Poisonous Prescriptions

Do Antibiotics Cause Asthma and Diabetes?

By

Dr. Lisa Landymore-Lim

Thank you to those who understood and encouraged…
Finally the journey which began in 1991 is complete…or
Perhaps this is just the beginning…

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Two people are admitted to the casualty department of a hospital suffering from nausea, vomiting and diarrhoea.

One, who ingested mercury, is said to be suffering from poisoning; the other who took an antibiotic, is said to be showing an allergic reaction.

In the first case the blame is put on the chemical, in the second, on the patient.

Lisa Landymore-Lim

"There will inevitably be drug disasters in the future; some will underline how subtle the unwanted effects of drugs can be – and with others it will seem the problem was right under our noses all the time."

Charles Medawar, London 1992.
(Power and Dependence – Social Audit on the Safety of Medicines)

About the Author

Lisa Landymore-Lim graduated from the School of Chemistry and Molecular Sciences, University of Sussex, England, with a First Class Honours degree in Chemistry by Thesis in 1983. Declining an offer of a postgraduate studentship at Cambridge University, England, she remained at Sussex to gain her Doctorate. During that time she received the School Prize for Chemistry and a scholarship from the Swedish Institute to attend the Biomedical Centre, Uppsala, Sweden.

She has worked briefly for the Medical Research Council (MRC) at the National Institute for Medical Research, Mill Hill, London in Peptide Chemistry and at the MRC Dunn Nutrition Unit, Cambridge.

Herald Sun, Friday, August 5, 1994

Scientist blames asthma on drugs

ANTIBIOTICS might cause asthma and insulin-dependant diabetes, a scientist has claimed.

Dr Lisa Landymore-Lim, a British chemist who has specialised in immunology and biomedical chemistry, also claims in her book, *Poisonous Prescriptions*, that some antibiotics are toxic to the ears and can cause hearing loss.

Dr Landymore-Lim came to Australia because of our high asthma.

She says more research is needed and has challenged institutes to compare the antibiotic use of child asthmatics, diabetics and their mothers with that of non-asthmatic and non-diabetic peers.

Dr Landymore-Lim believes they may cause the diseases in susceptible people.

A study she did in 1991 on diabetic children found 50 per cent of the children had been induced as babies and their mothers had had a certain drug during childbirth.

By HELEN CARTER, medical reporter

She said babies' and children's immune systems were immature and their kidneys took longer to excrete chemicals.

"If they have sufficient exposures as a child it could bring on juvenile diabetes," she claimed.

"I believe antibiotics damage the lungs.

"Australians have the highest rate of asthma in the world and take twice as many antibiotics as the Brits, Swedes and the Americans.

"The WA Health Department says there is no doubt the medical profession accepts that exposure to antibiotics during manufacture can cause asthma," she said.

National Asthma Campaign spokesman, Monash University medical lecturer Dr Michael Abramson said he thought it was extremely unlikely.

He said people who were occupationally exposed to powder antibiotics which were inhaled — such as doctors, nurses and manufacturers — could become allergic to antibiotics and some could develop asthma.

But most patients took antibiotics in capsule or syrup form so they were not inhaled.

"She is putting forward a hypothesis but most medicos would be sceptical although perhaps studies should be done," he said.

Dr LANDYMORE-LIM will speak at 8 tonight at the Mervyn Himbury Theological Studies Centre, 50 The Avenue, Parkville.

Country Life

Public health suffers as drug culture plagues us

Australians consume huge amounts of prescription drugs which have failed dismally to remedy our ills. British chemist Lisa Landymore-Lim was at Albany's Residency Museum last week making a photographic catalogue of the history of pharmaceuticals. She spoke to journalist PAT FRASER about how Australians in the past and present have poisoned themselves on prescription and over the counter drugs which cost infinitely less to produce than their retail price. Dr Landymore-Lim has a theory that the drug taking habit is exacting a terrible toll on community health.

PHARMACEUTICAL CONTROVERSY: Lisa Landymore-Lim believes prescription and over the counter medications have dire effects on community health.

These days the image of the 19th century snake oil salesman proffering bogus cure-alls is laughable to all intelligent people.

But a quick look through the pharmaceutical exhibits in Albany's Residency Museum demonstrates how deeply entrenched in the thinking of the day was the practice of seeking an unscientifically tested panacea in a bottle.

For example, vaseline, simple petroleum jelly, was considered a remedy for coughs, colds, croup and diphtheria, while Dr William's Pink Pills would fix the problem of pale people, presumably ones suffering from anything from pernicious anaemia to pale but healthy skin.

Worse still was the fact that doctors routinely prescribed morphine, mercury, arsenic and opium, all of which have side-effects, even causing early death.

But according to graduate of Sussex University in England, Dr Lisa Landymore-Lim, medical science has not progressed much further than the days when deadly narcotics such morphine were prescribed to babies.

