

rather full, full, rather large or large. It is, therefore, difficult to see how a useful comparison between Struthers' comparatively accurate measurements and Combe's subjective judgements of size could easily be made.

In the case of Andrew Combe's organs, the descriptive terms used suggest that the dimensions of all of the organs were at the upper end of the range. The connections between the talents and disposition of Andrew as observed during life, were then discussed in relation to the development of his brain as observed at the post-mortem examination, but in such vague terms as to make any comparison between the features of his brain and those of George Combe almost impossible.

Now that all of the measurements of the two skulls and brains are available once more, there seems little to be gained by attempting to undertake the detailed comparison requested by George. Consequently, virtually all of the time, and undoubtedly also the anxiety, expended by Struthers on this exercise would seem to have been wasted. It is still difficult to know why Struthers should have taken on this thankless task. It is possible, though unlikely, that he was ambivalent towards phrenology and that, while publicly stressing his disdain for the subject, he might have retained some uncertainties. He was certainly much in awe of the abilities of both George and Andrew Combe, and had probably been flattered by the request. It is unlikely that, unless further correspondence between Struthers and Cox and/or Gibbon becomes available, this question can be answered.

ACKNOWLEDGEMENTS

I thank Mr Jack Cable for expert photographic assistance, and Dr James Shaw for invaluable advice and discussion.

REFERENCES

- ¹ Walker EM, Shaw JP, Kaufman MH. Dr Andrew Combe (1797-1847), Edinburgh Physician and Phrenologist. *Proc R Coll Physicians Edin* 1995; **25**: 652-62.
- ² Combe G. Essay on the Constitution of Man, Considered in Relation to External Objects. Edinburgh: John Anderson Jr 1828.
- ³ Gibbon C. The Life of George Combe, author of 'The Constitution of Man'. 2 volumes. London: Macmillan & Company 1878.
- ⁴ Combe G. Hints for the Examination of the Brain of George Combe. Manuscript, dated 23 May 1858, signed Geo. Combe.
- ⁵ Combe G. The Life and Correspondence of Andrew Combe, MD. Edinburgh: McLachlan & Stewart 1850.
- ⁶ Struthers J. Letter to Robert Cox Esq, from Innerleithen, dated 23 August 1862.
- ⁷ Struthers J. Report on Examination of the Skull & Brain of George Combe. Manuscript, 94 pages + Index, 2 pages. Dated 23 August 1862, signed John Struthers.
- ⁸ Struthers J. Letter to Charles Gibbon Esq, dated 17 January 1878.
- ⁹ Struthers J. Historical Sketch of the Edinburgh Anatomical School. Edinburgh: MacLachlan & Stewart 1867.
- ¹⁰ Comrie JD. History of Scottish Medicine. 2nd Edition. 2 volumes. London: Bailliere, Tindall & Cox 1932.
- ¹¹ Obituary. Sir John Struthers, MD, FRCSE, LLD. *Brit Med J* 1899; **1**: 561-3.
- ¹² Combe G. Moral Philosophy; or, the Duties of Man considered in his Individual, Social, and Domestic Capacities. Edinburgh: MacLachlan, Stewart & Co. 1840.
- ¹³ Combe G. The Principles of Physiology applied to the Preservation of Health, and to the Improvement of Physical and Mental Education. Edinburgh: Adam & Charles Black 1834.
- ¹⁴ Combe G. Essays on Phrenology, or an enquiry into the Principles and Utility of the System of Drs Gall and Spurzheim, and into the Objections made into it. Edinburgh: Bell & Bradfute 1819 (subsequent editions were entitled System of Phrenology).
- ¹⁵ Sharpey W, Ellis GV (eds). Elements of Anatomy, by Jones Quain. 6th Edition. Volume 2, pp. 429-32. London: Walton & Maberly 1856.

EIGHTY-EIGHT YEARS OF THIS AND THAT: PART II

C. A. Clarke,* 43 Caldry Road, West Kirby, Wirral, Merseyside L48 2HF

MORE ABOUT LEPIDOPTERA

*The Clarke/Sheppard/Gill genetic collection*¹⁵

A memento to Philip is the Clarke/Sheppard/Gill collection of butterflies (and a few moths) in the Natural History Museum in London. This was started in 1982 and consists of about 5,000 specimens in 132 drawers, and reprints of the papers which we wrote together. I can give further information to anyone who is interested—mimicry is a great feature of the collection.

