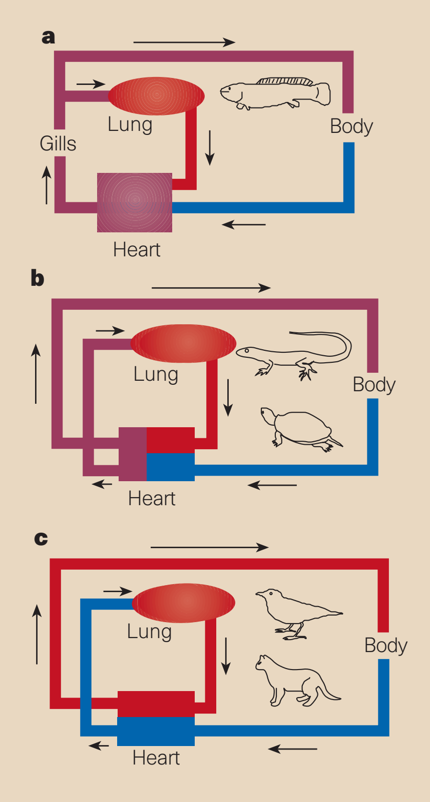

Figure 1 **Simplified circulatory-system diagrams of selected vertebrates.** a, **The circulatory system of certain air-breathing fishes is relatively inefficient at delivering oxygen to the body because blood flows from the lung back to the heart where it mixes with venous blood before being pumped to the body.** b, **Turtles and squamates (lizards and snakes) are able to maintain functional separation of arterial and venous blood, but they often shunt blood across a connection between the ventricles, thus mixing the flows.** c, **Birds and mammals have coronary arteries that feed oxygenated blood to both the left and right ventricles, and so have been able to evolve completely divided hearts. The myocardial oxygenation theory, proposed by Farmer[1] and discussed here, proposes a function for the apparently inefficient circulatory designs depicted in** a **and** b**. The hearts of most fishes, amphibians and reptiles lack coronary circulation, and instead obtain oxygen directly from the blood flowing through the chambers. Farmer suggests that oxygenated blood flowing from the lung to the heart of air-breathing fishes provides oxygen directly to the heart muscle, and that shunting from the left to the right side of the heart in reptiles provides oxygen to the right ventricle. Fully oxygenated blood is red; deoxygenated blood, blue; partially oxygenated blood, purple.**

attack, or possibly as a longer-term alternative to bypassing or clearing partially blocked coronary arteries.

Farmer formed her ideas about the oxygenation of spongy myocardium through the study of circulatory anatomy and physiology in a variety of non-mammalian vertebrates. Her theories will be testable through physiological studies of circulation, blood-gas concentrations and cardiac function during exercise in fishes, amphibians and reptiles. She also proposes another hypothesis, one that will be much tougher to test, in which lungs evolved in the common ancestor of fishes and tetrapods primarily to provide oxygen to the heart. According to the current view, lungs evolved mainly to increase the oxygen available to the whole body, and thus permitted the early bony fishes to invade poorly oxygenated aquatic environments, such as swamps[8,9]. Other views of lung evolution have also emphasized the importance of lungs in regulating the buoyancy of aquatic animals with dense, dermal armour[9,10].

Farmer marshals evidence for the plausibility of her evolutionary theories from palaeontology, ecology and physiology. It is difficult, however, to argue that a feature of an organism evolved for only one of several functions that the feature may serve today, without some evidence from an evolutionary analysis that one function evolved before another. It may not even be very useful to attempt to determine whether systemic oxygenation, myocardial oxygenation or buoyancy control was the most important selective factor in the evolution of lungs, because we can be certain that their evolution had inescapable consequences for all three.

Nonetheless, Farmer has done a great service in bringing this third important function of lungs to our attention, and in providing an elegant explanation for the evolutionary persistence of some seemingly inefficient circulatory designs. ☐

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Particle physics

Exotic meson plays hard-to-get

Frank Close

According to the popular media of the United States and now Europe, physicists have found the 'glue that holds life, the Universe and everything' together. The Web page of the E852 Collaboration at the Brookhaven National Laboratory in New York proclaims "we are in the news". In more measured language, in a paper published in *Physical Review Letters* this month[1], they have "evidence for exotic meson production"; and at the Hadron97 conference, held at Brookhaven on 26–31 August, these claims were critically evaluated. Something definitely seems to be going on, but precisely what is it?

