febribus et de morbis capitis et pectoris opus, Bologna 1683; possibly Leiden 1717, pp. 679 in 4°, prefaced by Boerhaave (BB, p. 41, 2:2) or Leiden 1730 (BB, p. 41, 2:14).

[48] B. S. Albinus (1697–1770), professor of anatomy at Leiden from 1719.

[49] François Tolet (1647–1724), Paris surgeon, (Traité de la lithotomie, Paris 1681, pp. 249 in 8°; possibly Utrecht 1693, pp. 172 in 8° (BB, p. 131, La Haye 1686, with 2 other, 0:17).

[50] 'Merchant on the Boompjes at Rotterdam' (*HMC*, Eglinton, p. 461).

[51] Possibly Lord Reay, cf. n. 59.

[52] Nicolaas Tulp (1593–1674), physician at Amsterdam also burgomaster, *Observationum medicarum libri tres cum aeneis figuris*, Amsterdam 1641 (BB, p. 93, Amsterdam 1672 in 8°, 0:12); also Leiden 1716, 1739, both pp. 392 in 16°.

[53] John Douglas (d. 1759), lithotomist at Westminster Hospital, brother to James Douglas, *Lithotomia Douglassiana*, London 1720; possibly London 1723, pp. 126 in 4° (BB, p. 80, 2:0); French ed. Paris 1724, pp. 192 in 8°.

[54] William Cheselden (1688–1752), surgeon at St. Thomas's, London, *The Anatomy of the Human Body*, London 1713 (BsG, p. 67, 1:00); possibly London 1730, pp. 355 in 8°.

[55] J. J. Wepfer (1620–1695), see 21 March, *Observationes anatomicae ex cadaveribus eorum quos sustulit apoplexia*, Schaffhausen 1658, pp. 304 in 8° (BB, p. 101, Amsterdam 1681, 0:7); possibly the enlarged edition *Historia apoplecticorum, cum observationibus celebrium medicorum*, Amsterdam 1710, pp. 464 in 8° or Leiden 1734, pp. 690 in 8°.

[56] Probably a Mr Mackay of Bighouse, a correspondent of Sinclair's, cf. SRO GD136/376/1.

[57] Hendrik van Deventer (1651–1724), leading Dutch obstetrician practising near The Hague, *Operationes chirurgicae novum lumen exhibentes obstetricantibus*, Leiden 1701, pp. 274 in 4°; possibly Leiden 1733 (BB, p. 54, 2:18) or *The Art of Midwifery Improv'd*, London 1728, pp. 328 in 8°.

[58] Francesco Redi (1626–1697), naturalist, physician to the Grand Duke of Tuscany, *Experimenta circa generationem insectorum cum figuris aeneis*, Amsterdam 1671, pp. 230 in 12°; also Amsterdam 1688, pp. 330 (1st ed. in Italian, Florence 1668). The other books by Redi may have been *De animalculis vivis quae in corporibus animalium vivorum reperiuntur observationes*, Amsterdam 1708, pp. 342 in 8° and/or *Opuscula varia physiologica*, Leiden 1729, pp. 216, 312, 342 in 12°.

[59] George Mackay, 3rd Lord Reay (1678–1748), who was educated in Holland. His second wife was a daughter of John Sinclair of Ulbster (*The Complete Peerage*).

[60] Probably Henry Munro (cf. Part I, n. 16), whose Jacobite sympathies are mentioned by Ezeckiel Hamilton (*HMC, Eglinton*, p. 468).

[61] Probably George Sinclair of Ulbster, cf. Part I, n. 26.

[62] Charles de Saint-Yves (1667–1733), a leading eye surgeon in Paris, *Nouveau traité des maladies des yeux*, Paris 1722, pp. 373 in 12°; possibly Amsterdam 1736, pp. 277 in 8° (Haller in Paris paid 2.15 livres = 27½ st.).

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EIGHTY-EIGHT YEARS OF THIS AND THAT: PART I

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WAR YEARS

War is terrible but occasionally an unexpected opportunity turns up because of it, and it did so for me in 1916 when I was nine. My father, an ardent territorial, came home on leave bursting with news, Kaiser Bill was about to bomb Leicester from his zeppelins. Though the threat seems to have been highly unlikely, this stimulated great activity and my young sister and I were evacuated to Houghton-on-the-Hill, a small village six miles to the east of our home. There our education continued under a 16-year old governess, Margaret Foster, and it was 'Fossie' who introduced me most skilfully to butterflies and moths, so that I became an obsessive collector until, at fourteen, I was sent away to boarding school. There the butterfly nonsense was soon knocked out of me. I spent most of my early days at Oundle endeavouring to hide from my contemporaries that I had previously attended the local 'grammar' and had not been sent away to a prep school. Contrary to the belief of many that I benefited from the teaching given at Oundle in science, I was usually bottom of my class in that subject and top in classics.

From Oundle I went off to Strasbourg University for three months to learn French and then to Caius College Cambridge, leaving there in 1929 with a 2nd class honours degree in Natural Science and a scholarship to Guy's medical school. I enjoyed various junior staff appointments at Guy's after qualifying and served as house physician to John Ryle, J. J. Conybeare, C. P. Symonds and Denny Brown. I had also brief periods with dermatology and physiology. From 1936–1939 I joined in a life insurance practice in the City.

