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SEXUALLY TRANSMITTED DISEASES: THE CINDERELLA OF TROPICAL MEDICINE*

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HISTORICAL REVIEW

To appreciate what are the significant contributory factors to sexually transmitted diseases (STD) today in Africa one has to understand part of the historical development of Western civilisation in that Continent.

Traditional society in Africa was either nomadic or agricultural. There were few towns and no large conurbations. Trading took place at local markets. Africa was ruled by tribal groups each of which had its own territorial rights. Larger, more land acquisitive tribes and ethnic groups had larger tracts of territory. Other smaller groups lived in isolation in remote areas or in fear of these stronger, more aggressive or war-like tribes. There were strong tribal taboos and cultural patterns which dictated and governed lifestyles. Religion, the power of ancestral spirits and the power of *thahu* [taboo] and *ũrogi* [the 'curse that kills'] were dominant factors in the keeping of law and order within tribal groups, particularly of the Bantu. Life expectancy was short and death-rates high due to disease, in particular malaria and dysentery, and to famine, drought and the effects of war and tribal feuds.

It was into this background that the early colonisers arrived, essentially as traders. In the course of their trading they opened up routes to the inland areas from which would come timber, ivory, skins and precious minerals. Some of them were devout God-fearing men who requested their home churches to send out doctors, teachers, agriculturalists and ministers of religion to deal with what they saw as the main causes of death—disease, ignorance, famine and malnutrition, and superstition. As a result death-rates fell. At the same time, because of the teaching of religion certain tribal traditions were curtailed or ultimately brought to a stop. The cessation of some of these, one could argue was for the better, such as female circumcision and polygamy, while the loss of others which prevented incest or premarital sexual activity and operated through *thahu* [strong taboo] was a disadvantage.

At the same time other colonisers came into the country to farm the land. The establishment of farms created buffer zones between warring tribes, settling the feuds and bringing peace to the land, hence the term settler. With them came a cash economy and westernisation and in time businesses, importers and exporters, and all those with the skills that add up to a modern western civilisation.

Following the marked fall in death-rates, the population began to increase. Traditionally land had belonged to nomadic tribes who grazed over it, apart

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from those areas which had been used by the more agricultural tribal groups. With the settling of the land, individual chiefs claimed tracts of land of various sizes. These were then divided up amongst the different families and ultimately a man's land was divided between his children when he died and later subdivided between his grandchildren. This brought increased land use in agriculture, animal husbandry and forestry.

Plots of land, the inheritance of the younger generations, became smaller and smaller and less viable as individual units and so a different pattern of living began to evolve. Young people drifted away from the homelands and travelled to work in the towns and cities. Some travelled for further education as secondary and tertiary education became available. Others travelled to work in businesses and on settlers' farms. Although, in some areas settlers provided not only education and medical services, but also land on their farms for their workers. There was increase of urbanisation but the homelands and agricultural plots, however small, remained an integral part of African culture—they were a man's insurance and ultimately his retirement home. Thus, they were not sold off but frequently a man left his wife at home to care for the land while he went in search of employment and an income to supplement what could be earned off the land.

The evolution of the pattern of travel for work as described is largely that seen in East Africa. Elsewhere in Africa although the final consequences are similar, the initial motivation for travel for work varied. For example, in Rhodesia, later Zimbabwe, it was the need to pay a poll tax in cash that drove many men to the towns to work for monetary wages. In South Africa the mining industry employed men not only from South Africa but also from neighbouring countries. The migrant labour force lived in hostels for months on end possibly returning home once a year for a few days.

As has occurred over the centuries, and up to today, with men from western and industrialised cultures during war and with 'travel to work', so too for many African men it was totally unnatural to be living away from home and without a woman. Thus some took second wives or found a 'girl friend', of if they did not, they availed themselves of the services of prostitutes and prostitution began to increase. Moreover there were and are few recreational activities or facilities open to the migrant labourers or those who had drifted to the cities in search of work other than bars, beer halls, beer gardens or bottle stalls all with their attendant hostesses. One of the practical consequences of wages being paid in cash was, and is, the inevitable temptation to spend much of the wage packet immediately on alcohol and women. With transportation of goods over long distances by road there came the development of the overnight stopping places, small trading posts with bars, possibly hostels and prostitutes.