Dr Landymore-Lim is about to release a book, Poisonous Prescriptions, in which she examines the effects of modern prescription medicines on community health.

Her findings are not good news, particularly for Australians.

Like the USA, we are rapidly developing into a nation devoid of harmless home-cures found in England, which tend to divert people away from drug consuming.

The consequences of our consumption are every bit as dangerous as last century, except they are less overt and likely to have longer term, and even more disastrous, effects.

It appears medical practitioners are hobbled to the drug companies through a training which teaches them to prescribe drugs, and in turn patients are demanding those drugs.

On top of this drug companies provide funding for research, thereby obfuscating and hampering results about the long term effects which research might otherwise indicate.

Dr Landymore-Lim says it is little wonder that better informed patients are turning more and more to naturopathic cures.

She cites an article published in The Bulletin in 1992 which reveals that Australians are on a drug binge, consuming twice as many antibiotics per capita as Sweden and far more than the USA and Britain.

Australia is out-consuming the USA, considered a major drug-consumer of the world with revenues from the health industry exceeding $360 billion a year, second only to those of the defence industry.

Dr Landymore-Lim notes, several decades ago asthma, diabetes and cancer were serious diseases which struck an unlucky few.

And despite the proliferation of modern pharmaceutical products and medical technology, these health problems are not declining.

"In fact, they seem to be increasing," Dr Landymore-Lim says.

She quotes research from the Wellcome Museum in London where it is claimed that more than 60 per cent of drugs are prescribed unnecessarily.

Most conditions would improve of their own accord, or couldn't be improved with drug therapy, the research suggests.

> ' The fact is dispensing drugs can be a lucrative business '

Dr Landymore-Lim finds it particularly surprising that in Australia, with a warm climate and high standard of living, there is such a high incidence of asthma.

She says this is a case of drugs tending to damage the body's immune system so it becomes less able to cope with infection.

In the UK an incidence of asthma in about four per cent of the population accounts for two million sufferers.

But in Australia with a low population density an incidence of 10 per cent accounts for 1.5 million sufferers.

A disproportionate number among children in both countries suggests an environmental rather than genetic agent.

The same situation applies with the antibiotic, amoxycillin, used to control throat and ear infections.

Children given this drug are known to suffer two to eight times the recurrence of the disease.

The antibiotic upsets the bacterial flora in the child, thereby causing further infection.

Also British research has shown where dispensing doctors were more liberal with prescribing drugs there has been an associated high incidence of disease.

"One would hope that these findings could be attributed to coincidence," Dr Landymore-Lim says.

"But the fact is that dispensing drugs can be a lucrative business.

"For the first 1000 prescriptions dispensed each month by a GP in the UK in 1992, a fee of 1.70 pounds (Sterling) was received."

Dr Landymore-Lim says that in Britain people who have been exposed in their working environment to antibiotics and subsequently develop asthma, may be entitled to compensation.

Then it is little wonder that children, also, may start to cough and wheeze after several exposures to antibiotics.

"Frequently children are given antibiotics as a preventative measure against asthma, especially if they are already coughing a bit," Dr Landymore-Lim says.

"It is not surprising they are already coughing and wheezing because often children are given beconase steroid (beclomethasone) to control asthma which can cause a sore throat or wheezing."

In the USA the vicious cycle of such drug taking has been called the American Death Ceremony.

"It starts with the person taking an aspirin for their headache," Dr Landymore-Lim says.

"After a while the person may need extra aspirin to control the headache which eventually burns a hole in their stomach causing a gastric ulcer.

"That, in turn, may end up in infection requiring penicillin which eventually messes up the immune system — and so the whole cycle keeps repeating itself."

It goes without saying the cost of this problem to the health industry is enormous.

Dr Landymore-Lim is particularly concerned about the prevalence of asthma and diabetes in Australian children.

She believes there is a strong link between overuse of the antibiotic amoxycillin and asthma.

She also implicates antibiotics, barbiturate tranquillisers, oxytocin (hormone used to induce labour) and ergometrine (used to stop postpartum bleeding) in the onset of diabetes.

Some diuretics, such as those often given to young women for the treatment of pre-menstrual water retention, and antihypertensives (drugs used to control high blood pressure) may also cause diabetes.

Dr Landymore-Lim points out that in Britain it takes less than 50 pounds Sterling, about A$240, to make a child diabetic through overuse of prescribed drugs.

"It will cost the British Government half a million pounds per child to treat the child at today's prices — never mind what it will cost 20 or 30 years down the track," she says.

"They are often faced with amputations, kidney problems and infections, so often must take more drugs."

Rather than being considered humanity's best friend, antibiotics could now be considered in a completely different light.

"I had a theory that all these problems were coming from prescribed drugs," Dr Landymore-Lim says.

"The stakes were too high to give up.

"If I'm right in these theories it will be of immense importance because we will be able to stamp out diabetes and asthma."

