of malaria infections, when the parasite (*Plasmodium falciparum*) is replicating inside red blood cells. The parasite then causes an infected blood cell to rupture and release the newly developed merozoites (Fig. 1), which infect other red blood cells. (Synchronous rupture is responsible for the periodic fevers that characterize malaria infections.) Unlike most of the cells in the body, red blood cells do not carry MHC class I proteins on their surface. The merozoites replicating within the cells are therefore not subject to immune surveillance by cytotoxic T lymphocytes. However, a parasite in an infected blood cell is susceptible to being cleared (as are ageing blood cells) as it passes through the spleen. To counter this risk, the parasite inserts PfEMP1 receptors into the surface of the blood cell; this facilitates binding to capillaries and delays passage through the spleen. The PfEMP1 receptors are thus the major target for antibody-mediated immune responses, and have consequently evolved to undergo antigenic variation during the course of the infection.

The model[2] can explain a number of epidemiological puzzles — for example, that the duration of malaria infection is longer in older than in younger children — as well as accounting for the delayed expansion of different antigenic variants despite the very high antigenic switching rate (which might otherwise be expected to result in nearly synchronous expression of the variants)[3]. But Recker *et al.* have not yet compared the predictions of their model with other models of antigenic variation[4,5].

Much remains to be done before we understand the dynamics of the merozoite stage of malaria infections. A prime task is to combine models of antigenic variation with those that allow for the effects of anaemia (caused by rupture of infected blood cells)[6] and fevers[7], and to estimate the relevant parameters from experimental data. Different models for the dynamics of antigenic variation must be compared, and we also need a better quantitative understanding of the immune responses elicited by the pathogen — in particular, why certain antigens elicit a greater response (immunodominance) and which factors are responsible for transient responses to some epitopes and for long-lasting immunological memory of others.

Recker and colleagues' model[2] is an elegant twist on our current ideas about antigenic variation in malaria. But a closer interplay between different models and carefully designed experiments (perhaps using malaria-infected laboratory mice) will be essential in finding the route forward. ■

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G. MURTI/SPL

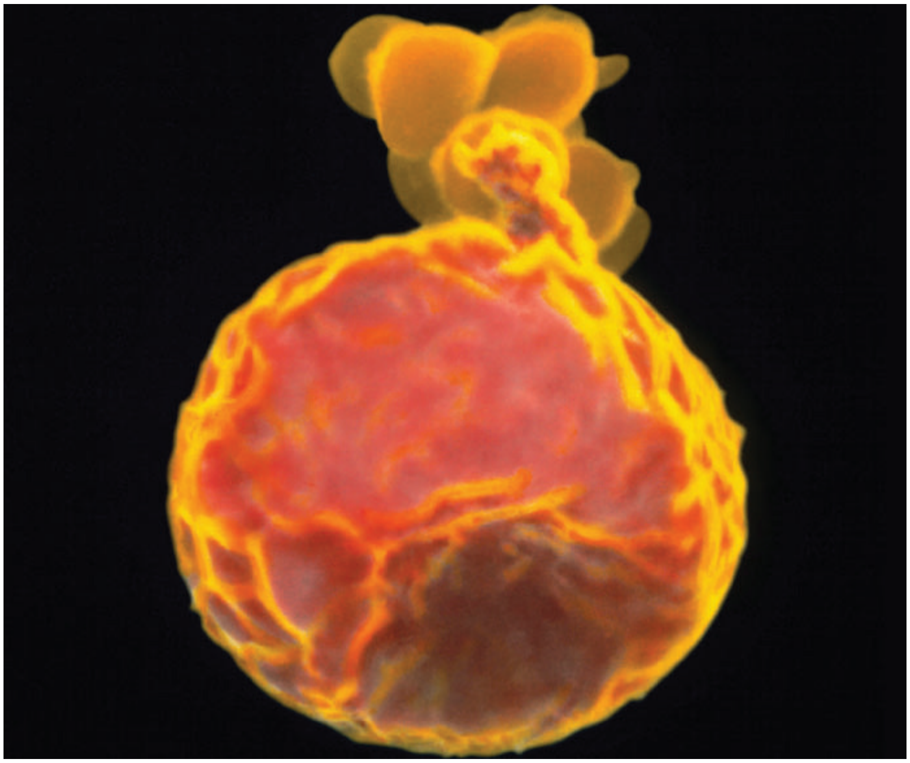

Figure 1 **The merozoites of the malaria parasite, *Plasmodium falciparum*, erupt from an infected blood cell, and will carry the infection into other blood cells. Recker *et al.*[2] suggest that the parasite might have evolved a devious, and counterintuitive, trick to prolong its evasion of antibody responses that are directed against infected blood cells.**

Global change

Hydrocarbon-driven warming

Gerald R. Dickens

A dramatic historical episode of global warming seems to have been driven by the release of huge amounts of hydrocarbons. New evidence for what might have happened comes from the sea floor off Norway.