The advent of World War II entirely altered my career, for it took me back not only to clinical medicine but also to entomology. It happened like this. In June 1939 I was getting bored with insurance work in the City of London (it had only given me one claim to fame, I had examined Winston Churchill in 1938) and as I had obtained an MD and had passed the examination for membership of the Royal College of Physicians (MRCP) and war was threatening, I decided to have a shot at joining the RNVSR. This was successful and I was called up on the fateful day, the third of September. My brother-in-law, Colin Ellis, wrote the following poem at this time:

1914–1939

The same old comrades in the same old trench
The same old Germans and the same old French
The same old courage and the same old hope
The same old papers with the same old dope
The same old knitting by the same old trouts
The same old stirring of the same old doubts
The same old answer to the same old guess
The same old men have made the same old mess.

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FIGURE 1
Surgeon-Lieutenant C. A. Clarke, 1939.

NAVAL SERVICE

I chose the Navy because I liked sailing, particularly racing, and I picked up my wife-to-be on the lawn of the Itchenor Sailing Club in 1934. My best man was great at cruising, but I was too often seasick so diverted to dingy racing; 12 square metre Sharpies before the war and Fireflies and bigger dinghy classes after it. I regarded myself as a competent club helmsman but when I was selected for the Olympic Trials at Torbay in 1948 I was soon sorted out!

Home waters

I spent the first six weeks of the war improving my snooker at Chatham and was then posted to HM Hospital Ship *Amarapoora*, which was being fitted out in Liverpool. I telephoned Surgeon Captain 'Jake' Martin, aged sixty (my boss-to-be) and asked which was the best hotel in Liverpool to stay in until the ship was ready. He replied 'The best hotel is the Adelphi, but Surgeon Lieutenants will stay at the Shaftesbury'! We sailed for Scapa Flow in November and were stationed there for over two years, acting as a base hospital as there was only a sick bay on shore. Shortly before we arrived in Scapa, HMS *Royal Oak* had been sunk by the German submarine-commander Prien, who crept into the Flow and out again. The losses in the battleship were terrible, the warning having been erroneously given as an air attack, so that nearly everyone went below decks. The few who did not, simply jumped overboard and swam the 100 yards or so to the shore.

When the Home Fleet arrived, in December 1939, we became very busy and Scapa became one of the safest places in the UK, most of the bombing being on the mainland. My wife, Féo, managed to get my sailing dinghy sent from Itchenor to Scapa by train (at a cost of £2.10s) and I used to race wearing a tin hat. We sailed round HMS *Hood* the day before she left on what was sadly to be her last voyage, but, just beforehand, we took off from her a sailor seriously ill with appendicitis. He was near death's door then, but after an operation became a lucky *Hood* survivor.

A minor conflict occurred on the *Amarapoora* between Jake, the Surgeon Captain and Duncan the Captain of the ship, as to who was the senior officer, particularly on visits between ships. It was settled by a compromise. When we visited an HM ship, 'Jake' was the boss, but when a Merchant Navy one it was Duncan.

In the hospital ship we dealt with the common diseases and I only mention a rather exceptional one. Meningococcal meningitis as usual in wartime was rife, but there were occasional cases (5 at least in the *Amarapoora*[1]) where there was no evidence of meningitis but a PUO markedly similar to malaria, and a rash which appeared when the temperature rose. These patients did not appear seriously ill but the raised temperature and the spots persisted for many weeks. Meningococcus was grown in the blood culture. When sulphonamides arrived the symptoms quickly responded and I thought the condition must be meningococcal bacteraemia. I wrote to Dr John Ryle, whose house physician I had been at Guy's and who had mentioned the disease to me and he agreed with my diagnosis. Nowadays meningococcal bacteraemia seems to have disappeared and all seriously ill cases are said to have meningococcal septicaemia.

Our convalescent cases were transferred further south to Kingseat by a small hospital ship, the *Isle of Jersey*, with the officers of which we formed great liaisons, and Dr Basil Levy is one that sticks in my mind as being a very amusing fellow.

In 1942 we left Scapa and went to North Africa via Gibraltar, where I was ill for about a fortnight with infective hepatitis. 'Everybody' (on both sides of the war) had the illness and it postponed the battle of Alamein. In our Army it was much commoner in the officers than in ratings. The ratings had an easy explanation—that the officers drank too much gin—but the doctors, presumed to be more scientific, noted that officers had their cutlery and china washed en masse whereas the ratings each cleaned his own spoon and mug and infection did not spread so readily.

Our next voyage took us from Gibraltar to Algiers where there was a lot going on, and we took on board many sick and wounded due for home, and also some mentally deranged American soldiers. I was in charge of the Yanks, and they terrified me, but I managed to solve the problem. We had on board some sick German prisoners of war, among them a sergeant called Adolf, and under his supervision they provided guards for me on my ward rounds.

And so home to Avonmouth, with one episode on the way when a Luftwaffe aeroplane flew straight over our mast and we trembled, but the German POWs said 'There's nothing to be frightened of—not even the British bomb our hospital ships'.

I left the *Amarapoora* in Avonmouth, and landed a job as medical specialist (in responsibility roughly the equivalent of a present day senior registrar) at the

Royal Naval Hospital in Seaforth, Liverpool. I was there for about a year, and luckily got to know several Liverpool consultants, particularly Robert Coope, physician, and Jim Oldham, surgeon, who were most useful to me later on.