Report by Pat Fraser in the Country Life section of the Albany Advertiser, 1994. Reproduced courtesy of the Albany Advertiser, Western Australia.

WHAT DOCTORS DON'T TELL YOU

DECEMBER 1994

CONTROL YOUR HEALTH
VOLUME 5, NO. 9

Diabetes has always been considered hereditary. But some new detective work suggests that drugs, particularly antibiotics, could be behind the surge in cases among children.

Diabetes

Possible drug connection

With virtually no solid scientific evidence, diabetes has always been considered hereditary. While researching her doctorate in chemistry, Lisa Lansdymore-Lim decided to study groups of diabetic patients. Her surprising findings—showing a possible link between early-onset diabetes and high exposure to prescription drugs in utero and early childhood—provide early evidence that diabetes could be caused by prescription drugs.

The results of epidemiological studies show tremendous variation in the incidence of diabetes in children internationally. In Hokkaido, Japan, about two of every 100,000 children have diabetes, compared with approximately 30/100,000 in Finland. In the US and Western Europe, the current incidence rate for diabetes is second only to asthma among severe chronic diseases of childhood, with considerable geographical variation. In terms of total numbers, in the UK some 1000 children under the age of 15 years were diagnosed during 1988, whilst it is estimated that in the US, some 22,000 children under the age of 15 years developed diabetes during the three years 1978-1980.

Another factor which points towards environmental agents as the cause is that Japanese children in the US have four times the risk of becoming diabetic as do children in Japan. Jewish and French children in Canada are two to three times more likely to suffer from diabetes than children of the same origin living in their native country.

When I began studying diabetic children attending children's hospitals in the south of England and in Kent, I was surprised to discover that many children had been diagnosed as diabetic before the age of 10.

'A high proportion of diabetic children had been exposed to drugs in the womb.'

This led me to amalgamate all data obtained for diabetics diagnosed before 23 years of age, and to compare the age at which they were diagnosed with the year of onset. What I discovered was a decline in the average age at onset with each successive decade. In the Sixties, the average age of the onset of diabetes was up to 12; in the Eighties, this had dropped to up to the age of four.

This decline in incidence up to the age of four years suggests that there may have been an agent responsible for causing diabetes, to which children were subjected either in utero or around the time of birth.

In my interviews with some 170 mothers of diabetic children during the pilot study I observed the following:

- Many children had suffered from recurring tonsillitis, asthma, prolonged eczema or recurrent exfoliative dermatitis.
- Some mothers had taken certain drugs to prevent miscarriage or morning sickness, or had taken antibiotics to treat infections during pregnancy.
- Some children had always been sickly when compared to other children in the same family, and others had apparently been perfectly healthy before they were diagnosed.

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What Doctors Don't Tell You, 4 Wallace Road, London N1 2PG (071-354-4892) Editor: Lynne McTaggart Office Manager: Diane Wray Order Fulfillment: Jackie Caldwell Editorial Assistant: Dorothy Rothermel Co-publisher: Bryan Hubbert Designer: Clerkenwell Design Group Printed by Prontaprint Press Publisher: The Wallace Press ISSN 1353-1247

Front page of the British publication WHAT DOCTORS DON'T TELL YOU (WDDTY), Vol 5, No. 9 describing the author's concerns in relation to diabetes. Reproduced courtesy of WDDTY.

Antibiotics linked to high asthma rate

By JOANNE COOPER

THE increasing incidence of asthma in Australian children — the world's highest — may be linked to commonly prescribed antibiotics and penicillin, according to a British researcher.

Drugs given to pregnant women and children for common complaints, such as coughing, earaches and chest infections, could induce the early onset of asthma in children who were genetically susceptible, independent researcher Dr Lisa Landymore-Lim said yesterday.

Dr Landymore-Lim also said her three-year study conducted in Britain showed links between prescription drugs and hearing problems and diabetes in children and adults.

She moved back to Perth, where she grew up, in June after being told Australia had the world's highest levels of asthma, with one in four children under five being diagnosed with the disease.

"Pollution is often blamed in Europe, but here there's not much pollution, so it really shows something else must be triggering asthma attacks," she said.

She noticed these side effects of prescription drugs during a survey of the effects of smoking during pregnancy and the benefits of breast-feeding in 1991. Dr Landymore-Lim has since studied the backgrounds of children who developed diseases while young.

"Wheeziness was often reported following several exposures to antibiotics, amoxycillin (a penicillin) and erythromycin in particular," she said.

"And the younger the age at which antibiotics were regularly prescribed, the younger the age at which asthmatic symptoms were reported."

She criticised doctors for not making patients aware of possible side effects of drugs, and of over-prescribing.

Report by Joanne Cooper, The Australian, Monday January 3rd, 1994.

Diabetes data alarms

● Lisa Landymore-Lim is surprised at WA's level of child diabetes.

