Addendum—We believe that a discussion has taken place with the manufacturers of Plamil who have agreed to alter the labelling of their product.

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In My Own Time

The rhesus story

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Oscar Wilde propounds somewhere the engaging conceit that nature follows art, maintaining, for instance, that the marvellous colours of a sunset were to be seen only after Turner started to paint them in that way. By the same token, just occasionally the story of scientific research seems to follow the kind of tidy, logical stepwise progression which we more often associate with the highly contrived theme of a novel that is suitably boiled down for the *Readers Digest*. Such is the rhesus story, almost too good to be true, with its classical sequence of the disease first being defined; its cause then identified, leading on to a rational treatment, for a time available to the baby only after birth, but later extended to the baby before birth; culminating in the grand finale—the disease prevented. And, to boot, all this has indeed taken place “in my own time.”

Blood of a newborn baby

In the 1930s several groups of workers were gradually formulating the idea that among the heterogeneous group of newborn babies who developed jaundice and anaemia or both, there were three recognisable clinical pictures—icterus gravis neonatorum, hydrops fetalis, and congenital anaemia—which were all variants of a single underlying disorder, characterised by the signs of blood destruction (haemolysis) together with regeneration (erythroblastosis). Foremost among proponents of this idea were J C Hawksley and R Lightwood working in Leonard Parsons's unit in Birmingham, and K D Blackfan and L K

Diamond in Boston, USA (Diamond's name will recur more than once in this story).

So the matter rested until 1940, when K Landsteiner at the Rockefeller Institute, and A S Wiener working in a blood transfusion laboratory in Brooklyn, published a brief paper on “An agglutinable factor in human blood recognised by immune sera for rhesus blood.” An antibody raised in rabbits injected with the red cells of a rhesus monkey had been found to react with the red cells of some humans, which thus contained what was to be termed “Rh factor.” Few clinicians glancing at this paper of less than 20 lines would have recognised it as a truly seminal observation from which much was to stem. On the other hand, it is striking how, in this story, workers in blood transfusion laboratories have so often played a conspicuous part. Thus in the same year (1940) Wiener was able to relate rhesus agglutino-gen to cases of otherwise unexplained blood transfusion reactions. The crucial linking of this Rh factor with haemolytic disease of the newborn came the following year (1941), when Levine published his paper on “The role of immunisation in the pathogenesis of erythroblastosis fetalis,” which provided unequivocal evidence that most cases of haemolytic disease of the newborn were due to immunisation of a Rh-negative mother by the Rh-positive fetus. He also made the point that in transfusing an affected infant, blood from a Rh-negative donor should be used.

Fortunately, the battle of the Atlantic, then at its height, did not prevent ideas from crossing that ocean, and by 1942 Janet Gimson (Roscoe) at The Hospital for Sick Children, Great Ormond Street, was transfusing blood to a series of babies with haemolytic disease, with P L Mollison (another name that recurs more than once in this story) typing the blood from a Medical Research Council blood transfusion unit outside London. Contemporaneously, work on the genetics of the blood groups was being pursued at the Galton Laboratory, which at the outset of war had been moved from London to Cambridge. Also working in Cambridge was the brilliant geneticist R A

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Fisher, and this fortunate conjunction led to his collaboration with two workers in the Galton Laboratory, R R Race and A E Mourant. Fisher's prediction that the Rh factor would be found to be made up of three pairs of genes came in 1943, and this, in turn, led to the now generally adopted CDE notation. Race has told us that R A Fisher himself was CDe/cde and had many injections of blood containing the antigen E, but to his disappointment he failed to make anti-E, which was much needed at the time. (The strong rearguard action fought by Wiener, who favoured a different notation, may be read by those interested in old controversies in the correspondence columns of the *BMJ* of 1948.) Not only did wartime Cambridge produce the fruitful Fisher-Race concept but it also led to another landmark in the rhesus story. R R A Coombs was working on immunological problems in a different laboratory, but in the same building as Race, and so was wont to exchange ideas with him over the proverbial cup of tea. This led to the evolution of the Coombs test, a simple and reliable test for recognising the presence of antibody-coated red cells, which remains the standard means of identifying the newborn infant affected by haemolytic disease.