Meanwhile wives may sometimes find it hard to make ends meet whether working at home on the family land or in an urban environment where the nuclear family has travelled when a poor harvest followed adverse weather conditions. When and if their share of their husband's monthly salary does not reach them or is inadequate to cover the costs of food, schooling and an emergency like medical treatment, some married women may have no alternative to prostitution to enable them to support their children. This recent break with traditional practice whereby women were expected to remain faithful to their husbands seems to occur more in urban areas.

STD in Africa

STD in Africa is characterised by high prevalence rates, antibiotic resistance, and high complication rates. Complications for women include pelvic infection, frequently with resulting infertility and ectopic pregnancy, and gynaecological morbidity.[1–4] STD especially gonorrhoea also causes infertility in men; in certain areas up to 50% of infertility has been due to the husbands' azospermia, secondary to gonococcal infection (C. Rendle-Short, personal communication). It is noteable that 30 to 40% of gynaecological admissions in Africa are due to the sequelae of pelvic infections and STD.[5,6] STD may also be an aetiological factor for cervical cancer which is the commonest cancer in developing countries. In obstetric practice, STD frequently results in adverse pregnancy outcome in terms of intra-uterine death, stillbirth and neonatal infections as well as puerperal sepsis and even maternal death.[7,8] These human tragedies have their further consequences, social, economic and psychological.

STD the neglected disease of tropical medicine

A review of publications on the subject of STD in tropical medicine shows that of papers reviewed in the Tropical Diseases Bulletin (1991) less than 1% related to STD, while 2% related to the epidemiology of HIV and AIDS. In a computerised search by the librarian of the Royal College of Obstetricians and Gynaecologists for publications on STD/female/Africa only one paper was found in the Transactions of the Royal Society of Tropical Medicine and Hygiene 1977–1992. It is of course possible that some STD publications may not have been submitted to tropical disease journals but rather to specialist journals in the field of genito-urinary medicine.

To put STDs in perspective, the global incidence is estimated by the World Health Organization (WHO) to be in excess of 125 million per annum, most of which occur in developing countries particularly in Africa. For comparison 5 million individuals are receiving treatment for active leprosy; trypanosomiasis in South America claims 7 million people; schistosomiasis affects 180–200 million world wide, filariasis 200 million and trachoma 400–500 million.

The WHO estimate of 125 million STD cases per annum may be an underestimate, if one considers notification for one country alone. For example, in Ethiopia gonorrhoea notification to the Ministry of Health for the year 1989/90 was 90,000 cases. However based on epidemiological studies,[9,10] the population, and population growth rate, it can be estimated that 140,000 pregnant women annually may have asymptomatic gonorrhoea and 42,000 prostitutes in Addis Ababa alone have gonorrhoea, a total of 182,000 women in two selected groups, before including infected men, sexually active teenagers or neonates.

Causes for the underestimation of STD incidence by WHO are essentially related to non-notification for which there are many co-factors including: non-diagnosis of STD; high prevalence of asymptomatic infections; lack of clinical suspicion that STD is a likely cause of gynaecological pathology, infertility or neonatal infections; poor or non-existent diagnostic facilities;[5] overworked doctors and other health workers who have neither the time nor facilities to investigate patients completely, nor the time to fill in notification slips for individual patients. These factors apply particularly to clinics serving rural areas in which most of the population live. The promotion of national government