BRITISH scientist Lisa Landymore-Lim is surprised at the high rate of childhood diabetes in WA.

But more alarmingly, her research indicates that common antibiotics could trigger the disease.

Dr Landymore-Lim, of Subiaco, is in the final stages of writing a book, *Poisonous Prescriptions*.

The title speaks for itself — the drugs she refers to include penicillin-based antibiotics commonly prescribed for simple colds and viruses.

"WA has one of the highest rates of child diabetes in the world," Dr Landymore-Lim said. "Twenty-two children in 100,000 suffer from it."

She said Australians took twice as many antibiotics as Swedes and more than Britons and Americans.

Dr Landymore-Lim had been doing research in England on the effect of chemicals in cigarette smoke.

"No-one has ever come across the diabetes link — it's a nightmare," she said.

"After speaking to about 170 mothers, I found that quite a few who had diabetic children had had a chemical history, either during pregnancy or labour, or their children had at an early age.

"I think there is a pattern with these drugs.

"I can't prove anything as I need a very large study, but have presented my data in the book."

Dr Landymore-Lim visited WA on a visa, but has had that extended so she can continue her study into the connection between chemicals and illness.

"Children would need several exposures and there's probably a genetical component as well," she said.

"But if it's accepted antibiotics can cause asthma, why not diabetes?

"The public need to make enough noise, and I will have to do further studies."

Dr Landymore-Lim said that one exposure to antibiotics would not cause diabetes.

"It would depend on the child's age and the number of exposures."

Dr Landymore-Lim is trying to raise sponsorship for her book of drug related data, which will be released in the U.S., U.K. and Australia.

She is still looking for data. Write to PO Box 1237, Subiaco, 6008.

Reproduced courtesy of the News Chronicle, Western Australia, February 16, 1994

8 Health Observer, September 1994

OPINION • OPINION • OPINION • OPINION • OPIN

ARE WE HELPING THE ASTHMA EPIDEMIC?

By scientist and author of Poisonous Prescriptions, Dr. Lisa Landymore-Lim (BSc., DPhil)

The usual official line to concerns raised about a chemical that may have disastrous consequences on health, is that monitoring systems are operational and there is not a problem. A study of the history of medicine when limbs were once amputated and cleaned with the same sponge that was sitting in a bucket of water and had been used on several previous patients; the common use of mercury, arsenic, strychnine and opium before it was realised that they caused more health problems than they cured; the addictions caused by morphine which was even used for babies (*Mrs Winslow's Soothing Syrup*) who were teething; and blindness in premature babies who were given oxygen therapy, reveals that since scientists and doctors are not infallible, iatrogenic (doctor-induced) health problems can result from medical practices.

In view of the current international epidemics of diabetes and asthma, for which there have been no definitive causes identified, I am unable to uncover a sound reason for precluding the possibility that prescription drugs are a major factor in the aetiology of both diseases. Genetic pre-disposition which is perhaps thought to be a predominant factor, is not necessarily a cause, as may be exemplified by smoking and lung cancer. The genetic susceptibility of an individual may play a role, but in the absence of tobacco smoke as a *trigger* agent, there is far less risk of the development of lung cancer.

My hypothesis which suggests that medicinal drugs are to blame for the bulk ofdiabetes and asthma in industrialised countries, evolved following a pilot-study to look at whether smoking during pregnancy

possibly being instrumental in the onset of diabetes. The response from companies questioned, was that no long-term follow-up studies of babies or children exposed had ever been undertaken. Therefore, there is every possibility that some toxic effects of the drugs have gone undetected.

farmers have been known to develop asthma from giving their cows penicillin injections; chickbreeders have become asthmatic from handling feed laced with antibiotics; and workers in the pharmaceutical industry manufacturing antibiotics (eg. spiramycin, erythromycin, cephalosporins, ampicillin,

diabetes association, would ideally need information on total lifetime exposure to all drugs. Incidentally, the antibiotic streptozotocin and chemical alloxan are used routinely in laboratories internationally to make animals diabetic. Examination of the structure of alloxan shows that it is structurally very similar to the drug phenobarbitone. Poisonous Prescriptions explains how these drugs may destroy the zinc containing beta-cells of the pancreas.

In the course of studying the health records of diabetic children, records of non-diabetic children were studied for comparison. As a scientist, with no prior knowledge of asthma, the pattern that I saw caused me to suspect that antibiotics were causing some children to start coughing, develop respiratory problems and finally

cause asthma."

From my experience, even doctors, pharmacists and drug information officers of pharmaceutical companies are unaware of this association. Some groups consider this asthma to be "occupational asthma" and either fail to see the connection, or have chosen to ignore what could be a vital clue in trying to discover the cause of our present epidemics of asthma. As I explain in Poisonous Prescriptions, I believe that we have situation similar to asbestos, which was once considered to be an occupational disease. A representative of the Health Department of W.A. when asked whether he had considered that antibiotics might be the cause of the present epidemic, was sufficiently open-minded to say that "It's possible".