Service in Australia

And so to my last year in the Navy. In October 1944 Féo and I were on leave for a few days tramping the hills in the Lake District; when we got back to our digs there was a telegram which I opened in trepidation. 'Proceed to Royal Naval Hospital, Sydney, Australia'. Immediate extrasystoles! I had endured (or more accurately quite enjoyed) four years of war, but although the situation in Europe was improving there seemed little chance that Japan would ever pack up and I thought that I should end my days in the southern hemisphere. But remembering what the headmaster of Oundle (Sanderson) had told us—'The secret of a happy life is to live dangerously'. I did not argue. The job seemed to have good prospects.

So in November 1944 for a second time I sailed away from Liverpool. We were the first British instalment for the Sydney Naval hospital. There were eight officers to a cabin, because the top deck was wholly occupied by the new governor of New South Wales, complete with wife, children and nannies. We were prety bolshie about that.

The ship did 23 knots, and after a destroyer escort down St George's Channel away we went at full bat—too fast for the submarines. She was a great ship but awkwardly, happened to be christened the *Empress of Japan*. For obvious reasons this had become unsuitable and she had been renamed the *Empress of Scotland*, but there had not been time to change the cabin notices, which were all in Japanese.

We made Sydney via the Panama Canal in 28 days and here it nearly all ended. None of us had seen the lights of a city for five years, and there was Sydney lit up for Christmas. The ship was going slightly astern preparatory to anchoring and there was a cross wind; everyone, of course, rushed to the landward side to get the view—at least 2,000 of us. The *Empress* began to heel over and there came a frantic shout from the bridge 'balance the ship'. We did, and she righted, but I had not appreciated that a ship of 23,000 tons could behave like a dinghy.

The hospital was not ready for us as it had only recently been evacuated by the Americans, who had gone up north; we stayed in a famous family hotel, Petty's, long since pulled down, where we spent about a month. At a reception party we had our first casualty. Our toothie—I forget his name—slid down and off the bannisters and broke his neck. Happily he survived.

Hospitality from the Prince Alfred Hospital included grand rounds every Sunday morning, led by Kempson Maddox. The war seemed miles away, though the Sydneyites frequently reminded us that a Japanese submarine had shelled the harbour. Somehow it had got through the defences, but, unlike Prien at Scapa, it did not get out again.

Eventually the naval hospital was ready and my job was marvellous, all the main specialities were represented and well staffed and I learnt medicine at a great rate. The discipline was admirable and I had entire clinical freedom, except on one memorable occasion. I had under my care a most attractive VAD with tuberculous pleural effusion. When she recovered I made the standard recommendation that she be invalided home, but I was told by the surgeon commander that she would do better if we kept her in the Antipodes. The reasoning was biased, but I was only a two striper so I had to cave in!

Ian Sneddon, a Sheffield dermatologist, came out in a troopship. We became great friends and bought a dinghy which we sailed in Botany Bay. The sailing both there and in Sydney Harbour was excellent and we raced VJs, 16 footers, and watched the incredible Sydney Harbour 18s with 2,000 feet of sail, but the design was old-fashioned and to windward would have been seen off by a 14 foot international. Betting was not legal, but there was a bookies' launch which followed each race and the crew had numbers on their backs like football players today.

The day of victory in Europe came and passed us by. In the Antipodes eternity still seemed ahead, but about July 1945 our neurosurgeon told us we should be home by Christmas (he was obviously in the know) and in August came Hiroshima and Nagasaki and the war was over—just as we had got fully organised.

VJ day I shall never forget. There was a strong breeze and Ian and I were celebrating by a sail in Botany Bay. A gust came and over we went. I knew it—after six years of war we should be 'taken' by a shark at the moment of victory. But the shadow of the sail is said to be protective and we managed to swim ashore, dragging the boat with us.

Neuropathies in prisoners-of-war

There was a final medical spin-off. British prisoners of war from Hong Kong came south to us after the defeat of Japan and we saw the most fantastic array of neurological problems. Ian and I wrote a paper about them[2] and had a film made illustrating the clinical features.

The neurological syndrome developed with remarkable constancy and chronological order. Within 3 months of imprisonment (in December 1941), swelling of the ankles was followed by weakness and paraesthesia of the limbs, difficulty in walking and failure of vision and hearing. Towards the end of 1942 and early in 1943 skin lesions suggesting pellagra were noted, stomatitis and dermatitis of the scrotum, the latter being extremely common. At this stage also 'electric' feet occurred, characterised by a burning sensation and extreme hyperaesthesia of the soles. The skin symptoms and to some extent the 'electric' feet responded well to nicotinic acid when this became available in 1943, but the neuritic symptoms remained stationary. Although at some time during imprisonment most of the prisoners had diarrhoea, chronic diarrhoea was not a feature in the history.

Of the 200 mixed medical and surgical cases reviewed in Sydney, 74 showed grossly abnormal neurological signs as follows:

Optic atrophy and ataxic paraplegia	31 cases
Ataxic paraplegia only	21 cases
Optic atrophy only	13 cases
Optic atrophy, nerve deafness and ataxic paraplegia	6 cases
Optic atrophy and nerve deafness	3 cases

The condition was considered to be due to a nutritional neuropathy but the response to dietetic and vitamin therapy was poor. The daily rations while they were in the prison camps were often less than 1 lb of rice (1600 Kcals) and little

else. The rice was usually polished and had often become mouldy during storage. The general feeling at the time was that rice was the main culprit.