Panaxia dominula, the Scarlet Tiger Moth

Philip left us a most fascinating and argumentative problem. The moth is found principally in colonies in the South of England and there are three genetically controlled forms, f. *typica* (one of the homozygotes) f. *medionigra* (the heterozygote) and f. *bimacula* (the other, rare, homozygote) (Fig. 6). All forms are recognisable but there is variability in the numbers of the three forms in different colonies. The moth had been one of E. B. Ford's pet subjects and there had been great controversy between him and R. A. Fisher on the one hand and Sewall Wright on the other. Is the variability of the proportions of the forms due to natural selection or to drift (i.e. migration or chance)?

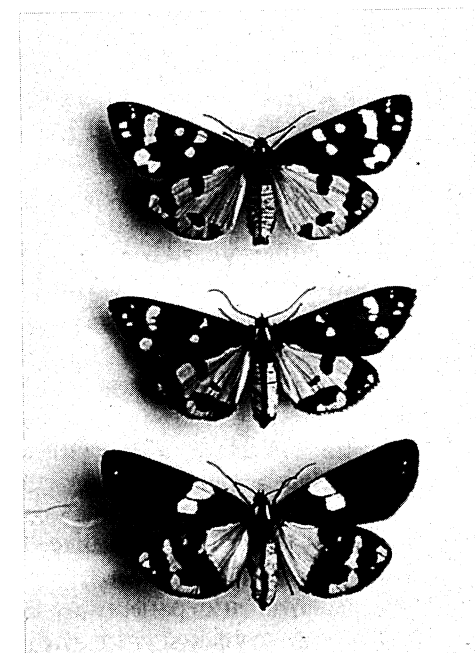


FIGURE 6

Three forms of the Scarlet Tiger Moth a. f. *typica* b. f. *medionigra* c. f. *bimacula*.

*Emeritus Professor of Medicine, University of Liverpool.

The area where *dominula* occurs in largest numbers is Cothill, near Oxford, where there are several colonies and with considerable variability in the populations over the years.

Philip was one of Ford's workers, and he had the idea of starting colonies in areas where *dominula* does not naturally occur and where he could put down known numbers of any of the forms (as small caterpillars) and where there could be no contamination from other colonies. One of these areas was 80 miles north of the normal range of the moth, on a disused railway line at West Kirby, Wirral, very close to his and my home. There in 1961 he put down about 13,000 newly hatched caterpillars obtained from Cothill by back-crossing *medionigra* to *typica*, giving a gene frequency of *medionigra* of 25 per cent in the first generation. With random mating and no selection these should in subsequent generations give a ratio of 9 f. *typica* to 6 f. *medionigra* to 1 f. *bimacula*. So far, we can find no clear records by Philip Sheppard between 1961 and his death in 1976, but quite accidentally I rediscovered the colony in 1988 and Table 2 gives our yearly data, based on bred larvae, and the proportions of the forms agree well with the wild moths observed each year in the colony. It will be seen that the ratios favour random mating and no selection which is in contradiction to the findings in Cothill where the population of *medionigra* is very variable, which we think is mostly because of migration from adjacent colonies.¹⁶

TABLE 2

Year	Dates collected as caterpillars (n)	Moth emergences from collected caterpillars			Total
		Typical	<i>medionigra</i>	<i>bimacula</i>	
1989	1.5-13.5 (30)	14	12	2	28
1990	1.5-9.5 (26)	16	7	1	24
1991	1.5-9.5 (51)	32	19	0	51
1992	1.5-13.5 (45)	32	11	0	43
1993	15.4-24.4 (51)	24	20	0	44
1994	18.4-28.4	31	17	0	48
1995	11.4-26.4	24	22	2	48

MOTHS AND INDUSTRIAL POLLUTION

This story is of considerable interest, particularly as regards the Peppered Moth *Biston betularia*; there is no doubt that pollution constitutes a risk to health. Thus, a good many years ago Professor Patrick Lawther, a friend of mine who was a chest specialist, asked some of his bronchitic patients to keep a diary of their symptoms in order to see how these correlated with the weather, particularly fogs, and with the levels of air pollution by smoke and SO₂. He found that exacerbations of bronchitis were closely related to increases of air pollution.¹⁷ There had been concern about the nation's health, (particularly after the 1952 London fog) and this led to the passing of the Clean Air Act in 1956, which made provision to limit the emission of smoke and for local authorities to

establish smoke free zones. The effect was remarkable, the emissions of smoke in 1976 being only one fifth of those in 1956. By contrast, total emissions of sulphur dioxide have risen during this period, mainly attributable to the use of oil and gas by power stations. The history of air pollution in Britain is therefore one of a dramatic increase during and after the industrial revolution, levelling off at the turn of the century, and a pronounced decrease in the last 25 years.¹⁸