Information currently available and the response of learned bodies, have

Health Observer, Western Australia, 1994. Distributed to hospitals and health workers.

Drugs 'may prove bitter pill'

By Medical Writer
BARRY HAILSTONE

Are widely prescribed drugs causing more illnesses than they cure? That's the question all Australians should be asking, says British researcher Dr Lisa Landymore-Lim.

The campaigner blames inappropriate and indiscriminate drug prescribing for the increasing incidences of illnesses, particularly asthma and diabetes.

"In many instances the risks outweigh the benefits," she said in Adelaide yesterday.

She said she believed the increasing incidence — the world's highest — of asthma in Australian children could be linked to the practice of freely prescribing common antibiotics, particularly penicillin, for non life-threatening conditions such as sore throats, colds and influenza.

It is a theory she developed after researching the toxic effects of drugs with a British Medical Research Council unit in Cambridge.

Similarly, she said little-analysed research findings also indicated that oxytocin — a drug used to initiate labor in pregnant women — had the ability to trigger diabetes in susceptible infants.

Dr Landymore-Lim said there was enough questionable evidence in medical research findings on adverse drug actions to warrant large-scale epidemiological research projects to highlight "poisonous prescriptions".

Australians were avid but ill-informed consumers of drugs who ought to consider that chemicals such as mercury, arsenic, strychnine and morphine were once commonly prescribed until many years later it was recognised that they had probably been responsible for more injury than death, she said.

"Since ampicillin, amoxycillin and erythromycin are known to be toxic to ears it should be of concern to all parents and patients to learn that these drugs which may be given for ear infections may actually cause damage to the ear which is not immediately apparent," she said.

Dr Landymore-Lim, 36, who is a self-funded campaigner for drug reform, has written a book *Poisonous Prescriptions*, which calls on health authorities to establish a government task force to look at diseases caused by drugs.

She will give a public lecture tomorrow night at the Australian National (railways) building, 1 Richmond Rd, Keswick. Tickets can be booked by calling 250 1506.

Dr Landymore-Lim: "questionable evidence." Picture: CAMPBELL BROC

Report by Barry Hailstone, reproduced courtesy of the Adelaide Advertiser, Australia 1994.

UK researcher warns on over-use of drugs

By MAIRI BARTON

COMMONLY prescribed drugs can be linked to the high rate of asthma in Australian children, says a British researcher who visited Dunsborough last week.

Dr Lisa Landymore-Lim said asthma had spread in the past decade because some antibiotics and penicillin made people prone to the disease.

Australia had the world's highest asthma rate — with one in four children under five diagnosed with the disease.

The 1990 Busselton Health Survey figures showed Busselton adults had a higher asthma risk than the total Australian population — 16 per cent compared with a national figure of 10 per cent.

Dr Landymore—Lim, an independent researcher who was in Dunsborough on a camp for disabled children, criticised doctors for over-prescribing.

She said drugs were not tested enough for side-effects before they were given to people and patients

Dr Landymore-Lim

were not made aware of possible side-effects.

People also were conditioned to think only a prescription could cure them when minor conditions often cleared up on their own.

In 1992, 57 West Australians died of asthma, up 11 on the 1991 figure, according to figures released last week.

Dr Landymore-Lim said doctors often blamed the illness for side-effects caused by antibiotics.

"Very often within two weeks of taking a drug kids seem to cough more, have higher temperatures and develop wheezing," she said.

"Most of these drugs wouldn't be allowed on the market if they were discovered today because there are so many side-effects," she said.

She said it could be years before the full extent of harm caused by prescribed drugs was known.

"Doctors used arsenic, opium and mercury on patients for years before it was discovered they were harmful," she said.

"The problem with Western medicine is that doctors are taught that the way to treat a disease is with drugs and they are not taught about side-effects."

The Australian Medical Association's WA branch president Dr Keith Woollard did not dismiss the claims but said they needed to be backed by scientific fact.

He advised people to see their doctor if they were concerned about the possible effects of any drugs they were taking.

"The most common opinion over recent years is that house dust mite causes asthma," Dr Woollard said.

"But there are a lot of people looking for other reasons. If Dr Landymore-Lim has some good scientific fact and research then we would be interested in seeing it."

Report by Mairi Barton, reproduced courtesy of the Busselton-Margaret Times, Australia, Jan 13 1994.

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FOREWARD

Although the human body is remarkably resilient, it can't be expected to endure a continual onslaught of toxic chemicals without showing some signs of poisoning. Good health starts from pre-conception and any chemicals to which parents are exposed e.g. tobacco smoke, alcohol and drugs, can all play a part in the future quality of health of a developing foetus.