But this is not the whole story. On September 1st 1945 there appeared in *The Lancet* a paper, *Obscure neuropathy in the Middle East*, which was a report on 112 cases of German prisoners-of-war in our hands.[3] In the main the symptoms consisted of retrobulbar neuritis, nerve deafness and ataxic paraplegia, but many patients developed only the visual manifestations and the illness usually began with failing vision. A diagnosis of nutritional neuropathy seemed the most probable explanation of the illness since there was no evidence of poisoning, infection or other causes and there was absence of the illness among the camp staff and among the thousands of other troops in the area; although there had been an outbreak of pellagra previously in the camp very few of these prisoners had been affected. The neurological syndrome did not appear in other camps where pellagra had been a serious problem.

The nutrients in the diet for this camp were as follows:

Energy	3574 Kcal	Vitamin A	2740 IU
Protein	136 g	Thiamine	2·3 mg
Carbohydrates	409 g	Riboflavine	1·8 mg
Fats	138 g	Nicotinic acid	36·4 mg
		Ascorbic acid	69·4 mg

It is of course well recognised that dietetic intake should be calculated not from rations authorised or issued, but from meals actually served, and that due allowance must be made for wastage and for cooking. Further, under war conditions items in short supply may have to be replaced by available substitutes from time to time. In this particular camp the cooking methods were found to be far from ideal.

Ian Sneddon and I did not know of the afore-mentioned paper by Spillane and Scott while we were seeing the cases in Sydney but we learnt about it in the discussion at the RSM which followed our POW film shown there on February 19th 1946 (Spillane was there).[4] At first there had been no difficulty in explaining the symptoms in the Japanese camps—it was due to deficiencies in the rice, but this could not have been the case in the similar syndrome described by Spillane and Scott. Our general theory is that poor diet in a foreign country is the explanation but it is interesting that the syndrome which both Spillane and Scott and we described had not been reported before.

The follow-up

Seven years later Bill Sircus and I thought it would be interesting to see what had happened to some of the Sydney patients; in particular we wanted to find out whether the condition of those seriously disabled had remained stationary, become worse or improved. We had 53 case histories, wrote to the men and got 34 replies, and somewhat later we examined in Liverpool eight of the typical cases.[5] A characteristic story was as follows:

'I do not seem to have control over my toes. . . . My balance has improved a little, although when washing my face with my eyes closed it is not so good, but I have full confidence standing in the bath with my eyes open. My eyes seem a little better some days. I can read the headlines of a paper, but I must confess I would be lost without my high-power reading glass, which has three lenses. It helps me a lot. I hold it about 1 inch from my eyes and two inches from the

paper. I am a 'borderline' case at St Dunstan's.' The most striking feature of the whole follow-up was the difference between patients in coping with their disability—some just 'drew their breath and drew their pay' while others showed remarkable capability in overcoming their disabilities, one of them even became a physiotherapist.

A final aspect of Australia that I shall never forget was the butterflies. Monarchs and Swallowtails were everywhere but little did I know how greatly they were going to influence my future career. 'Fossie' did indeed come to life again in the southern hemisphere.

Demobilisation

I came home from Australia in a P&O troopship in November 1945, and we had a moving experience in Fremantle, for there we landed hundreds of Aussie servicemen who were coming home from fighting the war 'up north'. The town band was there to meet us, and back it came at 5.00 am the next morning when we sailed for Southampton—and there were cheering crowds to see us off. The Japs had been beaten and the millennium was ahead.

Twenty-three years later I flew into Perth on a medical assignment, and as we landed there was again cheering. I thought 'It can't be for me'. It wasn't. It was for the Crown Prince and Crown Princess of Japan. *O tempora, O mores.*

Arriving in Southampton at Christmas time in pouring rain, the brave boys came home but there was no band, and the winter was perishing. I made my way to Leicester and joined my family (Charles Clarke, aged two, said 'kangaloo' to me) and we all stayed with my mother—me a brave boy with pockets full of glowing 'flimsies', our POW film and anticipation of a marvellous job. Everyone would be wanting me. But slowly it dawned that there were many others with equal credentials, and for three months I was jobless. Féo and I used to sit for hours in front of a gas fire in the spare room scouring the *BMJ* and *The Lancet* (my mother's gas bill reached the astronomical figure for those days of £20). There was nothing doing at Guy's—the Dean suggested general practice at Emsworth, 'the sailing was excellent'—and I was turned down at Guildford. But in March 1946 I applied for a registrar's job going at the Queen Elizabeth Hospital at Birmingham. I asked my old chiefs John Ryle and C. P. Symonds to back me. I landed it after a tussle. But was I medically qualified? Could I *prove* it? I was baffled, but it turned out that my predecessor, the best registrar they had ever had, had turned out to be a physiotherapist!

I loved the QE. The salary was £300 a year and Féo and I and our three sons lived in digs in a working class area and I bicycled each day to the hospital and never took a day off.

