1 *Consanguineous marriage, past and present*

Introduction

Major problems can arise when a term with a quite specific scientific definition becomes part of everyday speech. A prime example of this phenomenon is the word *mutation*, acknowledged within science as denoting a change in genetic structure and the driving force of evolution. But to members of the general public a mutation almost inevitably denotes a change that is at best disadvantageous and in many cases is life-threatening. Unfortunately, the terms *inbred* and *inbreeding* also fall into this category and, as a result, it has become virtually impossible to persuade members of the general public that inbreeding, and by extension marriage between biological relatives, can be anything other than harmful.

Yet in the animal kingdom there are many examples of deliberate inbreeding that have resulted in healthy and fertile stock, in particular the mouse strains which are routinely used in biomedical research. It has been claimed that all of the common laboratory strains of mice can be traced back to a single female (Ferris *et al*., 1982), and after continuous brother–sister mating for a minimum of 20 generations, it was estimated that the animals would have inherited identical gene copies from each parent at approximately 98.6% of their loci (Beck *et al*., 2000). Since some mouse strains have been maintained by sib-mating for more than 150 generations, in effect they now are genetically identical except for sex differences.

While there is no record of such sustained close inbreeding in human populations, even in Pharaonic Egypt, the anthropological literature contains ample evidence that unions between close biological kin have been commonplace and successful in many traditional human societies. Thus, in the cross-cultural ethnographic tabulations established by G.P. Murdock of the University of Pittsburgh, 353 of the 763 societies listed either permitted or favoured first- and/or second-cousin marriage (Murdock, 1967).

The continuing popularity of consanguineous unions in many present-day rural and urban populations is apparent from the detailed information presented in the Global Consanguinity DataBase (www.consang.net). Intra-familial unions between couples related as second cousins or closer are