Exchange and control

The logic of removing circulating Rh-antibody together with the affected infant's Rh-positive red cells, and replacing the latter by Rh-negative blood—exsanguination or exchange transfusion—was first applied by L K Diamond in Boston. In 1947 Diamond visited Britain and I recall his producing from his pocket a short length of the narrow-calibre plastic tubing used for cannulating the umbilical vein, and how we in Newcastle preserved this precious sample for the first few exchange transfusions we did.

The plastic tubing we had in those early days made exchange transfusions difficult and laborious. Cannulation of the umbilical vein was not always successful, and I have a nightmare memory of attempting to carry out an exchange transfusion on a desperately ill baby via a needle placed precariously in the internal jugular vein, my co-worker being S Doxiadis, now Minister of Health in the Greek government. Later the introduction of flexible wide-bore catheters made the procedure far easier, although it has always remained a rather long and tedious business, demanding experience plus scrupulous attention to detail if complications (occasionally lethal) are to be avoided. In Cambridge we eventually evolved an attractively simple syringeless method for carrying out an exchange—the baby's own arterial pressure being used to expel blood via a catheter in the umbilical artery, the replacing donor blood being dripped in via a catheter in the umbilical vein.

By the early 1950s it was generally accepted that the baby with haemolytic disease could be managed either by early induction of labour (which also seems to have been pioneered by Diamond and his colleagues in Boston) or by allowing delivery at term. This was followed by either simple transfusion with Rh-negative blood or by exchange transfusion, but criteria for selecting which type of treatment should be given were lacking. P L Mollison, who was working for the MRC, therefore undertook the organisation of a controlled trial. Even today, this 1952 trial can be seen as a remarkable achievement: 12 centres took part, and particular attention was paid to standardising haemoglobinometry, since cord blood Hb concentration was the main index of severity of disease. After two years, 185 babies with haemolytic disease had been treated, the majority coming from Newcastle, where W Walker had started to collect what was to become probably the largest and most completely documented series anywhere of haemolytic disease of the newborn. In the trial, exchange transfusion was proved superior to simple transfusion; early induction, as applied unselectively, seemed to be disadvantageous.

Nevertheless, it was realised that early induction, if applied selectively to the more severe cases of haemolytic disease, might have a place, and the next advance, therefore, was in prediction—

to determine antenatally whether the fetus carried by a woman with Rh-antibodies was affected, and if so whether severely or not. To this end D C A Bevis in Manchester suggested in 1950 the possible value of measuring the pigments in liquor amnii, which was often noted to be strongly coloured in severe cases of haemolytic disease of the newborn. His early experiments employed reagents giving a colour reaction with ferrous ions and success was meagre, but in 1956 Bevis showed that the spectrophotometer provided an appropriate method for measuring the often small amounts of bilirubin present in the liquor surrounding an affected fetus, and that bilirubin concentration so measured correlated well with severity of the disease. Thereafter, amniocentesis quickly became an established method of prediction and a means by which cases suitable for early induction could be identified. In retrospect, we can see that this use of diagnostic amniocentesis opened the way to a whole host of other diagnostic procedures depending on sampling amniotic fluid, and thus was the beginning of the new science of fetal medicine.

Rhesus research over the next decade was mainly of the i-dotting and t-crossing variety, until 1963, when A W Liley in Auckland, New Zealand, electrified us by doing what had seemed impossible—the intrauterine transfusion (on two occasions) of a severely affected fetus. It had long been known that red cells introduced into the peritoneal cavity were rapidly and almost quantitatively transferred into the circulation, but it was an ingenious idea of Liley's to apply this principle in this new context. Liley's original technique is still largely followed, except that ultrasound now helps to locate the placenta.

There we may leave the rhesus story so far as the treatment of the affected infant is concerned, and turn to the equally satisfying story of the prevention of rhesus disease. This has its roots as far back as 1943, when Levine made the astute observation that, in those abortions and stillbirths which were *not* attributable to rhesus factor, ABO incompatibility between mother and father was comparatively common. But it was not till a good deal later that R R Race and Ruth Singer in 1950 put two and two together and drew the conclusion that "if Rh sensitisation is due to fetal red cells entering the maternal circulation, it seems possible that if they carry, for example, the A antigen, and the maternal serum contains anti-A, then these invading cells may be eliminated before they have time to act as an Rh antigen."