The horizon got brighter. I had my sights on Liverpool because of my year's service there, and about July was interviewed for a job by Henry Cohen, the Professor of Medicine. I landed a consultant post at the Northern Hospital and started work in September 1946 and continued in Liverpool medicine until I retired in 1972.

LIVERPOOL

Adventures in genetics: butterflies

In addition to being fully occupied with medicine, I was determined also to fulfil my childhood ambition and breed the Swallowtail butterfly, *Papilio machaon.*

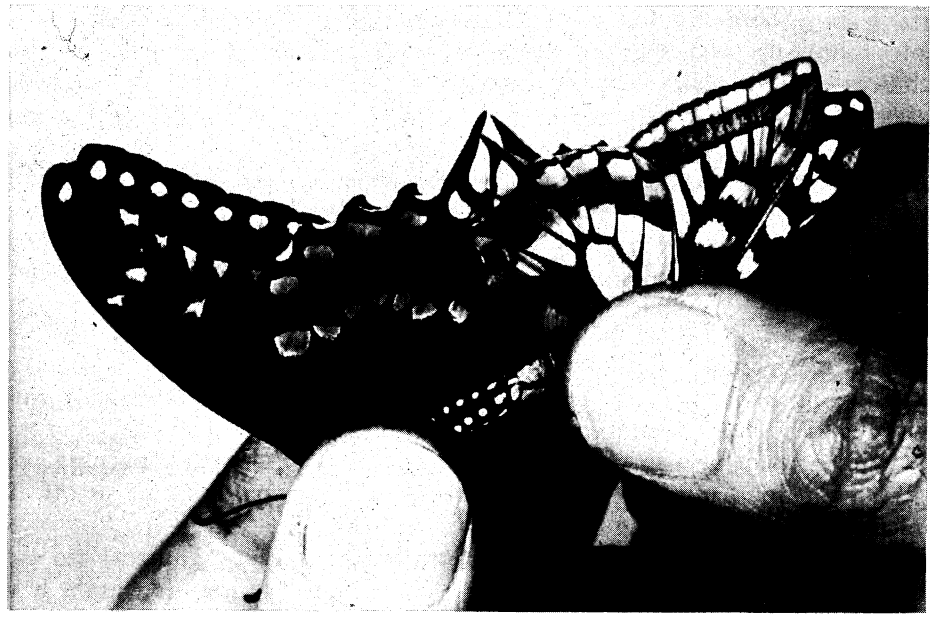


FIGURE 2
Hand mating between a male *Papilio machaon* (right) and female *P. polyxenes* (left).

Male and female butterflies rarely mate spontaneously in a cage, they need space for courtship flights, but I devised a technique for making them mate ('hand-mating') (Fig 2) and I thus achieved my collector's aim.[6] The next development came in October 1952. One Sunday afternoon I happened to have a female of the black North American Swallowtail, *Papilio polyxenes*, as well as a male of *P. machaon*, which is a close relative. Hand-mating worked between the two species, as it usually does in Swallowtails, and I produced F_1 hybrids and then the back cross which was most striking—the insects were *either* yellow *or* black (Figs 3 and 4); in other words there was only a single gene difference between the two 'species'. At about this time I answered an advertisement in an entomological paper and had the most incredibly lucky break. The advertisement was from a young ex-RAF geneticist, P. M. Sheppard, who was working in E. B. Ford's department in Oxford, and he wanted some *machaon* pupae. I supplied him and also told him my hybrid story. He was interested and we agreed to collaborate, first on the Swallowtails generally and later to study the genetics of mimicry in tropical butterflies. This needs a note of explanation. It is well known that certain butterflies gain protection by having evolved wing patterns which closely resemble those of other, quite unrelated, butterflies which are distasteful to birds and other predators (Fig 5). Philip was an expert on this subject, Batesian mimicry, and we pursued work on it for many years and published numerous papers together.[7]

Our joint work prospered at first by correspondence, but in the late 1950s there was a vacancy for a lecturer in genetics at the University of Liverpool. Philip asked me about this, but knowing a negative baby when I saw one, I was discouraging and said I thought Liverpool would not suit him. Three weeks later