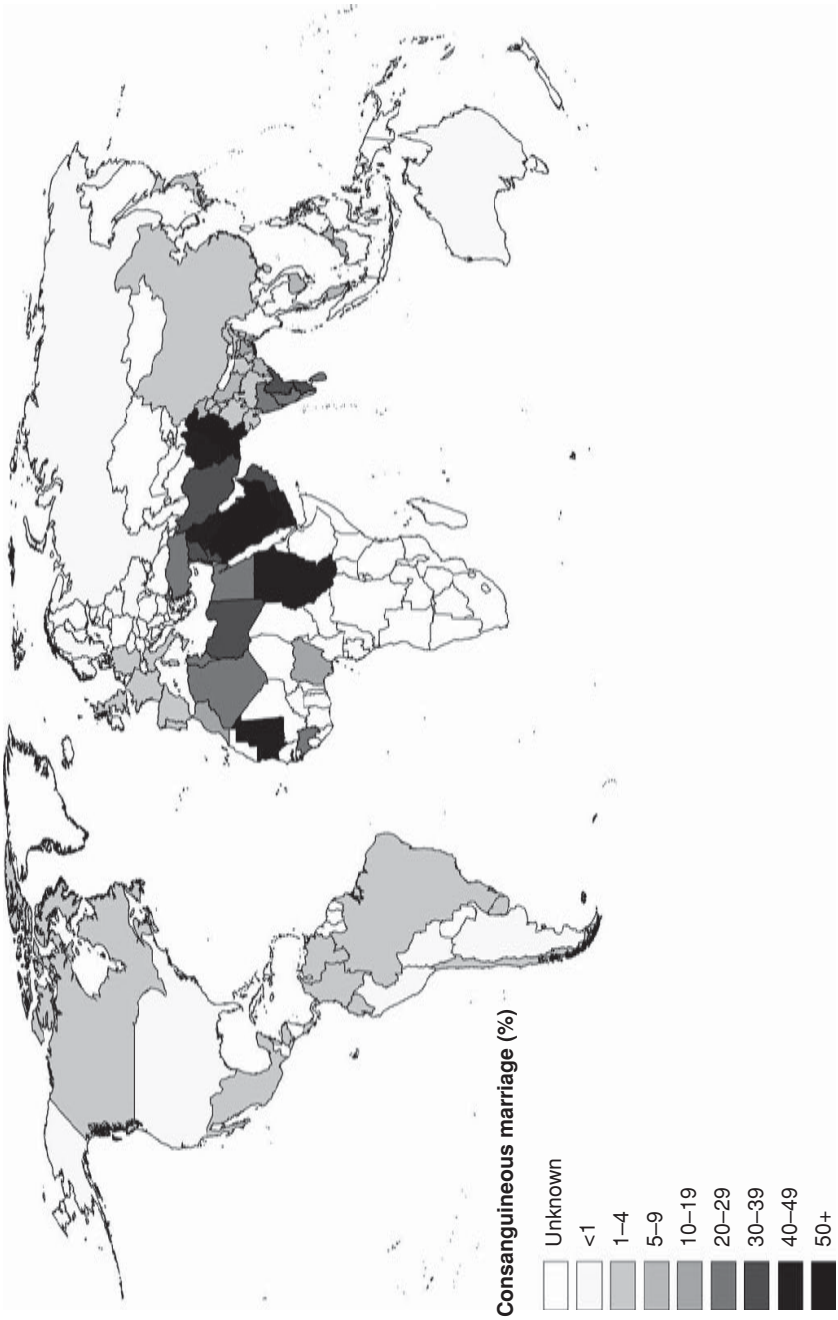

Figure 1.1 Global distribution of marriages between couples related as second cousins or closer ($F \geq 0.0156$). *Source:* www.consang.net

Table 1.1 *Current global prevalence of consanguineous relationships*

Consanguinity in population (%)	Percentage of global population	Population size (millions)
<1	15.5	1068
1–9	43.9	3026
10–19	0.5	35
20–29	6.5	448
30–39	2.1	145
40–49	3.2	221
50+	3.3	227
Unknown	25.1	1730

Sources: Global Consanguinity Website, www.consang.net; PRB (2011)

especially favoured in regions such as North and Sub-Saharan Africa, the Middle East, and Central and South Asia, and among the many emigrant communities from these regions now resident in Europe, the Americas and Oceania (Figure 1.1). In these populations 20% to more than 50% of marriages are contracted between couples who are related as second cousins or closer, with first-cousin marriage by far the most common form of consanguineous union. As will be discussed in Chapters 2–5, the rates and types of consanguineous union often vary according to historical, religious, legal and societal norms, but currently in excess of 1100 million people live in countries where consanguinity is highly favoured (Table 1.1).

These data should come as no real surprise, as even a cursory consideration of the size and structure of early human societies reveals that close kin mating must have been near-obligatory. It has been estimated that the Out-of-Africa migration of our human ancestors some 60 000–70 000 years ago involved potential breeding populations of as few as 700 individuals, to a maximum of some 10 000 persons (Harpending *et al.*, 1998; Zhivotovsky *et al.*, 2003; Liu *et al.*, 2006a; Tenesa *et al.*, 2007). Given their hunter-gatherer lifestyle, subdivision into separate small kindred groupings, and the suggestion that they exited Africa in two distinct waves (Rasmussen *et al.*, 2011), extensive inbreeding was well-nigh inevitable. Yet in the course of just 2400–2800 generations, their descendants who are scattered across the globe currently total some 5.9 billion, with an additional 1.1 billion relatives whose forebears had opted to remain in Africa (PRB, 2011). Statistics of this nature both indicate that all humans are genetically related to some degree and strongly suggest that close kin mating is not inevitably associated with an unfavourable health or reproductive outcome.