TABLE 1

Positive serological tests for syphilis in women attending antenatal clinics

Country	*Positive syphilis serology*		Reference
	VDRL/RPR (%)	*TPHA/FTA-Abs* (%)	
Swaziland	13	44	Guinness *et al.* (1988)
	10	33	Meheus *et al.* (1980)
Ethiopia	28	27	Duncan *et al.* (in press)
	18	17	Perine (1983)
Gambia (rural)	26	13	Greenwood (cited by Mabey (1986))
(rural)	15	11	Mabey (1986)
(urban)	9	1	Mabey *et al.* (1984)
South Africa (urban)	12	19	Klugman *et al.* (1991)
(rural)		12	O'Farrell *et al.* (1989)
Cameroon		17	Ndumbe *et al.* (1992)
Tanzania	19	16	Cooper-Poole (1986)
Malawi	18	14	Watson (1985)
Gabon		14	Mefane & Toung-Mve (1987)
Zambia	15	29	Watts *et al.* (1984)
(rural)	12·5		Hira *et al.* (1982)
	9		Hira *et al.* (1990)
Mozambique	5–15	2–10	Liljestrand *et al.* (1985)
Somalia	3	3	Jama *et al.* (1987a)
Nigeria	3	0·4	Gini *et al.* (1989)
Zimbabwe	0·5		Latif (1981)

awareness and motivation to eradicate STD is an important factor in the fight against STD worldwide.[11]

Epidemiological surveys in selected population groups yield useful data on STD prevalence in the community, of whom antenatal patients are considered as a normal risk group[12] reflecting a group of healthy women of reproductive age.

Specific STDs

Prevalence rates for syphilis in women attending antenatal clinics in some African countries are shown in Table 1. Syphilitic infection in the mother during pregnancy may result in abortion, intra-uterine death, intra-uterine growth retardation and congenital syphilis which will cause death in up to 40% of affected infants. Rates for congenital syphilis are 850/100,000 live births in Lusaka and 3,200/100,000 live births in Addis Ababa.[26,16]

Prevalence rates for *Neisseria gonorrhoeae* and genital chlamydial infection in women attending antenatal clinics are shown in Tables 2 and 3. Gonococcal and chlamydial infection in the mother, frequently asymptomatic, can cause acute salpingitis, puerperal sepsis and ophthalmia neonatorum.

Chlamydial serovars A-C, D-K and LGV are all sexually transmissible, although *Chlamydia trachomatis* D-K and *Lymphogranuloma venereum* 1-3, genital chlamydiae, are normally classified as STD while *C. trachomatis* A-C are not. Genital chlamydiae cause infertility in both male and female, pelvic sepsis, post-abortal and puerperal sepsis, and, in the neonate ophthalmia neonatorum, inclusion conjunctivitis which appears usually in the second week of life, naso-pharyngitis, otitis media and afebrile pneumonia which appear 2 to 3 months after the birth. Genital chlamydiae have replaced *N. gonorrhoeae* as the most

TABLE 2
Gonorrhoea in women attending antenatal clinics

Country	Gonorrhoea (%) Culture	Gonorrhoea (%) Serology	Reference
Cameroon	33*		Ndumbe *et al.* (1992)
(urban)	14		Galega *et al.* (1984)
	25 (PPS) #		Galega *et al.* (1984)
South Africa (urban)	12		Welgemoed *et al.* (1986)
(rural)	6		O'Farrell *et al.* (1989)
Zambia	11		Hira (1986)
Kenya	10		Braddick *et al.* (1990)
	10		Temmerman *et al.* (1988)
	34 (PPS) #		Temmerman *et al.* (1988)
	7		Laga *et al.* (1986)
Ethiopia		10**	Duncan *et al.* (in press)
	9		Perine *et al.* (1980)
	28 (PPS) #		Perine *et al.* (1980)
Gambia	7		Mabey *et al.* (1982)
Malawi	7*		Watson (1985)
Zimbabwe	5 (PN) # #		Mason *et al.* (1989)
	18 (PPS) #		Mason *et al.* (1989)
	2		Weissenberger *et al.* (1977)
Swaziland	4		Meheus *et al.* (1980)
Ghana	3		Bentsi *et al.* (1985)
Nigeria	3		Osoba *et al.* (19874