I was interested in the early information and was aware of pollution in relation to the Peppered Moth from the work initiated in about 1940 by a colleague, Bernard Kettlewell.¹⁹ The story was as follows:

Before 1840 the Peppered Moth only had one form, the pale one, f. *typica*, though there was an occasional black mutant, f. *carbonaria*, but with the coming of the industrial revolution this prospered and by the end of the century in places like Manchester and Liverpool the moths were mainly black, the explanation given being that *carbonaria* was protected from birds by its camouflage when resting on the polluted bark of trees.

Bernard paid us a visit around 1956 at our house on Caldry Common (100 acres covered with birch trees) at West Kirby, about 11 miles west of Liverpool, and he said we ought to study *betularia* there, particularly to find out the proportions of f. *typica* and f. *carbonaria*. This we started to do in 1959 and every year up to the present (1994) we have caught the moths in June and July using each night a mercury vapour lamp and, when available, bred virgin females, which also attract the males. The total number of *betularia* caught by us between 1959 and 1994 is 17,648, nearly all males.* The catch each year is by far the biggest reported in UK, averaging around 500 a year. About 1975 the proportion of *carbonaria* started to drop markedly, and by 1994 it had been reduced to 18.7 per cent from 94 per cent in 1959, but the total *betularia* did not drop.

I had never thought of our seaside home as being in a polluted area, but my wife had noted that when the wind was in the east our white spaniel dog looked sooty, and washing on the line in the garden was similarly blackened. So maybe *carbonaria* had been protected until the Clean Air Act (after which dog and washing improved).

This idea of camouflage protecting the black moths has been widely adopted as an ideal example of natural selection at work within a human lifetime, and which is readily comprehensible to the layman and to schoolchildren, but in recent years there have been several minor queries and one major one. Bernard Kettlewell had magnificent photographs showing how *carbonaria* was camouflaged on sooty bark whereas *typica* stands out, but *betularia* have very rarely been observed in nature in the daytime and no one knows where the moths rest. Those in Bernard's photograph were posed for demonstration (a good picture is worth a thousand words!) (Fig 7). Several other species have melanic forms unrelated to bird predation and the cause of melanism is not always known.

Lastly, and most important of all, it has recently been found that in the north of the United States *carbonaria* has also decreased in frequency from 84.9 per cent in 1959 to 16 per cent in 1994.²⁰ While the parallel evolution of melanism in American and British Peppered Moths is striking, common causes are not obvious.²¹ Without closer inspection of what once seemed a well-understood phenomenon we are left with conjecture—considering the astonishingly rapid

*We only trapped 81 females over the 35 years: males, as usual, are expendable.



FIGURE 7

f. carbonaria and *f. typica* on sooty bark. A good picture is worth a thousand words!

decline in frequency of the melanics, we may soon lose the opportunity to understand this episode in the history of a species we thought we knew well. Experts in difficulty again!

In 1992 The College of William and Mary in Virginia, whose professor of biology, Bruce Grant, had helped a great deal with my work on melanism in moths, honoured me with a doctorate of science. This award brought my honorary doctorates (the first being Edinburgh) into double figures and was especially appreciated.

IN VITRO FERTILISATION

As a physician, *in vitro* fertilisation (IVF) is not really in my line, but I have been interested in it because I feel it needs emphasising that in general it is still in the experimental stage.^{22, 23} In Man the press leaps to report any successful outcome (only about 1 in 10) but does not mention the many failures and there is also the puzzle of why it can be done in cattle, sheep and pigs but not in horses.

Because there are occasional successes in Man, quite illogically I thought that it should be possible to do it in the Lepidoptera, where it would have considerable importance both for research breeding and in butterfly farms, and it is useful to start by describing the anatomy of the female genitalia (Fig 8). At mating, spermatozoa are introduced in one or more little sacs (spermatophores) into the copulatory opening of the female, from there they proceed to the bursa copulatrix. Here, after a few hours, the membrane of the spermatophore dissolves and the spermatozoa make their way (either through muscular contractions of the

passages or by chemical stimuli) through the ductus seminalis into the common oviduct and thence by another fine duct into the receptaculum seminis.