The outstanding examples of intense global warming and massive greenhouse-gas emissions occurred during a brief episode, known as the 'initial Eocene thermal maximum' (IETM), about 55 million years ago. Superimposed on already warm climates, Earth's surface temperatures soared by 5–10 °C within a geological instant[1,2]. At the same time, an enormous amount of carbon dioxide, apparently produced through oxidation of hydrocarbons, rapidly entered the global carbon cycle[3]. Scientists have only reluctantly taken the IETM as an analogue for examining our planet's future, however, because direct evidence for the actual release of hydrocarbons, and the driving mechanism, has remained elusive. This will change if the observations and ideas of Svensen and colleagues[4] (page 542 of this issue) prove to be correct.

There is seemingly incontrovertible evidence of the injection of huge amounts of organically derived CO_2 during the IETM. Numerous isotope records, constructed using data from primary carbonate or organic matter, display an extraordinary drop in the ratio of ^{13}C to ^{12}C at that time, clearly signalling a perturbation of the entire carbon pool on Earth's surface[3]. Given the coeval dissolution of deep marine carbonate[5,6], and the short duration of the isotope excursion (< 20,000 years[1,5–7]), at least 1,500 gigatonnes (Gt) of carbon as CO_2 must have suddenly been injected into the ocean or atmosphere

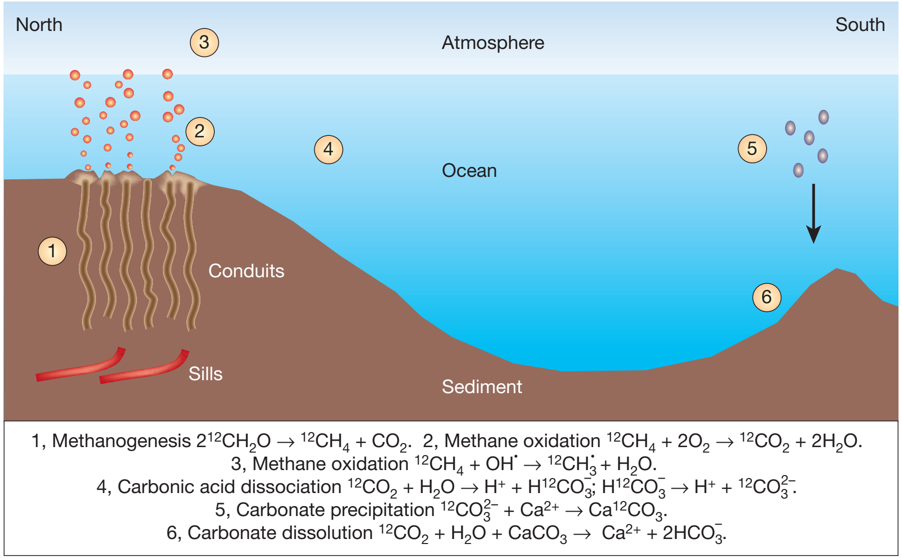

Figure 1 **Methane release during the initial Eocene thermal maximum (IETM), around 55 million years ago. This overall scheme incorporates both sediment-core data[5,8] and the new seismic observations of Svensen *et al.*[4]. Sediment with abundant ^{13}C-depleted organic carbon ($^{12}CH_2O$) was penetrated by hot sills, resulting in the release of massive amounts of newly formed or previously generated ^{13}C-depleted methane ($^{12}CH_4$). Conduits channelled the gas–fluid mixture to the sea floor, and the CH_4 was then oxidized to ^{13}C-depleted carbon dioxide ($^{12}CO_2$) in the ocean and atmosphere, with consequent extreme warming. Such oxidation resulted in finely layered strata devoid of carbonate in the North Atlantic, and a global negative carbon-isotope anomaly[9]: these phenomena are seen in sediment cores at the onset of the IETM. The numbered sequence shows the chain of generic reactions involved.**

from a ^{13}C-deficient source[3]. The only satisfactory explanation for this is the release and oxidation of carbon from a large reservoir of organic material (the biological generation of organic compounds preferentially incorporates ^{12}C).