Once foetal growth has commenced, this tiny developing human being is often exposed to any chemicals to which his or her mother is exposed. This includes many toxic chemicals in processed foods, pesticides on and in fresh fruit and vegetables, antibiotics and drugs in poultry and meat together with any chemicals from prescription and over-the-counter (OTC) drugs that she may take. No OTC or prescription drug has been studied to show that it has no long-term adverse effects on the foetus and therefore its safe use during pregnancy must be suspect.

Having survived pregnancy, the foetus is usually exposed to a variety of drugs during labour. This may arise as a result of the mother being administered pethidine, an epidural, caesarean, induction drugs or drugs to prevent bleeding post-delivery. Whilst breast-feeding is to be preferred over formula-feeding, even the mother who is breast-feeding may be unsuspectingly dosing her child with chemicals, if she herself is in receipt of drugs, perhaps antibiotics for mastitis.

The usually healthy newborn is then often subjected to a variety of chemicals through the use of vaccinations. Vaccinations are

chemical preparations that may contain the chemicals mercury, formaldehyde (used to preserve corpses), phenol (carcinogen) and biological material from diseased humans and animals. Repeated exposures, which are sometimes a legal requirement, are likely during what is a delicate and important maturation phase, especially for the immune system.

It should therefore come as no surprise to learn that newborn and infants frequently suffer from minor problems, which lead to further chemical assault through the ingestion of pharmaceutical preparations, most frequently antibiotics. However, the introduction of all these chemicals, ostensibly to protect and improve health, seems to parallel our current epidemics of allergies, asthma, diabetes and hearing problems.

To my knowledge Poisonous Prescriptions, first published in 1994, was the first publication to point the finger at antibiotics for being responsible for our current epidemics of asthma and the only one with data to suggest that commonly prescribed drugs may be implicated in the onset of diabetes. As can be seen from the media articles on my website, I was documented in 1994 as claiming that antibiotics were, in my opinion, causing ear problems in children, deafness, asthma and diabetes. I sought the help of the media in an attempt to inform the public of the possible dangers of drugs and to stimulate debate and further research.

Self-publication of Poisonous Prescriptions became the route I was forced to take as attempts to gain the interest of the medical profession in the UK were unsuccessful. Apart from a few medically qualified people in drug companies and the department of health in the UK, who understood and appreciated the validity of my concerns, those Professors of Child Health who were in a position to initiate

further research, literally scoffed at my suggestions. To quote one professor, “Millions are spent on research into diabetes annually. None has shown that antibiotics cause diabetes!” I knew that it was pointless to reply “But Sir, no one has yet asked the question!”

My dilemma was what to do if I couldn’t get the medical profession to listen. In a desperate attempt to gain access to more records of diabetic children to study, I enlisted the help of local diabetic groups and The Daily Telegraph, UK. My reason for this was to see whether similar patterns of drug exposure existed in other groups in different parts of the country, as this would possibly support my claims or suggest that they might be unfounded. Whilst the numbers of children’s records gained in this way are small, very interesting data was obtained, which only increased my belief that the possible role of drugs in diabetes and asthma causation needed to be explored.

Ideally of course, one would do extensive studies to test one’s hypothesis. However in the absence of an opportunity to conduct further research, I decided that I had sufficient information to warrant raising public awareness about the adverse effects of drugs.

I managed to self-publish Poisonous Prescriptions in Australia in 1994, yet my attempts to continue this research even in an unpaid capacity in Australia were also unsuccessful. One Professor of Child Health, when interviewing me, asked me what my interests were. His face fell as I explained my research and concerns. When he spoke, his considered reply was “Here at ….Hospital, we are funded by the drug companies to give drugs to pregnant women, to determine whether this prevents asthma in their child.” With that he knew that I understood that he either would not or could not have me in his research group.

In 1996, the Wellington Asthma Research Group at the Wellington School of Medicine, New Zealand reported that antibiotic use in infancy may be associated with an increased risk of developing asthma. They reported that asthmatic children had more exposures to antibiotics and the younger the age of exposure to antibiotics, the younger the age at which children became asthmatic.

Another study, from the United Kingdom published in 2002, showed that mothers who took more than three antibiotics during pregnancy were more likely to have asthmatic children. More recently, an American study, funded by the National Institute of Health, reported in November 2002 that children who had antibiotic exposure were more likely to become asthmatic.

The medical profession already accepts that exposure to antibiotics during manufacture, through the inhalation of antibiotic dust, can cause asthma. This however is considered to be occupationally related. My research suggests that exposure to antibiotics arising from ingestion, may also confer a risk of asthma. In 2005 the British Medical Journal (editorial) reported that asthma in young children in Victoria, Australia had fallen since 1994. The reason for this is unknown. However, as the article “Scientist blames asthma on drugs” (Sun Herald, Victoria) shows, I was giving public talks warning the public of the dangers of antibiotics at this time. Prime News TV, Canberra, in the nation’s capitol, also ran an interview with myself as did other newspapers and radio stations nationally.