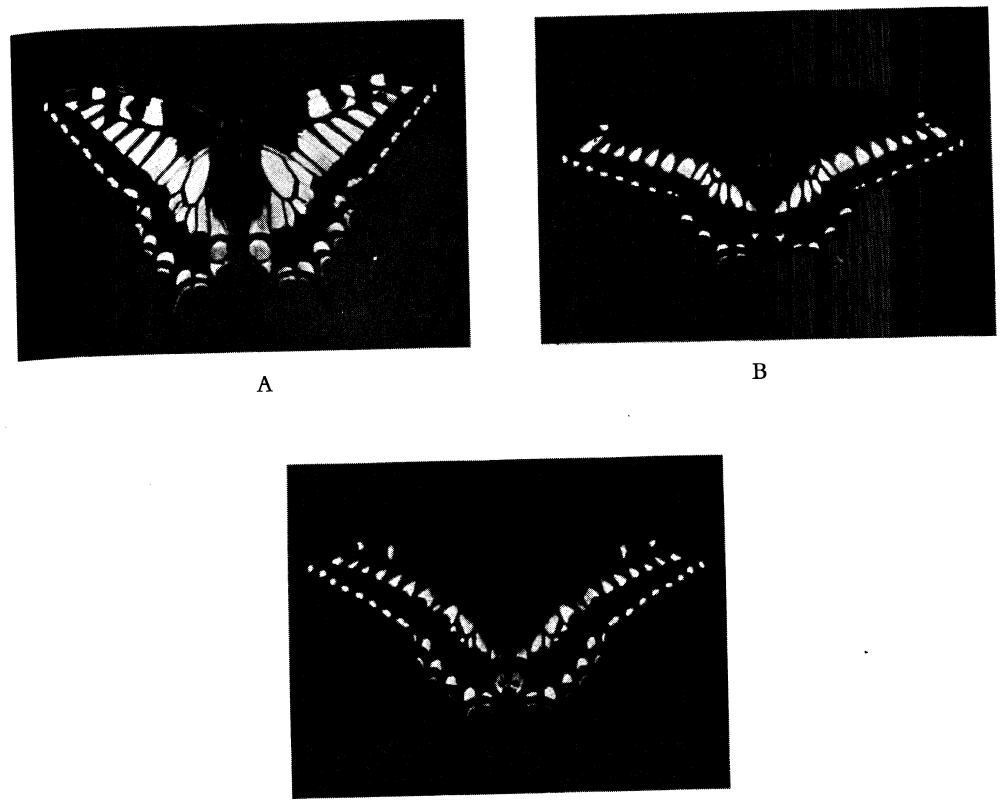


FIGURE 3
Swallowtail butterflies. A. *P. machaon* ♂ B. *P. polyxenes* ♂ C. F_1 ♂ hybrid (*machaon* × *polyxenes*).

I had a telephone call asking for more information and I knew then that the fish was hooked. He came in 1956 and we collaborated for 20 years, I becoming Professor of Medicine and he Professor of Genetics.

Blood groups

Soon after his arrival in Liverpool an episode occurred that I remember well. When motoring down to the Norfolk Broads to look at Swallowtails, I asked Philip how I could apply my small but increasing knowledge of genetics to medicine. 'Blood groups' he said, and blood groups it was.

Twenty-five years ago the journals were full of associations between one or other of the ABO groups and diseases such as carcinoma of the stomach (group A) and duodenal ulcer (group O). Aird, Bentall and Fraser Roberts were the magic names then and in Liverpool we were in the thick of it together with Dr Richard McConnell who was my registrar. However, we were pulled up short by Lionel Penrose, who said he would not believe the duodenal ulcer group O association until someone had used unaffected sibs as controls—only these would overcome the possibility of racial stratification. We took up the challenge, and the research involved finding families where there was segregation for ulcer (easy) and also segregation for the ABO groups, i.e. some sibs had to be group O and

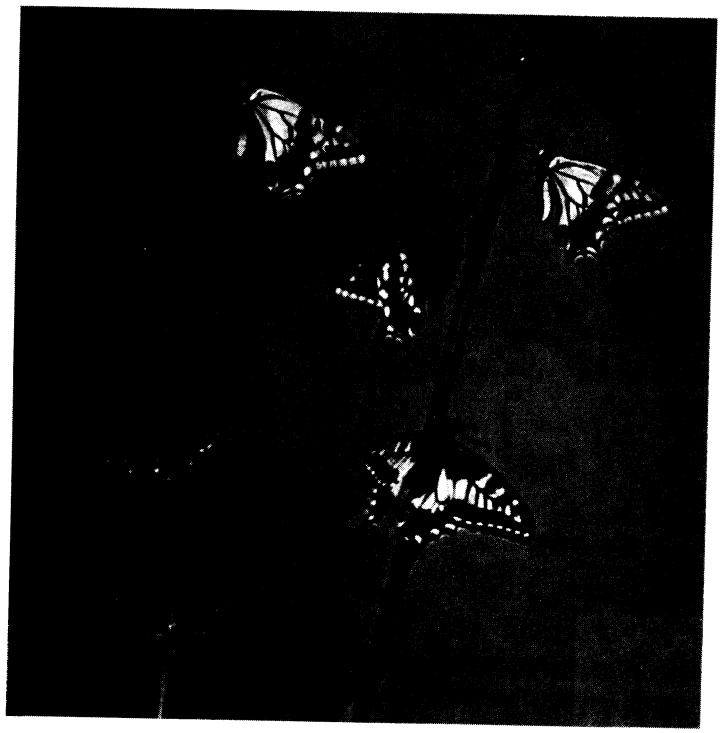
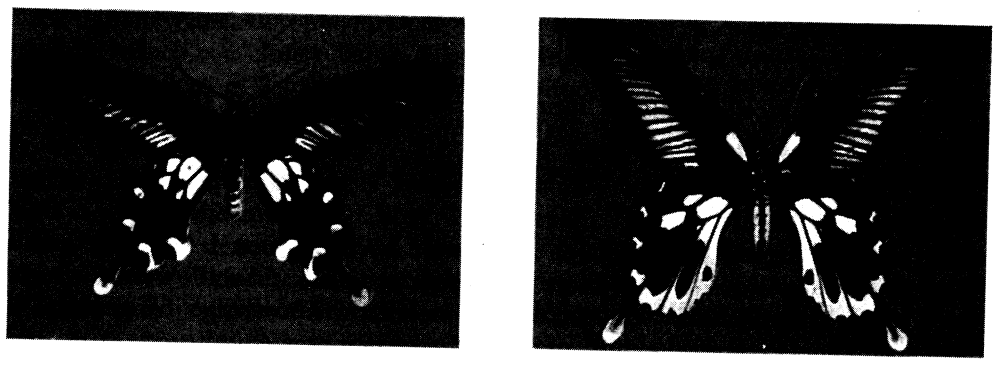


FIGURE 4
Back-cross from F_1 hybrids producing either yellow or black insects.