*Detection by Gonozyme, Abbot Diagnostics.
**Seropositive at titre ⩾1/320 suggestive of current infection (Duncan *et al.* 1991a).
PPS prevalence (%) for symptomatic women with puerperal sepsis.
PN prevalence (%) for asymptomatic postnatal women.

important single aetiological agent of neonatal infections, worldwide, causing up to 32% of all cases.[37]

Maternal herpes simplex virus 2 (HSV2) infection during pregnancy can cause spontaneous abortion, congenital malformations particularly of the central nervous system (CNS), prematurity and neonatal infections of the skin and CNS.

From the prevalence rates of STD in antenatal patients it is clear that STD in Africa is a major problem. Because of the mothers' concern for a healthy baby, screening and treating pregnant women and their husbands/sexual partners is recommended as a first step which will be acceptable to the mothers.[15]

Factors for the transmission of STD

Pilot studies in Addis Ababa showed that 9% of parturient women and 9% of out-patient attenders at the gynaecological out-patient department (GOPD) were culture-positive for *N. gonorrhoeae*.[4] A sero-epidemiological study was therefore established to investigate further the prevalence of STD in clinic attenders in Addis Ababa. Early age at first coitus was shown to be a significant factor for both STD and cervical cancer.[52,53] Early age at first coitus was associated with ethnic group, religion and with origin of residence, those from the countryside being married younger than those in the city. In Ethiopia, at the time the study was carried out the vast majority (over 99%) of women were married for the first time as virgins. Sexual debut therefore occurred within marriage. Early age at first coitus was very significantly associated with income, the poorest being

TABLE 3
C. trachomatis infection in women attending antenatal clinics

Country	Culture (%)	Serology (%)	Reference
South Africa		71	Klugman *et al.* (1991)
	11		O'Farrell *et al.* (1989)
Ethiopia		54*	Duncan *et al.* (1992)
		31**	Duncan *et al.* (1992)
Cameroon	43***		Ndumbe *et al.* (1992)
Algiers		27	Kadi *et al.* (1990)
Nigeria	11		Walker *et al.* (1989)
		10	Darougar *et al.* (1982)
	7		Aladesanmi *et al.* (1989)
Kenya	10		Laga *et al.* (1986)
	8		Braddick *et al.* (1990)
	7 (PN) #		Temmerman *et al.* (1988)
	20 (PPS) # #		Temmerman *et al.* (1988)
Zaire	9		Beaujean *et al.* (1990)
Gabon	8		Leclerc *et al.* (1988)
Gambia	7		Mabey *et al.* (1982)
		35	Mabey *et al.* (1985)
Zimbabwe	6 (PN) #		Mason *et al.* (1989)
	14 (PPS) # #		Mason *et al.* (1989)
Ghana	4		Dreschler *et al.* (1988)
	8 (PPS) # #		Bentsi *et al.* (1985)

*IgG titre ⩾1/16.
**IgG titre ⩾1/64, or IgM ⩾1/8 suggestive of active/present infection (Duncan *et al.* 1992).
***Detection by Chlamidiazyme, Abbott Diagnostics.
PN prevalence rate in asymptomatic healthy postnatal women.
PPS prevalence in women with puerperal sepsis or endometritis.

married much younger than the richest in the community.[8] Early age at first coitus was highly significantly associated with the number of husbands (serial monogamy within marriage as polyandry was not practised) and thus the total number of sexual partners: the earlier the first marriage and hence first coitus, the shorter the duration of that first marriage, the greater likelihood of the marriage ending in divorce, with subsequent remarriage and further divorce taking place, and ultimately the girl running away from home to seek her fortune in the city or drifting into prostitution. In particular, it was notable that those with a stable first marriage to the first husband were rather older at first marriage, while those who had drifted into prostitution were married younger. Almost 25% of the cohort of women first sexually active aged 12 or under drifted into prostitution.[54] Moreover, in countries where widows and divorcees are not supported by social welfare, because of poverty some women have to resort to prostitution to provide for themselves and their children, while students use the same means to pay for their education fees, their books and their clothes. The prevalence rates for STD and cervical cancer, not surprisingly, were far higher in those women who were involved in prostitution than in women still married to their first husband (Figure 1).