In several sediment sections from the north and central Atlantic Ocean, the IETM is marked by finely layered deposits devoid of carbonate[5,8]. Combined with the isotope information, that suggests the addition of substantial amounts of methane to this ocean basin, and its oxidation (Fig. 1), because methane oxidation consumes dissolved oxygen (which precludes fauna from turning the sediment over) and produces CO_2 (which dissolves carbonate)[9]. The dual discoveries of the apparent existence of warm, deep waters at the IETM[1], and vast amounts of methane-containing gas hydrates — ice-like crystals of gas and water — along continental slopes[10], thus led to the following proposal[3,5,6,9]: like those of today, gas hydrates in marine sediments included large amounts of ^{13}C-depleted biogenic methane; some change in conditions at the start of the IETM caused relatively warm water to sink in the oceans, and that warming resulted in the dissociation of the gas hydrate; the free methane thus released escaped from the sea floor, and was then oxidized to CO_2 in the ocean or atmosphere.

Such a massive release of methane should have left physical traces, especially in North Atlantic sediments where the chemical evidence for such an event is strongest[9]. However, other than sediment slumping along the North American margin[6], which might be explained by processes other than gas release, no such evidence has been forthcoming. There are also problems with identifying a plausible environmental trigger for hydrocarbon release from marine sediments[3,11]. Alternative, but similarly unsatisfactory, explanations for the carbon input have included the impact of a volatile-rich comet[11] or burning of expansive peat deposits[12].

Svensen *et al.*[4] have examined data from an immense seismic array that shows features lying beneath the sea floor in two large sedimentary basins west of Norway. A truly remarkable find is their identification of several hundred kilometre-scale 'fluid-escape conduits' that terminate in marine strata deposited around 55 million years ago. A few such structures had been previously identified in the vicinity and were interpreted as submarine igneous volcanoes[13]. But these conduits, which are capped by craters and mounds, more closely resemble structures seen in modern sedimentary basins, where water and gas migrate from depth and spawn mud volcanoes and hydrocarbon seeps on the sea floor (Fig. 2)[14,15]. The ancient structures seem to be connected to volcanic sills[4,13], which delivered hot magma into organic-rich sediments throughout the North Atlantic around 55 million years ago. So the authors[4] argue that, during the IETM, the sills produced massive amounts of thermogenic methane and high-pressure fluids, which vented into the ocean through the conduits and perturbed the global carbon cycle (Fig. 1).

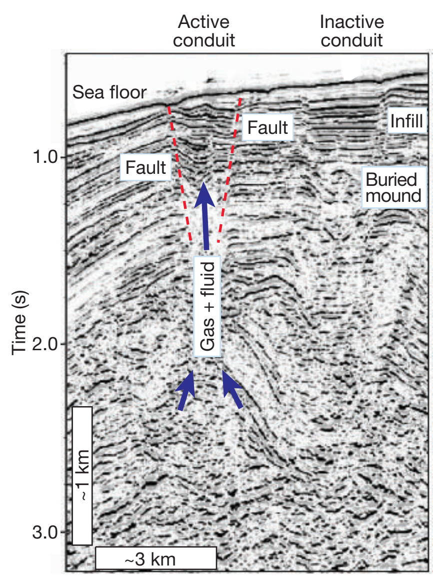

Figure 2 **Seismic profile of active and inactive 'fluid-escape conduits' on the upper continental slope southwest of the modern Niger River Delta. These features result from the migration of water, gas and sediment from depth, and resemble the 55-million-year-old structures identified by Svensen *et al.*[4] in the northeast Atlantic (see Fig. 2 on page 543). Note collapse of sediment along faults above both conduits, and sediment burial of the mound at the inactive conduit. The vertical axis is the two-way travel time of sound waves in seconds. (Reproduced from ref. 14.)**

All this provides tantalizing support for massive hydrocarbon discharge from the sea floor during the IETM. The composition of the expelled fluids, and the timing of their release, need to be better defined, however. And a convincing link between the conduits and environmental changes at the IETM will require evidence that significant quantities of ^{13}C-depleted carbon were actually produced in and released from sedimentary rather than volcanic[13] features, and that this occurred during the 20,000-year onset of the carbon isotope anomaly.

The simultaneous generation and release of methane by volcanic sills at the IETM solves the triggering problem. But it raises an equally contentious issue. Thermogenic methane resulting from the heating of sedimentary organic carbon contains a greater proportion of ^{13}C than does biogenic methane. So to explain the isotope anomaly, a greater amount of carbon than previously thought — more than 3,000 Gt — must have escaped[3,4]. The entire world's conventional deposits of oil and gas today amount to about 5,000 Gt of carbon[10]. The mechanism proposed by Svensen *et al.*[4] therefore requires the instantaneous generation and release of a truly stupendous amount of hydrocarbons. An alternative possibility is that the sills released biogenic methane that had already accumulated in North Atlantic strata and then, through the consequent environmental changes, carbon from other sources such as methane from widely dispersed gas hydrates.