A B

FIGURE 5
An example of Batesian mimicry A. *Parides coon* B. The mimic, *P. memnon f achates.*

some not O (much more difficult). When we analysed our data we found that Penrose was right, our results being nowhere near significant.[8]

Later we were able to turn the tables on some American work. Buckwalter and Tweed had shown a highly significant association between duodenal ulcer

and a particular Rhesus genotype (R_1R_2) and with the MN blood group.[9] To me this sounded 'too good to be true'. I asked our blood group technician Mr W. T. A. Donohoe what he thought of the finding. He looked at the data and then turned to me smiling and said 'Sir, (remember this is 30 years ago) this is all temporary due to previous blood transfusion'. How right he was, when non-transfused patients were tested the association vanished.[10]

The Rhesus factor

It was however the butterfly mimicry work which led to our interest in the Rhesus blood groups, because the inheritance of Rh and of the mimetic patterns was rather similar. Rh has three loci (on chromosome 1)—Dd, Cc and Ee, with supposed crossing over to account for the rarer genotypes. The butterflies too have a series of genes on the same chromosome, ('linked genes'), usually inherited as a unit (a supergene) and we found occasional crossing over giving rise to rarer patterns. Another parallel was in the genetic interactions, in that between the Rh and the ABO systems ABO incompatibility usually protects against Rh haemolytic disease, and in the butterflies only the females have the mimetic patterns in the species that we were investigating and the males do not, so the influence here is sex.

The genetic interaction between the Rh and ABO systems is of great practical importance and it was this interaction which gave us the idea of how to prevent Rh haemolytic disease of the newborn.

The reason that ABO incompatibility between mother and fetus usually protects against the disease is because a group O mother contains naturally occurring anti-A and/or anti-B in her plasma, some of it 'complete' and some 'incomplete'. If there is a transplacental haemorrhage at or near delivery, the baby's cells may be Rh-positive and group A. If the mother is Rhesus negative, the maternal anti-A clears these cells before the Rhesus antigen on them has time to stimulate anti-Rhesus antibody (Rhesus is a slow acting antigen). This is a naturally occurring protective phenomenon against Rh haemolytic disease of the newborn, and is one of the reasons why some Rhesus negative women have no problem even though they carry Rh positive infants.

The ABO/Rhesus interaction gave us (at the start, Ronnie Finn, Richard McConnell and myself, and later John Woodrow and Shona Towers) the idea of injecting the mother with anti-Rhesus antibody (anti-D)—in the much more common situation (80% of cases) where there is *compatibility* on the ABO system (e.g. a mother is group O and Rh negative, and the fetus is also group O but Rh positive) and here, after a transplacental haemorrhage, the mother is at risk. This was a 'hair of the dog' cure if ever there was one and presently they are thinking about something like it for AIDS. But in fact we would be mimicking the naturally occurring protective mechanism, as the Rhesus antibody that we gave would get rid of any Rhesus positive cells that had leaked across from baby to mother. The injected antibody only persists for a few weeks, whereas if a mother is immunised by her baby she continues to produce antibodies for the rest of her life.

But how were we to test it out? We could not try it on women of childbearing age. We started our experiments on volunteers, on Rh negative male policemen, who were magnificently cooperative and when warned that we might produce all sorts of dire results, including leukaemia, said 'We trust you,

doctor'—this was many years ago. They believed they might really be doing some good if the experiments were successful, and mercifully there were no ethical committees in those days. We had consciences, however, and never took a step without consulting experts, whom we bombarded with difficult questions.

One expert, Rob Race, who had been enormously helpful in advising us originally, set us on one wrong track because he thought we should use 'complete' anti-Rh as this was the type which was thought to protect in ABO incompatibility. But this did not work—it cleared the cells but did not prevent immunisation. However, his wife, Ruth Sanger, rescued us because she came home from a meeting of American Blood Banks with the report that Curt Stern and Maya Berger had prevented immunisation in volunteers by using *incomplete* anti-D, which coated the Rhesus positive cells but did not destroy them.[11] These workers however did not think of using their antibody to prevent haemolytic disease! This incomplete antibody *did* work[12] in our volunteers (and also in postmenopausal women), and we could now start our clinical trials using newly-delivered women within the first 72 hours after delivery. When finally we were proved successful the male volunteers were saluted in the local Liverpool paper with the headline 'Men of Merseyside Mothers-to-be'!

So we really were off. This initial research took about ten years and was necessary before we could start treating women of child-bearing age.[13] One of the best and most exciting things about the research was the way it was taken up all over the world (at least where Rh incompatibility was a problem, which it is not universally owing to variations in blood group distribution). We had endless correspondence with America, Australia, Canada, Hungary, France, Germany and, even in those Iron Curtain days, with Eastern Europe. Everywhere the results were consistent and so it has gone on and still does.[14] The decline in Rh deaths from 1977 to 1992 is shown in Table 1 and the current work is assessing the immunisation rate in mothers whose babies are affected but do not die, which is a much more difficult problem.