Analysis of seropositivity of gonococcal antibody showed 1089/1851 (58·8%) overall seropositive, seropositivity being highest in those with more than five sexual partners (88%), in those involved in prostitution (100% in barmaids), in those who gave a past self-history of having had either gonorrhoea or syphilis, in

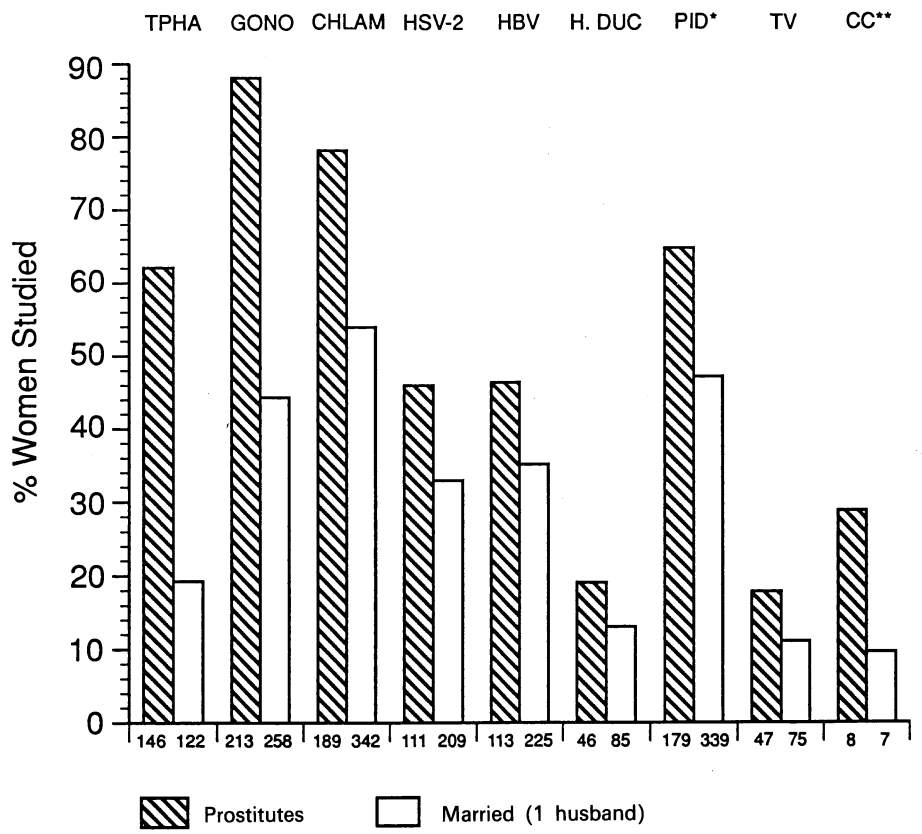

FIGURE 1

Prevalence rates for sexually transmitted disease (determined by serological tests), pelvic inflammatory disease and cervical cancer are shown for women involved in prostitution and women still married to their first sexual partner, their first husband. Women studied were taken from those attending the gynaecological out-patient department, and routine family planning, antenatal and postnatal clinics in Addis Ababa. STD and PID rates are % of the women studied; rates for cervical cancer are /1000 women.