As so often happens in medicine, it was a new technique, introduced without relation to the present matter, that triggered off a fresh advance. Kleihauer in Freiburg, West Germany, published in 1957 a simple acid-elution method for recognising HbF-containing red cells among a large population of other red cells. Two years later Zipursky, in Winnipeg, applied the Kleihauer technique to blood sampled from postpartum women and showed that fetal red cells were often then present in the mother's circulation. "It was this paper more than any other," C A Clarke says, "which stimulated the Liverpool group to go ahead with their ideas for preventing immunisation." The extraordinary story of how an amateur interest in butterflies led Clarke to set up work on genetics, which eventually turned from the genetics of butterflies to those of human blood groups, and how this led on to the discovery that fetal cells in the maternal circulation could be destroyed by administering anti-Rh in the form of gammaglobulin to the mother post partum, is told in *The Sources of Invention*, by Jewkes *et al.* When the Liverpool workers published their results in 1961, a team in the University of Columbia (Golman, Freda, and Pollack) were found to have been achieving similar clinical results, although they had arrived at their conclusions by a different route—including the use of male volunteers from Sing Sing prison.

Commendably soon after the researchers had shown that prevention of Rh disease was a practical possibility, the National Health Service in Britain, together with the blood transfusion centres, were initiating steps to make the requisite gammaglobulin available throughout the country. What at first sight seemed to be a most daunting prospect of Kleihauer-testing post partum

every mother potentially liable to become Rh-sensitised, and then giving gammaglobulin to those requiring it, in the event, proved to be perfectly feasible. By the early 1970s, new cases of rhesus sensitisation among pregnant women were already becoming uncommon, and babies with haemolytic disease, which during most of my time as a paediatrician occupied a large part of our energies, were becoming a rarity. Today there remain a few strongly sensitised women, dating from pre-gammaglobulin days, who still provide a challenge, and for them removal of circulating antibodies by plasmapheresis may have a place in management of pregnancy.

MATERIA NON MEDICA

Swedish slang

One often hears the advice given to a would-be visitor to Scandinavia: "Don't bother about the language, everybody speaks English." Certainly this is nearly true in Sweden and, given random samples of two groups of people from London and Stockholm, it is just possible these days that the observation might be more true for Stockholm than London.

Swedish is, however, an interesting language in its origins and its melody. It is known that the Welsh take readily to Swedish. There was probably enough Old Nordic in the language of the Anglo-Saxons for the Vikings to communicate directly with their English victims when they plundered them in the ninth and tenth centuries. The words common to English and Swedish are often easily recognisable, although usage and spelling may have changed slightly—for example, "stol" for "chair," "bok" for "book," "kniv" for "knife," "bord" for "table."

As a student of Swedish I had, sooner rather than later, to face up to slang in spoken Swedish. It was then that I discovered the joys of Hald Gibson's *Svensk Slangordbok* (*Swedish Slang Dictionary*). Much of it is untranslatable into English, but it is worthy of comment none the less. Swedes, for example, have nearly 100 slang words for "girl." With difficulty I could think of only 10 in English, although there may well be some regional ones I do not know about. None of the English words, however, carried quite the descriptive possibilities of the Swedish. An American can be an "Amris" or "Jänkare" (pronounced "yenkarer"). Britons are not apparently favoured with special slang names. There are 12 words for "doctor," including "knox" (any allusion to Edinburgh's shady anatomist?) and "skelettmeikaniker"—which needs no translation.

Unfortunately much slang is transient and I do not doubt that Gibson can happily bring out new editions of his book every five years for the rest of his days. For the moment I can savour the pleasure of typing this on my "slammertacka."—E R NYE (Stockholm, Sweden).

The man who brought the Dali to Scotland

On a recent visit to Glasgow I was reminded by Professor A C Kennedy that a medical man had been director of the city's art galleries and museums during and after the last war. Tom Honeyman (1891-1971) must have been one of those rare individuals with the enviable gift of instinctively recognising the quality of a painting, because he began buying pictures early. After 10 years as a general practitioner and part-time physiologist he abandoned medicine to join an old-established firm of Glasgow art dealers which subsequently moved to London. Just before the war he returned to his native city as director, at a salary which he estimated to be a fifth of what he was earning in London. He gives a fascinating account of the art world and of the tough going of running a major museum for 15 years, during most of which there was either war or austerity, in his autobiography, *Art and Authority*, published just before his death.