A better understanding of the relationship between the sills, conduits and carbon-cycle perturbation at the IETM will require more work. But if that relationship is one of cause and effect, the significance of the IETM escalates dramatically. In the hydrate-dissociation scenario[3,6], deep-ocean warming drove the massive release of carbon, making events at the IETM an intriguing but imperfect analogue of current fossil-fuel emissions. The volcanic triggering of methane release from the sea floor, whether that methane was biogenic or thermogenic, instead implies that sudden hydrocarbon input caused extreme warming, a view consistent with analyses[2] of temperatures at the IETM. Given the comparable estimates for carbon release at the IETM (1,500 to 3,000 Gt)[3,4], and anthropogenic release of carbon into the atmosphere over the coming centuries (3,000–4,000 Gt), environmental change during the IETM should become the subject of general investigation. ■

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Neurobiology

A matter of balance

Martyn Goulding

The types of chemical signal that a neuron synthesizes and communicates with were thought to be genetically encoded and largely invariable. It seems, though, that if a neuron's activity changes, so too do its signals.

Nerve cells use chemical signals known as neurotransmitters to communicate with each other. These molecules come in many different flavours, and the combination of flavours used by any given neuron represents a key property that determines not only its function within a circuit, but also the circuit's overall output. How exactly neurons regulate the profile of neurotransmitters that they express — their neurotransmitter 'phenotype'— is poorly understood, although it is known that most neurons synthesize a highly restricted repertoire of neurotransmitters, and that the regulatory events governing this repertoire occur in the embryo, soon after a neuron is born and begins to take on a particular identity. Numerous studies[1–4] have also led to the view that a neuron's transmitter phenotype is tied closely to the genetic programme that controls its developmental fate, such that a neuron's identity and its neurotransmitter profile are inextricably interwoven.

On page 523 of this issue[5], however, Borodinsky and colleagues challenge this view. These authors provide evidence that, in the spinal cord of developing frogs, profiles of neurotransmitter expression can change in response to differing degrees of neuronal activity. Although it was well known that neurons can alter the *levels* of expression of particular neurotransmitters after changes in circuit activity, what is interesting about the new study is that it shows that embryonic spinal-cord neurons can also alter the *types* of neurotransmitter that they produce — and that they do this independently of changes in cell identity. Moreover, these changes in neurotransmitter phenotype, which seem to be encoded by the patterns of Ca^{2+} spikes — a measure of activity — that the neurons produce, occur in a system that was thought to be genetically 'hardwired'.

Previously, patterns of Ca^{2+} spikes were shown to modulate the expression of neurotransmitters *in vitro*[6]. Borodinsky *et al.*[5] have now taken an elegant approach to assessing the role of Ca^{2+}-dependent activity in neurotransmitter expression *in vivo*. First, they noted that different populations of embryonic neurons exhibit distinctive patterns of Ca^{2+} spikes. Then they studied the effects of experimentally manipulating this activity, by engineering the developing spinal cord to overexpress one of two types of ion channel: a potassium channel that hyperpolarizes neurons and so reduces Ca^{2+} spike activity, or a sodium channel that increases the frequency of spike activity. By injecting messenger RNA transcripts encoding one of these channels at the two-cell stage of embryonic

100 YEARS AGO

In the course of an interview reported in the *Westminster Gazette* of Friday last, Lord Kelvin is reported to have expressed himself as being decidedly of the opinion that the source of energy of the heat emitted by radium is not in the element itself. He remarked:— "It seems to me absolutely certain that if emission of heat at the rate of 90 calories per gram per hour found by Curie at ordinary temperature, or even at the lower rate of 38 found by Dewar and Curie from a specimen of radium at the temperature of liquid oxygen, can go on month after month, energy must somehow be supplied from without."

ALSO

A Reuter message from Wellington, New Zealand, reports that the King has sent the following telegram to Captain Scott, leader of the National Antarctic Expedition:— "I have read with interest your report, which Sir Clements Markham sent me. I congratulate you and your gallant crew on your splendid achievements, and wish the *Discovery* a safe journey home. I hope to see you on your return to England."

From *Nature* 2 June 1904.

50 YEARS AGO

It is no bad thing that a broadsheet entitled "Graduate wives"… has provoked considerable discussion regarding the value of university education for women, and perhaps more particularly when that education has only been possible because of the help received from public funds in some form or another. That latter point was not specifically covered by the inquiry, although it is noted that many thousands of pounds of public money are spent on the education of the four thousand women graduates who leave the universities of Great Britain every year... the fact that the majority of those covered by this inquiry made no direct use of their academic qualifications after marriage does not imply that the public money expended on their university education has been wasted, though it may well induce some re-examination of the system of university awards and a fuller consideration of the whole purpose of university education. As the broadsheet points out, the indirect contribution which a trained mind and cultured outlook can make to family life and to the life of the nation generally is very great indeed.

From *Nature* 5 June 1954.