TPHA = serological test for syphilis; Gono = gonococcal antibody test; Chlam = antibodies for *C. trachomatis* D-K and *Lymphogranuloma venereum* 1-3 (genital chlamydiae); HSV 2 = *herpes simplex virus* 2; HBV = hepatitis B virus; H.DUC = *Haemophilus ducreyi*; PID = = pelvic inflammatory disease; TV = *Trichomonas vaginalis* (diagnosed by cytology); CC = cervical cancer (diagnosed clinically or by cervical cytology).

women who attended on account of primary infertility or for family planning advice. The latter two groups had the highest seropositivity (39% and 31% respectively) at titre $\geqslant 1/320$ which is indicative of recent or active gonococcal infection. Asymptomatic antenatal clinic attenders had 43% seropositivity, 10% at titre $\geqslant 1/320$, while 54% other clinic attenders with no clinical evidence of pelvic infection were seropositive, 18% with titre $\geqslant 1/320$: this indicates the asymptomatic nature of many gonococcal infections in women.[9] It has been said 'A promiscuous female pool (PFP) with many silent infections infects a larger number of promiscuous males; these men feed back gonorrhoea into the PFP and may also infect a non-promiscuous secondary contact, usually the wife'.[55,56] It is clear that control of gonorrhoea (STD and all its sequelae) requires greater recognition of the problems by the health services at a government level.[11]

Why is early sexual debut such an important factor for transmission/acquisition of STD? The prepubertal girl and indeed many young teenagers are physically immature: because they are anatomically small and undeveloped sexual intercourse is traumatic. Secondly, the vaginal epithelium which is normally 2–3 cell layers thick in the prepubertal girl only develops a multi-cell layer thickness (approximately 80 cell layers) as a result of oestrogenic stimulation. Progesterone, secreted in response to cyclic ovulation, may not be present within the first two years after the menarche. Progesterone is esential for storage of glycogen in the vaginal epithelium: lactobacilli cause the conversion of glycogen to lactic acid thus creating an anti-bacterial acid milieu in the vagina. Secretory IgA normally only reaches full adult levels by the early twenties and low adult levels by the age of sixteen. Finally there is a behavioural 'male factor': for a young girl to be sexually active usually requires an older, experienced and therefore potentially infected partner.[52]

It is worth noting that similar risk factors for STD transmission in young teenagers also apply to those who practise anal sex, namely (i) anatomical factors—the muscle tone of the anal sphincter which is easily traumatised while the epithelium of the rectum has a single cell layer thickness which is easily torn; (ii) a physiological factor—semen contains collagenase and spermine which damages the basement membrane of colonic mucusa thus allowing increased penetration of pathogenic bacteria and viruses[57] while interfering with the normal colonic function of fluid absorption from faecal matter; (iii) an immunological factor—nitrates taken to aid relaxation of the anal sphincter are immunosuppressive; (iv) a behavioural factor—many of those practising anal sex have multiple partners. One can thus appreciate why it is in countries where anal sex is practised that infection with HIV, HBV and other STD occurs more commonly than with vaginal sex. For most African cultures STD, including HIV, transmission by homosexuals and bisexuals has not been an issue, although 'there can scarcely be a part of the "third world" which is free from adult western homosexuals' [travelling on vacation][58] and in some African languages AIDS is referred to as the white man's disease, while STD is referred to as women's disease. Recent reports indicate that this may change. In an AIDS educational video, street boys orphaned by AIDS are in their own words 'sleeping together as man with man'. Homosexual rape is occurring, as it is worldwide, in penal institutions. Decriminalisation of homosexuality has been promised within the new South African constitution. In western countries, of which Britain is an example, decriminalisation of homosexuality has increased the visibility of the homosexual subculture/homosexuality,[59] and thus the availability of casual promiscuous sexual encounters.[60]

Cervical cancer

Early sexual activity is one of the most important aetiological factors for cervical cancer worldwide. Cervical cancer is numerically the number one cancer of all

developing countries, currently estimated at 369,500 per annum.[61] Global prevalence shows it to be highest in sub-Saharan Africa, Asia, Central and South America. Factors for cervical cancer are early coitus, multiple partners, high parity, male factor and human papilloma virus infection (STD). If it had not been eclipsed by the AIDS pandemic, cervical cancer and the human papilloma virus epidemic would have had far greater recongition and publicity.