I don't know what the people of Glasgow think of him, but I guess he will go down in art history for three things at least. Scottish shipping magnates had been among the earliest buyers of modern French paintings (as had Honeyman himself), and because of his connections he was able to acquire such fine examples that one expert later remarked "No student of French art can afford to miss seeing what is in the Glasgow Art Gallery." Secondly, Sir William Burrell has put on record that Honeyman's knowledge was "one of the principal

In going over the rhesus story, it is striking how decisive advances have come from such a wide diversity of centres throughout the Western World. To list only the sources of the papers I have mentioned, they include Birmingham, London, Cambridge, Manchester, and Liverpool in Britain; Boston and New York in USA; Winnipeg in Canada; Auckland in New Zealand; and Freiburg in Germany. Brevity has been a welcome feature of several of these papers—three of the key papers occupy no more than half a page of the journal. Finally, I have benefited greatly from Sir Cyril Clarke's excellent commentaries in his *Rhesus Haemolytic Disease—selected papers and extracts*.

factors" which influenced him and his wife to leave their collection to Glasgow. Now that Pollok Park is being refurbished let's hope that the whole of this remarkable collection will soon be on view.

In 1951 Honeyman saw Salvador Dali's "Christ of St John of the Cross" exhibited at his old gallery in London. He was so moved that he had the painting sent up to Glasgow, where, to his delighted surprise, all the various corporation committees unanimously recommended its purchase at a specially reduced price of £8200 including the copyright, which proved to be a gold mine. The storm of criticism and abuse that erupted must have been one of the most furious in the story of art, and it led Honeyman to remark 20 years later that he was remembered only as the man who brought the Dali to Scotland. Today Glasgow has many treasures, and the Dali in its remarkable setting at Kelvingrove is acknowledged to be one of the finest. It is nice to think that it is there because of the "vision" of a medical truant.—ALEX PATON (physician, Birmingham).

Dead wood fungi

When trees die in a garden or stumps are left after felling fungi often grow on the remains to add interest by their form, colour, or even their edibility. A common stump coloniser is the sulphur tuft, where the yellow cap contrasts with greenish gills; the sulphur-tinted flesh is bitter if eaten although not poisonous. More palatable, however, are the tiered fruiting bodies of the destructive honey fungus. This spreads relentlessly by its black cords which progress between bark and wood. Perhaps unexpectedly, honey fungi are good eating; moreover, they look attractive with prominent rings on yellow-brown stalks below their caps of similar and subtle shade.

A conspicuous, tough, and brown-scaled fungus is *Pholiota squarrosa*, common in autumn at the base of deciduous trees; the handsome and often multiple fruiting bodies have their stalks ringed by down-curved, dark tongues of membrane. Contrasting with this species is the smaller and more delicate *Coprinus micaceus* with a grooved, light-brown cap; it is seen on lawns but is growing really from dead tree roots. Sometimes its autumnal growth extends into the winter when, after a frost, the fungi look delightful when capped by rime; sadly, severe cold kills them and after a thaw they shrivel and twist to the ground.

Fallen branches may be the site of *Tremella mesenterica*, which is unmistakable as a knob of bright yellow which is soft, moist, and folded almost like the brain's cortex. Other convoluted forms of the *Tremellales*, often grey, sprout on grassland, although originating from dead, buried wood. Conifer wood is host to *Tremella encephala*; here the beige-coloured fungus has the appearance of a piece of walnut. Another colourful fungus is coral spot, where the fruiting bodies are dotted spectacularly over poles or cut sticks.

Also brightly coloured are the interiors of the cups of *Peziza coccinea*, which are not uncommon on fallen wood in winter; the red hue certainly suggests warmth and cheerfulness on dull and chill days. Then, as oak wood decays, it will turn green if infiltrated by the mycelial threads of *Chlorosplenium aeruginascens*, while blue fruiting cups ornament the surface.

So, when wood dies, fungal invaders can add fascination to the scene, thus providing some compensation for the loss of a valuable tree or shrub. Further, following careful identification and selection, it is worthwhile picking and cooking certain of the fruiting bodies, thereby benefiting by the enjoyment of a tasty meal.—A P RADFORD (general practitioner, Bristol).