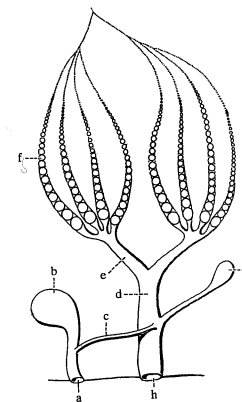


FIGURE 8

Female reproductive system in the Lepidoptera. (a) copulatory opening; (b) bursa copulatrix; (c) ductus seminalis; (d) common oviduct; (e) paired oviduct; (f) ovary; (g) receptaculum seminis; (h) ovipore.

When the mated female is about to lay, a muscular contraction occurs which pushes the egg towards the ovipore, and on its way causes a few spermatozoa to be squeezed out of the receptaculum seminis and into the oviduct where one enters the micropyle of the egg and fertilises it as it is laid. A good female will continue to lay eggs very quickly, and if the eggs are fertile they can be seen to be 'browning' after about 24 hours. When the female dies one more egg can be squeezed out through the ovipore or alternatively dissected out. The eggs still in the abdomen of the female, above this single fertile one, remain waiting in vain.

To study IVF in butterflies and moths we used many species, but an ideal one seemed to us to be *Hypolimnas bolina*, the Egg Fly, a tropical butterfly not unlike our Camberwell Beauty. Wild caught females are almost always mated, they travel well by standard air mail and on reaching England often live for several days, laying their eggs on stinging-nettle and sweet potato in a heated greenhouse. Fertility is confirmed when some caterpillars hatch, and then the laying female can be killed, and in the abdomen lie the unfertilised eggs glistening among the fat. To try and effect IVF the receptaculum is slit open and with a paint brush the sperm is mixed with the eggs using various different solutions, and sometimes injected through the micropyle, *but no fertility has ever resulted*. This is in spite of the fact that, in the naturally mated female preliminaries such as additions from adjuvant glands and 'capacitation'* of the sperm would presumably have already taken place *in vivo*.²²

John Hunter

Failure of IVF in the Lepidoptera has I think been universal in modern times, but

*Capacitation is effected by mixing the sperm with a variety of chemicals, one ingredient being calcium. The head of the sperm (the acrosome) has to bind to and penetrate the oocyte. Another aspect of capacitation is that it initiates the whiplash movement of the tail of the sperm.

on going through the literature we came across a paper by the famous John Hunter, written in 1792, where he claimed success in *Bombyx mori*, the Silk Moth.²⁴ His experiments were as follows:

Experiment 1. I took a female moth, as soon as she escaped from her pod, and kept her carefully by herself, on a clean card, till she began to lay: I then took males that were ready for copulation, opened them exposing their seminal ducts, and after cutting into these, collected their semen with a hair pencil: with this semen I covered the ova, as soon as they passed out of the vagina. The card with these eggs having a written account of the experiment on it, I kept in a box by itself. In the ensuing season, 8 of the ova hatched at the same time with others naturally impregnated. Thus then I ascertained that the eggs could be impregnated by art, after they were laid. The ova laid by females that had not been impregnated, did not stick where they were laid: so that the semen would appear not only to impregnate the ova, but also to be the means of attaching them.

To know whether that bag in the female silk-moth, which increased at the time of copulation, was filled with the semen of the male, I made the following experiment.

Experiment 2. I took a female moth, as soon as she had escaped from the pod, and kept her on a card till she began to lay. I then took females that were fully impregnated before they began to lay, and dissected out that bag which I supposed to be the receptacle for the male semen; and wetting a camel hair pencil with this matter, covered the ova as soon as they passed out of the vagina. These ova were laid carefully on the clean card, and kept till the ensuing season, when they all hatched at the same time with those naturally impregnated. This proves that this bag is receptacle for the semen, and gradually decreases as the eggs are laid.

These sound like genuine successful attempts and perfectly clear to repeat, but as has been said, we and others have failed entirely. It is possible that we have not taken enough notice of adjuvant glands and capacitation but neither did Hunter.