HIV

For many developing countries HIV infection is essentially a STD with transmission also through contact with infected blood and transplacentally. Projections show an alarming escalation in the pandemic, particularly in sub-Saharan Africa. 'It has taken the emergence of HIV/AIDS, a fatal STD, to highlight the problems of STD across Africa and the need to understand the epidemiology of these conditions, and to control transmission by all means that are socially and culturally acceptable. Such methods will result not only in control of STD, but of HIV/AIDS in particular'.[15] Education, particularly at school and high school level together with promotion of barrier contraception (condoms) has been the cornerstone of the WHO AIDS Control Programme. It is hence significant that faced with lack of condom use by high school students, recommendations include an urgent need to promote AIDS risk-reducing sexual behaviour among high school students, abstinence from sex until marriage and monogamy with or without marriage (closed heterosexual relationships), along with the use of condoms,[62] or as President Museveni of Uganda said, in 1991: 'In countries like ours, where a mother has to walk twenty miles to get an aspirin for her sick child . . . the practical questions of getting a constant supply of condoms or using them properly may never be resolved. Young people must be taught the values of abstinence and self-control.'

In conclusion this review indicates that STD are the neglected diseases of tropical medicine and require urgent research to evaluate the underlying problems before effective programmes for control can be implemented.

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HYPERGLYCAEMIA IN THE DEVELOPMENT OF CHRONIC COMPLICATIONS OF DIABETES MELLITUS: NO LONGER A QUESTION OF WHETHER, BUT HOW★

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Hyperglycaemia is the hallmark of diabetes mellitus. Indeed it is by measurement of blood glucose that we diagnose and define the condition. In practice raised blood glucose is the biochemical aberration in diabetes which, either by modification of diet or administration of oral hypoglycaemic drugs or insulin injection, is most responsive to therapeutic intervention. Because of the consistency of hyperglycaemia as a finding in untreated diabetes it is natural to speculate that excessive levels of glucose or related sugars are in some way responsible for most, if not all, of the ills which may subsequently befall diabetic patients. Our ability to manipulate the blood glucose towards normal adds attractiveness to this hypothesis, as both the patient and the attending physician are encouraged to believe that their successful therapeutic endeavours, easily demonstrated by simple blood tests, will yield handsome long-term health dividends. Also our realisation that it is almost impossible, in all but a very few patients, to achieve complete normalisation of the blood glucose provides the rationale, and, for the physician, the intellectual consolation, if our best efforts fail to prevent the relentless onslaught of vascular complications.

The question of whether there is a link between hyperglycaemia and the development of complications has, in my opinion, rightly been the burning issue in clinical diabetes since shortly after the discovery of insulin. My contention is that whether the link exists is no longer the appropriate question. Rather, we should be asking how? How does hyperglycaemia lead to the development of complications, and how are we going to prevent it?

Glycated haemoglobin

Why do I feel so confident that the argument about a link between control and complications is over? They key to this, I believe, is glycated haemoglobin. The chemical reaction which we now refer to as glycation—the non-enzymatic linkage between a reducing sugar and a receptive amino acid—was first described, in relation to food proteins by Maillard in 1912.[1] However, the relevance to clinical diabetes mellitus was not recognised until half a century later following the serendipitous finding by Huisman and Dozy that a minor negatively charged haemoglobin component referred to as HbA1c was increased in diabetic patients.[2] This finding was confirmed in several other studies during the 1960s and early 1970s, but it was not until 1976 that Fluckiger and Winterhalter showed that HbA1c is formed *in vitro* when purified haemoglobin is incubated with glucose.[3] This clearly indicated the non-enzymatic nature of the reaction; HbA1c is formed by the adduction of a glucose molecule to the amino-terminal valine of the beta

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