During the time of the Rhesus research we were enormously grateful to the Nuffield Foundation for giving £350,000 to build a medical genetics unit in Liverpool. I was its director and in 1970 I was elected a Fellow of the Royal Society and made a lot of very distinguished, if eccentric, new friends.

Philip Sheppard (FRS 1965, Darwin medal in 1974) lived to see the success of the work and we were able to collaborate on the butterflies and moths to the very end.

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TABLE 1[14]

Decline in deaths from Rhesus haemolytic disease of the newborn. Classification of deaths registered by the Office of Population Censuses and Surveys as due to haemolytic disease of fetus or newborn, 1977–92.

Category	*Year* 1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992
							Deaths due to anti-D*									
1a	53	40	40	31	14	17	4	1	5	8	1	3	2	0	0	0
1b	32	28	24	23	12	16	12	11	11	9	9	5	5	5	4	2
2	12	11	10	6	6	5	8	3	9	8	7	6	2	3	3	2
3	9	7	12	11	9	6	9	9	8	5	10	6	1	2	2	5
4	0	2	1	1	0	0	1	1	0	0	0	0	0	1	0	0
Total	*106*	*88*	*87*	*72*	*41*	*44*	*34*	*25*	*33*	*30*	*27*	*20*	*10*	*11*	*9*	*9*
Deaths/100,000 live births	18·4	14·6	13·5	10·9	6·4	7·0	5·4	3·9	5·0	4·5	3·9	2·9	1·5	1·6	1·3	1·3
							Haemolytic disease due to antibody other than anti-D (anti-c, anti-K, etc)									
5	4	3	3	4	3	4	4	5	4	4	0	4	3	4	2	6
							Deaths not due to haemolytic disease (that is, excluded after scrutiny of notes)									
6	45	49	21	27	13	19	17	19	15	18	8	7	10	8	4	15
Total deaths registered as due to haemolytic disease by the OPCS	115	140	111	103	57	67	55	49	52	52	35	31	23	23	15	30

*Category 1: mother believed to have been immunised by pregnancy after which she was not given injection of anti-Rh immunoglobulin; category 1a: immunising pregnancy occurred before 1970 (when anti-Rh immunoglobulin not widely available); category 1b: immunising pregnancy occurred from 1970 onwards; category 2: immunised during first pregnancy (anti-D detected during or within seven days after first pregnancy); category 3: immunised despite having been given anti-Rh immunoglobulin after one or more previous pregnancies (failure of prophylaxis); category 4: immunised against D by blood transfusion. (Reproduced from *J R Coll Physicians Lond* 1994; **28:** 311)

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Letter from Australia

SENSE AND SENSIBILITY

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Prohibition often enhances the allure of the prohibited, and documents marked 'Confidential' seem particularly enticing. If it is only males that are excluded from access, then the chances of compliance must be vanishingly small. In the case in question, interest was intensified by the fact that the prying eyes belonged to a senior member of the Liberal Opposition front bench, Ian McLachlan, who not only looked, but also made a copy of a forbidden document. The circumstances in which it had arrived on his desk bordered on farce: it had been sent in error by his political opponents, the Federal Labour government. The intended recipient was a different McLachlan, who was presumably female, or if not, could obviously be trusted to obey instructions not to read his own mail.

Those hoping to hear of a scandal of Royal dimension will be disappointed, although several figures in Australian public life professed themselves highly scandalised by McLachlan's misdemeanour. This was largely because the secrets it revealed had belonged to a group of Aboriginal women. Outbursts of moral indignation of this kind tend to occur when our politicians compete to demonstrate their sensitivity to Aboriginal sensibility. This might be an admirable characteristic, were it not for the suspicion that the Aboriginal needs are not always the primary motivation for such protestation. Much to everyone's surprise however, propriety was observed, when McLachlan suddenly confessed the error of his ways and resigned his shadow portfolio. This was unexpected, as the Westminster tradition of ministerial responsibility is usually felt to be rather wimpish in Australia. Even the Prime Minister, Paul Keating, whose political weaponry has more often included the bludgeon than the rapier, was temporarily at a loss for words. He soon recovered from this tame, unsporting surrender however, and directed his vitriol at the Leader of the Opposition, John Howard, lambasting him for insensitivity by proxy.

Political opportunism apart, the case does highlight the difficulties which abound at the junction of different cultures and belief systems. The women whose secrets were put at risk, belonged to the Ngarrindjeri people of the lower Murray region of South Australia. They had protested because property developers wished to build a bridge from the mainland just south of Adelaide to Hindmarsh Island, to allow access to a half-completed $170 million marina. The Government, as governments do when confronted with a difficult decision, called for an independent enquiry to dilute any opprobrium. The sole arbiter, Professor Cheryl Saunders, found that the women did indeed have a case, and as a consequence, the Government announced a 25 year ban on the bridge. Perhaps in the name of equity, the property developers should also have been given the opportunity to explain their view of the cultural significance of the bridge to an anthropologist. Presumably this is a tribe whose values are not thought to require anthropological attention.

Predictably, the developers appealed, and the Federal Court overturned the ban. The Government has now counter-appealed so the saga is not yet over. In