Not long ago, mercury was commonly used in medicine in a variety of compounds; even mercury cyanide was a medicinal preparation! However, today there are regulations restricting the levels of mercury vapour allowed in the workplace, and mercury compounds are rarely used in medicinal preparations. This is because

it is now appreciated that exposure via any route confers a risk of poisoning. After all, poison is poison. The warning in Poisonous Prescriptions is that we have merely supplemented other poisonous medicines for mercury and cyanide and just as in former centuries, we may be unwittingly poisoning ourselves when in search for a cure.

Patient expectations and our quick-fix mentality toward illness are partly to blame for doctors “doling out antibiotics like Halloween candy” (Michael Castleman, USA), despite research showing that the majority of ailments would resolve of their own accord. American research has shown that 81% of ear problems go away if left untreated. There is even greater irony in this unnecessary prescribing, when one learns that the antibiotics usually prescribed actually damage the ear and increase the likelihood of a recurrence of the problem!

It has always been my aim to make Poisonous Prescriptions available internationally. Fortunately the Australian Immigration Department considered the book to be ‘in the interests of Australia’, and when my application to immigrate was rejected in London, an appeal in Australia was successful. My application which was considered in London was rejected as I had no income, since I was ‘self-financing’! However, after eliciting the support of the media and submission of the book that had finally been published, I was successful in my appeal heard in Australia. I will always be grateful to those who encouraged me to appeal, since being successful enabled me to spread the word in Australia about the side-effects of drugs. I shall never forget those 100 people who helped with publishing costs by buying a copy of the book before it was even published. This is truly the ‘Spirit of Australia’!

Unfortunately, since everything has been self-financed, it has taken me a further twelve years to take the book overseas. Apart from minor alterations and for the first time, inclusion of images and media articles, the bulk of the book remains unchanged. Whilst this may date some statistics within, the story remains the same and even more relevant today as our dependence on drugs has increased.

This book was considered by some to be ahead of its time in 1994, and it probably still is, but perhaps the time for greater exposure was not right until now. Following increased concerns about antibiotic exposure over the past decade, due to MRSA and microbial resistance to antibiotics, perhaps only now will the majority listen. With public interest, we will be able to determine whether our blind acceptance of this pharmaceutical era and antibiotics, is responsible for what is possibly the greatest drug disaster to date.

One however should be aware that it is easy to provide information which can prevent the public from attributing any credibility to a story. For example, in 1994 the media obtained the following responses from Dr. Keith Wollard (president of the Western Australian branch of the Australian Medical Association) and Dr Michael Abramson, (National Asthma Campaign spokesman and Monash University medical lecturer), in answer to my concerns: “if she has any interesting results we would like to see them” and “..people who were occupationally exposed to powder antibiotics which were inhaled – such as doctors, nurses and manufacturers – could become allergic to antibiotics and some could develop asthma. But most patients took antibiotics in capsules or syrup form so they were not inhaled. She is putting forward a hypothesis but most medicos would be sceptical although perhaps studies should be done”, they said respectively.

When I did approach the AMA in Perth, W. Australia, to try to give a talk and show them my results, after repeated delay, they responded with a 'no', saying that it was hard enough for them to get doctors interested in their medical talks they put on. I also spoke to a senior executive of the Asthma Foundation, who after a couple of visits, somewhat uncomfortably replied they could not help, as most of their funding came from pharmaceutical companies.

The task therefore may not be easy, for there may be forces opposed to discovering the truth. These will include patients who do not want to hear that drugs they willingly took are responsible for their disability, doctors who will not want to feel instrumental in having made their patients ill and parents who may feel guilty for unwittingly being party to their child's illness or death. The commercial stakes too are high. Even during the 1930's the discovery, by a brilliant scientist Royal Rife in San Diego, USA, that certain frequencies were capable of destroying pathogenic bacteria and cancer in the human body were initially greeted by the medical profession with great acclaim, until medico-pharmaceutical cartels decided that his discoveries posed too great a threat to the health of their businesses. For it is only with diseases these corporations flourish.

Today, the medical profession can no longer argue that my concerns have no merit. For in 2005 in the UK, Study Team for Early Life Asthma Research (STELAR), with six professors and many doctors/scientists from around the UK, was funded to try to understand the factors involved in the development of asthma. The study will examine the following:

• *Prenatal factors: maternal health, nutrition during pregnancy, drugs taken during pregnancy, mother's smoking history;*

- *Perinatal factors: gestation, birth weight, neonatal problems, feeding history;*
- *Early childhood exposures: home environment – damp, moulds, overcrowding, environmental tobacco smoke, socio-economic factors, childhood nutrition, pet ownership, place of residence;*
- *Other health outcomes: symptoms in early childhood, features of other allergic disorders, visits to GPs and / hospital and medication use.*

Reproduced from the website www.asthma.org.uk

Readers of Poisonous Prescriptions will see that each of the above categories under investigation is covered in this book.