It is well established that the seeds of protons, neutrons and all strongly interacting particles ('hadrons') are quarks. According to the theory of quantum chromodynamics, which is part of the Standard Model of particle physics, quarks are gripped together by the exchange of gluons. Although this is established at high energies, the dynamics of gluons at low energies, where the forces become strong and the proton and other hadrons are formed, are obscure.

Hundreds of short-lived hadrons have been found during the past 50 years. They are 'resonances', where the quarks are excited into states of higher energy; but in none of these has the glue played other than a passive role. Yet according to quantum mechanics, the gluon degrees of freedom also should be excitable in the presence of quarks, forming 'hybrid' states in which both quarks and gluons are active components. The energy of the excitation adds mass to the system, and also allows characteristic correlations between various properties (such as spin and the behaviour of the wavefunction under certain transformations) that would normally be impossible.

In the rather primitive theoretical models of the early 1980s, we noticed that the lightest of these 'exotic' states could have a mass of around 1.5 giga-electron volts (GeV) — some 50 per cent more than a proton[2–4]. In the intervening 15 years theory has matured, and the mass of the lightest exotic is expected to be around 1.8 GeV, with a lifetime of 10^{-23} s and most probably decaying into a pion accompanied by more massive particles such as the η or f_1 (refs 5–8). And there have been a few hints of experimental detections.

In 1988 the GAMS Collaboration[9] reported a particle at 1.4 GeV, but this was quickly criticized and has been dismissed[10]. Then in 1993 two claims emerged, one from Japan's KEK laboratory[11] and the other from the VES collaboration at Serpukhov[12]. There were some differences of detail between this pair, and together with the emerging doubts about the earlier GAMS claim, there was a 'once bitten twice shy' reaction in the community. But the new publication from Brookhaven, and preliminary news from the Crystal Barrel collaboration at CERN, has led to a real resurgence of interest.

The VES experiment[12] used beams of pions with 37 GeV c^{-1} incident momentum to produce their exotic object, which was revealed through its decay into a π-meson and an η-meson. The new Brookhaven experiment[1] uses a less energetic incident pion beam, but the results are very similar: they see a π and an η, and the inferred mass and lifetime of the implied exotic particle are not inconsistent with the VES observations. So reports of a 'discovery' may be less than fair to the earlier Russian experiment; ironically so, as some members of the original VES team are collaborators in the BNL experiment.

The experiment does not see a clear resonance, but rather a spatial asymmetry in the distribution of the η and π together with a distinctive dependence on energy of a certain quantum-mechanical phase. These phenomena are interpreted as evidence for a quantum-mechanical interference between a well-known resonance (the 'a2') and the conjectured exotic particle. The effect is subtle, and there was some concern over whether a small error in quantifying the intensity of the a2 signal could have misled the researchers. However, confidence in the result was increased by a report at Hadron97 that the Crystal Barrel collaboration at CERN sees similar phenomena when they study the π and η produced in annihilations between antiprotons and matter (K. Peters, Univ. Bochum; E. Klempt, Univ. Bonn). Reassuringly, the production mechanism, research team and systematic uncertainties all differ from those in the BNL and VES experiments.

Were this the whole story, it would be natural to conclude that the long-sought evidence of an 'exotic' had been found. But the fuller panoply of evidence presented at Hadron97 has created an enigma.

In a related experiment at Brookhaven, attempts have been made to find the same exotic particle decaying into something other than a π and an η. A signal is seen, but now at around 1.6 rather than 1.4 GeV. In investigations looking at yet other predicted decay paths, an experiment at Brookhaven and an independent one in Russia see a signal at around 1.8 GeV.

Have we searched for over ten years suddenly to see three exotics come along at once, like the proverbial London buses? This seems unlikely. There may be a single, genuine, exotic resonance around 1.6 to 1.8 GeV, and then established quantum effects