However, as already stated, no one has been able to repeat this work—not even the Japanese experts—and it may be that Hunter's report is erroneous. Moths are extremely quick to mate, and it could be that he left the experiments to an assistant and the eggs were naturally fertilised, or even that it could be a very rare case of parthenogenesis (on two occasions). It is curious that Hunter does not mention the actual breeding of the caterpillars, or the fact that silk moth eggs, if fertile, darken in a few days, or that for six months of the year there are no mulberry leaves for them to feed on and they had no means of refrigeration in those days. The eggs used in Hunter's experiments are in the Hunterian Museum at the Royal College of Surgeons, where we have received every help, and had the eggs photographed, but it is difficult to come to any firm conclusion about them.

A referee initially commented that in our criticism of Hunter we had not followed exactly his technique in our work on *Hypolimnas bolina*, in that in *bolina* the unfertilised eggs had not been laid. We therefore repeated Hunter's experiments precisely, but sadly with exactly the same lack of success as before, despite collaboration from the Zoological Society of London (Dr Patricia Croft).²⁵

Like all great men, Hunter had his admirers and his detractors, as will be seen in the contemporary remarks quoted below:

John Hunter, FRS 1728–1793

Praise (Anonymous)

By his discoveries in anatomy and physiology it was Hunter who first placed surgery on a scientific basis. He worked on over 500 different species of animals and made numerous dissections of plants, and what he discovered formed an invaluable body of new truths. Examples are: the circulation of insects; the semi-circular canals of the Cetacea; the air cells of birds; the function of the red corpuscles of the blood; the nature of the freemartin;

observations on bees (they do not collect wax but secrete it); and *in vitro* fertilisation of the silk moth, *Bombyx mori*.

Medically, our knowledge of the mechanism of inflammation and of collateral circulation in the treatment of aneurism dates from his work, 'He sought for truth, for truth's sake alone'.

Detraction (Jesse Foot, a contemporary surgeon, wrote in 1794):

He cared not about the truth, nor the use which might be made of any investigations in nature: and if he could give his subject the air of novelty he cared not from whom he took his information. Both his repute for understanding and his hope for success depended upon his passing the idea as his own.

Although no one (except ?Hunter) has so far convincingly carried out IVF in the Lepidoptera, yet my feeling is that one should go on trying, because the natural sequence of events ought to be capable of being imitated.²⁵

A note of general interest shows how complicated things can get. In 1976 USA workers showed that hamster eggs denuded of their zona pellucida could be fertilised to several divisions by human sperm. This penetrates the cytoplasm and acts as a non-specific stimulus but only to a few cell divisions. It is probably not proper fertilisation and has been criticised on this count, but apparently it gives useful results when testing for infertility in human males. Interestingly, sperm from marsupials and budgerigars can also fuse with the cytoplasm of the hamster.²³

CHANGES IN MEDICAL OPINIONS

Over the years, as a general physician I have come into contact with very many aspects of medicine without being an expert in any of them, but I have become very interested in the changing attitudes of the profession towards 'risk factors' (and 'mistakes') stimulated, I suppose, by the great fun we had with the moth *dominula* and the experts. (see p 675).

Alcohol

Alcohol is my first example. Everyone realises that chronic alcoholism is a bad thing, and far more of a threat to families than, say, cigarette smoking. Sensible people would still agree with this, but when I was young alcohol was frowned upon in general; but now the story is that three drinks a day for males and two for females are not only pleasant but they increase the life span. Why can't girls have three? I suspect the experts fear that there would make them live even longer.

Dupuytren's contracture

The views on Dupuytren's contracture have also shifted. When I was a student the consultants gave a wink when they saw a patient with this and immediately thought of alcohol abuse. But since I developed it myself at the age of 40 (there is a marked familial element on my maternal side) I became more interested in the condition, and as luck would have it I got to know John Carson, who is the physician and surgeon in charge of the Royal Hospital, Chelsea, where 400 elderly ex-servicemen live. Together John and I looked at the hands of all the occupants. In the 55 cases of Dupuytren the ages ranged from 65 to 97 years (mean 76.2) and from 65 to 99 years in the 'controls' (mean 75.5).²⁶ Being ex-servicemen from all parts of the country there was not much question of abstinence but there was no difference in the incidence of heavy drinking in the

Dupuytren group compared with the controls, and moreover even if there had been it does not seem to have interfered with their life span. My view is that alcohol as a 'cause' of Dupuytren's contracture is a fairy story but the Scots will take a good deal of convincing that this is so, perhaps because the whisky consumption is on the high side in the whole adult population.