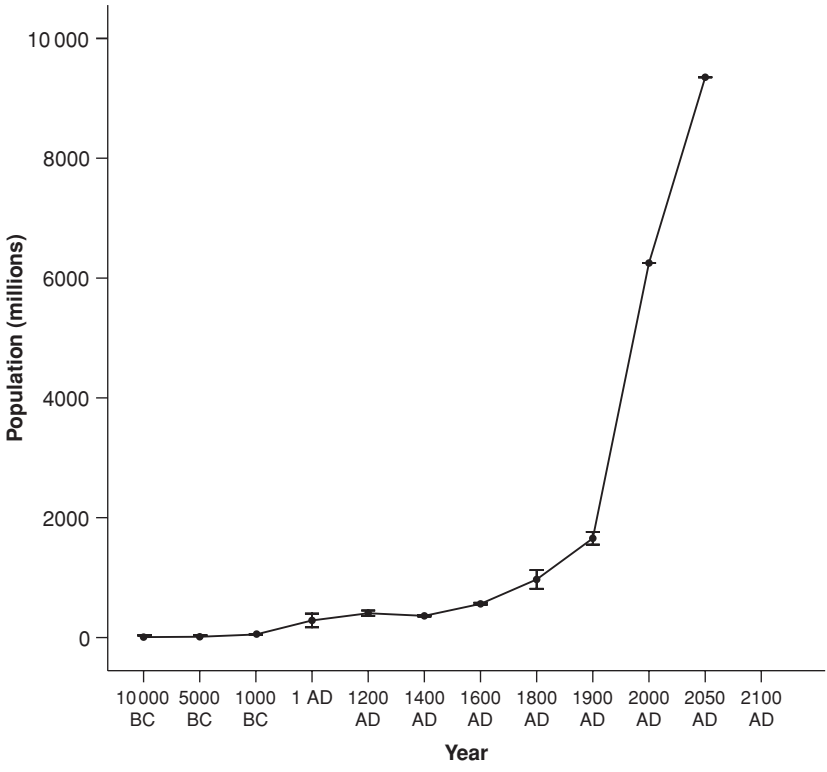

Figure 1.2 Global population growth, 10 000 BC to AD 2100. *Source:* USCB (2011)

Early urban development and social stratification

With urbanization and the establishment of increasingly sophisticated city states in Mesopotamia, Egypt and the Indus Valley around 3000 years ago, formal marriage was instituted and social stratification gradually became the norm. The net outcome of these changes was to restrict mate choice and to encourage endogamy and consanguinity within different social classes and strata. Thus, despite the slowly growing global population which, as indicated in Figure 1.2, is estimated to have numbered approximately 310 million by AD 1000 (USCB, 2011), most individuals married and reproduced within quite restricted local communities.

The Tribes of Israel provide a relevant and well-documented historical example of the influence of tribal subdivision dating back some 3000–4000 years, with the land and prescribed social and religious obligations subdivided

between the 12 sons of Jacob and their descendants. Intra-familial consanguineous unions were favoured, a pattern set by Jacob himself as both of his wives, Leah and Rachel, were his first cousins (Genesis 28–29). It is, however, difficult to estimate the degree to which historical clan and/or tribal endogamy resulted in genomic homozygosity in such early, numerically small populations. Especially since, as in the example of Jacob, while six of his sons were born to Leah and two sons to Rachel, the remaining four founding males of the Tribes of Israel were the sons of Jacob's two concubines, Zilpah and Bilhah, who formerly had been maidservants to Leah and Rachel (Genesis 30).

Some indication of the population structure and dynamics of these earlier human groups can be gained through the study of present-day societies, such as the Kel Kummer Tuareg tribe of the southern Sahara, which was founded in the seventeenth century and by the 1970s numbered approximately 300 persons. Among the Kel Kummer, strict tribal endogamy has been maintained and marriage between a man and his mother's brother's daughter is regarded as obligatory (Degos *et al*., 1974). By comparison, in other larger tribes, there is marked population stratification, with individuals and families born into traditional patrilineal clans and tribes. For example, the Abbad tribe in Jordan, which was established some 250 years ago, now comprises approximately 120 000 individual members divided into 76 male lineages of between 250 and 2000 individuals, with 47% of all marriages intra-clan and 90% contracted within the tribe (Nabulsi, 1995).

Human mating as a genetic continuum

Rather than inbreeding and outbreeding being regarded as separate and opposite reproductive strategies, it is more logical and credible to consider human mating as a genetic continuum that ranges across:

(i) Random mating: which is a rare event despite its incorporation in the Hardy–Weinberg principle that specifies an equilibrium relationship between gene frequencies and genotype frequencies within populations.
(ii) Positive assortative mating: with marriage occurring between couples who live in a specific geographical area and often in the same village or town; are of the same generation; and who share religious, educational and socioeconomic backgrounds.
(iii) Endogamous marriage: between partners preferentially and often obligatorily drawn from the same clan and tribe and therefore lineal descendants of a common male ancestor.

Table 1.2 *Human family and genetic relationships*

Biological relationship	Genetic relationships	Coefficient of relationship (r)	Coefficient of inbreeding (F)
Incest	First degree	0.5	0.25
Parent–child			
Sibling			
Half-sibling	Second degree	0.25	0.125
Uncle–niece			
Double first cousin			
First cousin	Third degree	0.125	0.0625
First cousin once removed	Fourth degree	0.0625	0.0313
Double second cousin			
Second cousin	Fifth degree	0.0313	0.0156
Second cousin once removed	Sixth degree	0.0156	0.0078
Double third cousin			
Third cousin	Seventh degree	0.0078	0.0039

(iv) Consanguineous marriage: in which the partners are known to share close biological ancestry, usually involving intra-familial marriage(s) within the preceding two to three generations.

It is apparent that positive assortative mating, endogamous marriage and consanguineous marriage are all examples of 'inbreeding', the differences among them being principally a question of degree. However, it could additionally be argued that while assortative mating is largely character-specific and so may be dependent on genes that determine attributes such as external appearance or temperament, consanguinity and to a lesser extent endogamy can influence the entire genome (Lewontin *et al*., 1967).

Basic measurements of consanguinity in human populations

As will be described in detail in Chapter 6, in all forms of consanguineous unions the partners share genes inherited from one or more common ancestors and, for example, in first-cousin marriages, the spouses are predicted to have 1/8 of their genes in common, described as the coefficient of relationship (r). This means that on average, their progeny will be homozygous at 1/16 of gene loci, i.e. they will have inherited identical gene copies from each parent at this fraction of sites in their genome. As shown in Table 1.2, an individual's level of consanguinity is conventionally expressed as the coefficient of inbreeding (F), which for first-cousin offspring is 0.0625. By comparison, in second-cousin marriages, the equivalent figures are that they have 1/32 of their genes in

common and therefore an F value for their progeny of 0.0156, while for first-degree (incestuous) relationships, the couple share 1/2 of their genes and their progeny will have an F value of 0.25. If the same mutant gene is inherited from both parents, an individual will express the equivalent recessive disorder, prenatally, at birth, or later in life depending on the nature and site of the mutation, thus contributing to the phenomenon of inbreeding depression.

Western attitudes to consanguineous marriage

In contemporary Western society, the term *inbred* is widely used as a term of denigration, and marriages between biological relatives often are treated, at best, with suspicion and frequently with embarrassed astonishment. Once again, this is somewhat surprising because long lists of eminent and highly successful persons can be compiled who either contracted consanguineous marriages (from the Latin *con sanguineus*, of the same blood) or had long-standing relationships with a close biological relative. Among males who married a first cousin are the musicians Edvard Grieg and Sergei Rachmaninov, the scientists Charles Darwin and Albert Einstein, literary figures ranging from the doyen of Victorian horror stories Edgar Allen Poe to H.G. Wells and Mario Vargas Llosa, and the pre-eminent free-market economist Friedrich Hayek.