Smoking

Cigarettes are I suspect at the peak of their trouble. I agree that they are not good for health, except perhaps as a relatively harmless sedative, but I find it very difficult to believe that they are the *cause* of many thousands of deaths a year. It is only very recently that smoking was allowed to be put on the death certificate as a contributory factor, and it still cannot be given as *the* cause. When I was young most young men smoked like chimneys (myself included) and there was minimal parental disapproval, and yet here most of us still are, and the interesting fact is that since the cigarette craze began (in the First World War really) the expectation of life has increased markedly. I think what has happened is that the proselytisers have taken over and exaggerated the ill effects of the craze. Passive smoking seems to me a very good example of this. Had the infant mortality rate (deaths under one year) gone *up* in the last 160 years 'passive smoking' would surely have been invoked as a cause, but in fact it has gone *down* from 148 per 1,000 in 1896 to 7 per 1,000 in 1991 in Liverpool. So I think that the dangers of cigarettes are exaggerated and far less dangerous than the drug taking which seems to be rife among the young at the present time. The Royal Colleges of Physicians of London and Edinburgh have banned smoking in the College buildings, but fortunately have left alcohol alone, though logically in my view it should have been banned as well. Frequent College dinners must be a hazard leading to alcoholism in a few cases.

Bicycling

It is interesting to look back 100 years and see of what the doctors were then disapproving. There was a splendid scare in the 1890s, all about the hazards of bicycling. The doctors soon pronounced on the health risks—cyclist's spine, cyclist's pudendum, cyclist's facies, cyclist's sore throat and there was also the suggestion that some of the lesions might be inherited.²⁷ And of course the ladies were in particular anatomical trouble. In 1895 Dr Herman is quoted as cautioning: 'If pedals are too far from the seat, the rider cannot make her feet follow the pedals without inclining the pelvis. Such side to side movements of the pelvis produces unnecessary strain on the muscles of the back and loins, and also friction against the sensitive external genitalia. If the saddle is badly shaped, the friction thus produced may lead to bruising, even to excoriations, and short of this, in women of certain temperament, to other effects on the sexual system, which we need not particularise'. Dr Playfair, in the same item is quoted: 'if there is any marked uterine or ovarian lesion, cycling, like other forms of exercise, should be prohibited, and it should not be practised during menstruation'.²⁸ But nevertheless the craze thrived, and to stop the rot the heavy guns had to be brought up, and 'cyclists heart' was invented. A BMJ leader in 1898 pontificates on over-exertion on a bicycle. The commonest effects are palpitation and temporary dilatation 'but the fact that temporary dilatation occurs at all is enough to show the great strain put upon the heart'.²⁹ Cycling-related heart disease was thus



FIGURE 9

A lady cyclist in St James' Park, 1897. (Hulton Deutsche Collection).

well on the way, but destined to become ridiculous when 100 per cent of the population was involved. This is the most ludicrous example of a 'risk factor' backed by the profession. The 'sweetie' in the photograph (Fig 9) looks most attractive and in the best of health. Personally as I said earlier I think I shall stick to what my Oundle headmaster said—that the secret of a happy life is to live dangerously. Medicine is much more scientific than it was 100 years ago but it has lost none of its proselytising zeal, and the rule still holds good that when the 'lower orders' begin to enjoy themselves they are fair game, and it is so much easier to lecture them than the top brass.

Asthma

A much more serious problem is that of asthma. When I was a student at Guy's I became interested in the management of asthma, particularly in childhood. There a psychiatrist, Dr Rogerson, long since dead, started an asthma clinic for children, and I copied him when I got the Liverpool job. It was not that we discarded obvious allergic and hereditary factors, but I had been taught always to look also at the general background of the child. Quite often maternal tension was a factor. In these cases we found that we got considerable success with our Liverpool patients if the child, when entirely well, slept away from home, i.e. in hospital, and went to school daily from there. Naturally any success we obtained was attributed by the allergists to the lack of house mites in the hospital. We also ran a children's play clinic once a week, and this culminated in 'An unscientific experiment'.³⁰ We organised a mammoth Christmas party at the Liverpool Northern Hospital, to which about 40 children who were supposedly particularly

'allergic' to dust and excitement were invited, together with their mothers. Over the weeks before, we built up great anticipation for it—there was to be a Father Christmas, presents, etc (and dust in plenty) but nobody had an attack and we attributed this to the fact that the mothers did not get anxious or apprehensive; we thought our party involved much less maternal strain since the child was not being sent among normal children with whom it might be unfavourably compared, and if it did break down it would be promptly treated.