Despite the successful lives of these notable persons, and the evidence from the Out-of-Africa migrations indicating that consanguinity can be compatible with successful reproduction and population expansion, there remains a suspicion that inbreeding is necessarily deleterious. But, if so, why do so many contemporary societies continue to favour consanguineous marriage? Conversely, if consanguinity is not especially harmful, then why are marriages between cousins frequently a source of mirth and derision in Western societies, even though they are legal in virtually all countries? Whether any single volume could answer even these very basic questions is dubious. But as a starting-point, by examining and analysing the plentiful information that is available on the prevalence of consanguineous unions and their outcomes in terms of partner compatibility, reproductive success and the health of their children, it should at least be possible to identify the roots of the prejudices that seem to surround the entire subject of close kin marriage.

There is convincing evidence that consanguineous marriage was quite widely prevalent in Europe prior to the middle of the nineteenth century (Huth, 1875), and indeed the theme of cousin marriage initially was strongly favoured by many eminent Victorian novelists, including Charles Dickens, Anthony Trollope, Emily Brontë and William Thackeray, with Thackeray, John Ruskin and Lewis Carroll themselves the progeny of cousin marriages (Anderson,

Table 1.3 *Consanguineous marriage within geographical isolates in the Americas and Europe*

The Americas		
Canada	Québec	Phillipe & Gomila (1972)
	Newfoundland	Bear *et al*. (1988)
USA	Tangier Island, Virginia	Mathias *et al*. (2000)
North Atlantic	Flores, Azores	Smith *et al*. (1992)
Caribbean	St Thomas, US Virgin Islands	Leslie *et al*. (1978)
	St Barthélémy, Antilles	Serre *et al*. (1982)
South Atlantic	Tristan da Cunha	Bailit *et al*. (1966)
		Roberts (1968)
Europe		
France	Arthez-d'Asson, Pyrenees	Serre *et al*. (1985)
	Vallouise, Briançon	Boëtsch *et al*. (2002)
Hungary	Ivad	Nemeskéri & Thoma (1961)
Italy	Upper Bologna Apennines	Pettener (1985)
Scotland	Inner Hebrides	Sheets (1980)
	Orkney Islands	Roberts *et al*. (1979)
Spain	Formentera, Balearic Islands	Valls (1969)
	Western Pyrenees	Abelson (1978)
	Sigüenza-Guadalajara	Caldéron *et al*. (1998)
	Gredos Mountains, Avala	Fuster *et al*. (2001)
Switzerland	Alpine isolates	Morton *et al*. (1973)

1986). The fictional narratives, where a heroine falls in love with her 'dearest coz', are therefore at odds with the popular belief that consanguineous unions were restricted to population isolates and arose only because of a shortage of marriageable unrelated partners.

Marriage in geographical, social and religious isolates

As previously described under positive assortative marriage, it is nevertheless true that the choice of a marriage partner will necessarily be restricted in small isolated populations with few potential spouses and, in such communities, all of the members may be related to some degree. Geographical isolates of this nature exist in the Americas and in many European countries (Table 1.3), and similar patterns are seen in enclosed religious communities, such as the North American Anabaptist sects, the Amish (Khoury *et al*., 1987; Dorsten *et al*., 1999), Hutterites (Mange, 1964; Martin *et al*., 1973) and Mennonites (Allen & Redekop, 1987; Moore, 1987); in a Brazilian Jewish community (Freire-Maia & Krieger, 1963); and in the Middle East among the Samaritans (Roberts & Bonné-Tamir, 1973), the Druze (Shlush *et al*., 2008), and the Mandaean community in Iraq which reveres John the Baptist.

In addition, ethnic and social groups frequently choose to marry within their own community, exemplified by the Ramah Navaho and Hopi Native American tribes (Spuhler & Kluckhorn, 1953; Woolf & Dukepoo, 1969); or are subject to social stigmatization by co-resident majority populations, as in Gypsy/Roma populations (Williams & Harper, 1977; Thomas *et al*., 1987; Kalaydjieva *et al*., 1996; Martin & Gamella, 2005) and Irish Traveller communities (Flynn, 1986; Gordon *et al*., 1991).

In some isolates, there is evidence of consanguinity avoidance, probably reflecting prevailing religious restrictions (Hussels, 1969; Leslie *et al*., 1981; Magalhães & Arce-Gomez, 1987). Whereas in others, the pattern of concordance between consanguineous marriage and religious practice seems to be more finely tuned, e.g. with second-cousin but not first-cousin marriages contracted in Eriskay, a Scottish Roman Catholic island community (Robinson, 1983).

Anecdotal tales of close kin unions – licit and illicit

In his essay entitled *The Great Revolution in Pitcairn*, Mark Twain provided an example of the deliberately humorous approach to inbreeding in an isolated human settlement, in this case the community on Pitcairn Island in the southern Pacific which was founded by the mutineers of HMS Bounty in 1789 (Huth, 1875; Twain, 1899). At the time of writing, Pitcairn had a total population of 90 persons, comprising 16 men, 19 women, 25 boys and 30 girls. According to Twain's fictional traveller to Pitcairn, on talking with a male islander, he remarked, 'You speak of that young woman as your cousin; a while ago you called her your aunt'. To which the islander replied, 'Well, she is my aunt, and my cousin, too. And also my stepsister, my niece, my fourth cousin, my thirty-third cousin, my forty-second cousin, my great-aunt, my grandmother, my widowed sister-in-law – and next week she will be my wife'. All good knockabout fun, at least for the majority of the world's population not resident on Pitcairn, which in the 1990s gained a rather less acceptable reputation associated with the sexual exploitation of young females by adult male islanders.

Although every Western country seems to have at least one region where, allegedly, inbreeding is rife and the adverse physical and mental outcomes are obvious, few studies have been published to support this belief. During the late 1940s, social attitudes towards consanguineous marriage were, however, investigated in a remote mountain community in eastern Kentucky (Brown, 1951), a region where according to popular account many families were married 'through and through'. It transpired that consanguineous marriages occurred both among families who the author defined as 'high-class' and others who were 'low-class'.

Because of the shortage of suitable spouses from other families of equal social status, high-class families did sometimes resort to marriages between partners who were second cousins or second cousins once removed but, as described by the author, they were: '. . . long-resident families of good background, *moral athletes*, hard workers and good livers, less isolated and more modern than other families in the area and people who emphasized self-improvement and who participated more widely in neighborhood affairs'. By comparison, their much more highly inbred 'low-class' counterparts: '. . . tended to be newcomers with *shady pasts*, morally lax, economically insecure, not ambitious, old-fashioned and *backward*, and people who participated relatively little in many neighborhood activities'. (Original author's emphases in both quotations.)

One large 'low-class' family was particularly notorious for sexual misconduct, drunkenness and behaviour discreetly described as 'other deviations from accepted norms', and the patriarch allegedly had fathered a child with his stepdaughter. Not surprisingly, they experienced difficulties in arranging marital alliances with other families in the locale; as a result, 18 of the patriarch's 70 grandchildren had married close kin, with 15 of the 18 married to their first cousins. The situation was succinctly summarized by a 'low-class' woman who had actually married into the family: 'I reckon they married each other because they couldn't get nobody else' (Brown, 1951).

Consanguineous marriage among European royalty and other dynasties

Colourful anecdotal material of this nature has tended to typify and reinforce attitudes against consanguineous marriage within Western society, but with double standards applied. Consanguineous marriage seems to be acceptable if families are well-to-do and generally regarded as pillars of society, especially if such marriages have been between more remote relatives. Hence, perhaps, the unquestioned acceptability of multi-generational intra-familial unions within many of the Royal Houses of Europe (Darlington, 1960). For example, with His Most Catholic Majesty King Philip II of Spain (1527–98) sequentially bound in matrimony with his double first cousin Maria of Portugal ($F = 0.125$), Mary Tudor a first cousin once removed ($F = 0.0313$), Elizabeth of Valois a non-relative, and finally with his niece Anne of Austria ($F = 0.125$).

The Spanish Habsburgs

Recently, the problems that can arise due to multi-generational consanguinity have been illustrated by a pedigree analysis of the Spanish Habsburg dynasty, conducted over 16 generations and comprising some 3000 individuals (Alvarez