The next step came from Dr (now Professor) Marcus Pembrey, then a research fellow in my department, who in 1969 collected, after much discussion, the details of 34 identical twin pairs where one of the pair had a common chronic disease such as asthma, Parkinsonism, or psoriasis, the other twin being normal. Discordant identical twins usually provide an ideal opportunity to study environmental influences on those multifactorial diseases with a strong genetic component, because the well twin acts as a perfectly matched control. A series of six papers was published by Pembrey in the *Practitioner* in 1972, the first being on bronchial asthma.³¹ The details of this pair, one of whom was asthmatic and the other not, indicated salient differences between the personalities and experience of the twins in childhood but later in life they still *looked* identical and were often mistaken for one another, even by their father, and when tested with 15 blood group sera their cells gave identical reactions. This suggests how important it is to look into the child's background.

I feel it is a sad reflection on the medical profession that asthma is now commoner than ever, in spite of drugs, particularly inhalers, and it is all put down to pollution; now motor cars are mostly blamed, and psychological background factors are rarely mentioned. These tend to be interpreted as 'old hat', whereas they are common sense though not high powered molecular genetics!

Cancer of the oesophagus in China

My interest in carcinoma of the oesophagus began in 1954 when Richard McConnell and I published a paper describing six members (all dead) of one family who had the disease.³² We learnt about them from an outpatient of mine who talked a great deal about her affected relatives and helped us to investigate their pedigrees. At that time we postulated that the most likely cause of the cancer was a dominant gene but we had no clue as to its nature though naturally at the time we persevered with the investigation of group A and secretor status associations.

Then in 1958 I had under my care at Broadgreen Hospital Liverpool a man of 37 who had carcinoma of the oesophagus, and my registrar asked me to diagnose a skin lesion affecting the palms of his hands. I said 'My boy, you ought to know what that is, it's tylosis' (though I had never seen a case myself I had heard about it). The patient told us that he had a cousin similarly affected with the two conditions, and the same was true of several other relatives. We discovered that he belonged to the same family as the one of 1954. This was the first report of the association of the two conditions and it looked as though our earlier guess of a dominant gene had been correct.³³

Time passed (I had been President of the Royal College of Physicians London from 1972–77) and I was delighted in 1978 to be invited by the Royal Society to be a member of a small team to make a short visit to China, to study oncology

there.³⁴ It was led by Michael Stoker, and the others were Walter Bodmer, Richard Doll, Avron Mitchison and, probably the most important of all, Elizabeth Wright, then director of the Great Britain–China Centre, who spoke fluent Chinese.

At the end of July we visited Linhsien, several hundred kilometres south west of Peking. This is an area with a high incidence of oesophageal cancer, and where the Peking Cancer Institute had a field station. A most important additional factor was that they had a heaven-sent model in the shape of their chickens, who allegedly were also liable to the disease, and the team felt that this should be research priority number 1. It might be that the hypopharyngeal tumour in chickens was unrelated to the squamous cell carcinoma found in man, but the high/low areas of incidence ran parallel. Richard Doll and Michael Stoker suggested that the Chinese Ministry of Agriculture should be approached to see if it would fund a big chicken farm containing many thousands of the birds. The farm should be stocked with chickens from an area where the prevalence of the carcinoma in Man was low, about 1 in 100,000. Additions to or subtractions from the diet of the birds could be made to try and find out which items might be responsible for bringing the cancer incidence in man up to 1 in 500. (The chickens were fed scraps from the human diet).

The Peking Field Station was very attracted to the idea that nitrosamines were the answers to their problems, but Richard Doll pointed out that, though they were known to be highly carcinogenic in animals, no tumour in Man had with certainty been related to them.

An important side issue in the high incidence area was what to do with young men who were not ill but who gave a positive screening-test. They tended to take to the mountains! Regarding progress since 1978, Richard Doll recently sent me details of American Chinese studies which suggest that the prevalence of oesophageal cancer remains high and that treatment has consisted mainly of various vitamins. There was no mention of chickens nor of our visit in 1978.

Longevity

I became interested in old age when I heard that the congratulatory messages which the Queen send to centenarians had greatly increased in number being 300 in 1955, 1,200 in 1970 and 3,300 in 1987, almost 90% being women.

Most environmental factors affecting longevity are well known, but less so is the improvement in the decline in infant mortality—that is, deaths in the first year of life. This has fallen from about 148/1,000 in 1896 to 7/1,000 in 1991 (Liverpool figures), which automatically means an increase in the average life span of the survivors.

The most interesting recent work on longevity relates to the suggestion that male and female embryos develop at different rates from the moment of conception onwards, the males faster than the females.³⁵ Thus the developmental advantage of XY over XX embryos will result in a higher proportion of XY embryos being able to implant and this would also explain the excess of male births over females (105–100) and more male than female abortions and stillbirths. Mittwoch³⁵ speculates 'that the male sex chromosome constitution codes for a higher metabolic rate in the embryo and sets the speed so as to accelerate the entire male life cycle. If so it would mean that the cost of this for the human male is on average five years of life'. Supporting this is a US finding on heart



FIGURE 10

Sir Cyril and Lady Clarke with female *P. aegeus*.

disease. The mortality was higher in males though the morbidity was similar for both sexes, but the 'weaker' sex tended to recover.

So after 88 years, my time is probably nearly up but there is still quite a lot of amusement around, and I would very much like to know why my pet animal (the butterfly) has the XX chromosome complement in the males and XY in the females, yet the latter live much longer than the tempestuous XX males. God does move in a mysterious way.

REFERENCES: Part II

- ¹⁵ Clarke CA. The Part II Clarke/Sheppard/Turner genetic collection of butterflies at the Natural History Museum, London. *J Lep Soc* 1991; **45** (3): 222-5.
- ¹⁶ Clarke, Sir C. *Panaxia dominula*, the Scarlet Tiger Moth: queries arising from an artificial colony rediscovered after 28 years. Presidential address to the RES, London. *Antenna* 1993; **17**: 177-83.
- ¹⁷ Lawther PJ *et al.* Air pollution and exacerbations of bronchitis. *Thorax* 1970; **25**: 172-7.
- ¹⁸ Bishop JA, Cook LM eds. Genetic consequences of man-made change. London: Academic Press 1981, p 409.
- ¹⁹ Kettlewell HBD. The evolution of melanism. Oxford: Clarendon Press 1973.
- ²⁰ Clarke CA *et al.* A long-term assessment of *Biston betularia* (L) in one UK locality (Caldy Common near West Kirby, Wirral) 1959-93 and glimpses elsewhere. *The Linnean* 1994; **10** (2): 18-26.
- ²¹ Grant B, Owen DF, Clarke CA. Decline of melanic moths. *Nature* 1995; **373**: 565.
- ²² Clarke CA. *In vitro* fertilization of insects. *AES Bull* 1988; **47**: 227-37.
- ²³ Clarke CA. *In vitro* fertilization: some comparative aspects. *J R Soc Med* 1990; **83**: 214-8.
- ²⁴ Hunter J. In: Observations on bees. *Phil Trans R Soc Lond* 1792; **XVII**: 186-8.
- ²⁵ Clarke CA. *In vitro* fertilization in *Bombyx mori*, the silkworm. Was John Hunter right or wrong in 1792? *Notes and Records, R Soc Lond* 1995; **49** (1): 85-92.

- ²⁶ Carson J, Clarke Sir C. Dupuytren's contracture in pensioners at the Royal Hospital Chelsea. *J R Coll Phys Lond* 1993; **27**: 25-7.
- ²⁷ Clarke C. The bicycle as a 'risk factor'. *J R Coll Phys Lond* 1988; **22**: 92-3.
- ²⁸ Cycling for women. *Br Med J* 1895; **2**: 1582-3.
- ²⁹ Bicycle heart. *Br Med J* 1898; **1**: 908.
- ³⁰ Clarke CA. Asthma in childhood. *Practitioner* 1950; **164**: 441-2.
- ³¹ Pembrey ME. Discordant identical twins. I: Bronchial asthma. *Practitioner* 1972; **209**: 110-3.
- ³² Clarke CA, McConnell RB. Six cases of carcinoma of the oesophagus occurring in one family. *Br Med J* 1954; **13**: 1137-8.
- ³³ Howel-Evans W *et al.* Carcinoma of the oesophagus with keratosis palmaris et plantaris (Tylosis). A study of two families. *Q J Med* 1958; **27**: 413-29.
- ³⁴ Report of Royal Society delegation led by Dr M. G. P. Stoker. July-August 1978. Royal Society 1979.
- ³⁵ Clarke CA, Mittwoch U. Puzzles in longevity. *Perspect Biol Med* 1994; **37** (3): 327-36.