It is time for the public to take responsibility and initiative for their health. Despite pharmaceutical corporations being at the top of the wealthiest businesses in the world, it is not inconceivable that they too could crumble in the wake of mass class actions.

1

Introduction

Given that a poison is any substance that when introduced into or absorbed by the body injures health or destroys life, most of today's pharmaceutical preparations, because of their harmful effects, may be labelled poisonous. *Poisonous Prescriptions* is intended to provide the reader with a brief insight into the history of medicine in relation to the use of drugs and their hidden dangers. It includes information about certain popular drugs in use today in the UK, USA, Australia and other major industrialized countries, and includes those commonly prescribed for babies and young children. It suggests that exposure to currently prescribed drugs may involve the user, and in the case of pregnant women, the foetus as well, in greater risks than are currently appreciated.

Medical practices, which often have not been thoroughly researched, historically evolve into trends. For example, it is hard to believe that not so long ago leeches occupied a place on the pharmacist's shelf and were used in the conviction that draining blood from the patient would affect a cure. Today, it is common knowledge that blood-letting (Figures 1.1 and 1.2) is not likely to improve a patient's chances of a speedy recovery and may even result in death. These days, medical practice is mainly chemically oriented with the use of pharmaceutical preparations. Unfortunately, the pharmaceutical companies understandably place their marketing emphasis on the beneficial effects of a drug and not on the potentially damaging ones. Despite animal testing and clinical trials, a drug is rarely tested to ensure that it does not cause a fatal disease many years after exposure.

Fig. 1.1 One form of blood-letting knife used to inflict stab wounds to patients. Engraved bone handle, origin USA.

Moreover, the inappropriateness of animal testing of drugs can be better appreciated when one considers the quite distinct animal and human food chains. Some wild boars for example can tolerate manioc roots which contain arsenic, a poison which is extremely toxic to humans.

It is my opinion that the science of drug therapy is still in its infancy, since information about drugs is still obtained, essentially, by trial and error. And as in years gone by, there are many harmful drugs in use that will continue to be available until sufficient concern is expressed or they cease to be commercially viable. Sadly, it is the latter event which is likely to result in their faster withdrawal from the marketplace.

Fig. 1.2 Doctor directing a nurse to inflict multiple cuts to a patient according to the Broussais system, in an attempt to cure him. This system was popular in the nineteenth century (Reproduced with permission from the Wellcome Library).

Pharmaceutical Preparations - the dangers

Each year, worldwide, there is enormous public and private expenditure on prescription and over-the-counter health preparations and remedies, in the widespread belief that they are solely beneficial.

However, this is not necessarily so - some of these drugs pose a *serious* threat to health both in the short and long-term.

Is there any way to convince people that pharmaceutical preparations including such apparently harmless items as mouthwashes, analgesics, decongestants and antibiotic throat lozenges are in fact media through which they expose themselves to what are potent chemicals? Chemicals that under laboratory standards would often carry the warning TOXIC or BIOHAZARD, and can initiate a *subtle* downward spiral of deteriorating health.

Prescription drugs are all too often considered a part of normal everyday life. In the United Kingdom around 1990, over a million prescriptions were issued daily. But these medicinal preparations contain chemicals which often have their origins in plant, insect, animal or organic matter, some of which may have been used rather unwisely in the past to try to cure a variety of ailments. In the UK a little more than a hundred years ago, chemicals such as strychnine, arsenic and opium were readily obtainable from a tradesman or pharmacy. Although natural in origin, these highly potent, toxic chemicals have the power to kill humans following the ingestion of a very small dose. Despite formerly being freely available and used for medicinal purposes for *hundreds* of years, these drugs are now rarely used, following the realisation that they are toxic and may in the past, have done more harm than good.

Nevertheless, due to the explosive growth of the pharmaceutical industry during the twentieth century, we now have a much greater variety of potentially toxic chemicals available for medicinal purposes. Whereas in the earlier half of the twentieth century we might have been forgiven for not recognising the potentially damaging nature of

these chemicals, even today, we still seem to be deluded into thinking that drugs obtained with or without a prescription are entirely beneficial and without risk.

Fig. 1.3 Here I am after a capital dose of STRYCHNINE!

“You need not be at all uneasy my dear Madam. If anything unpleasant should occur, you have the satisfaction at least of knowing that your husband has been POISONED according to act of parliament and I need not say what a pretty widow you’ll make.” (Reproduced with permission from the Wellcome Library)

Allowed onto the market place by legislation and prescribed by the medical profession, sometimes in response to demands for a pill

or potion as an easier option than a change in diet or life-style, medicinal drugs have become ubiquitous. However, we, the consumers, have been insufficiently educated as to their possible undesirable effects. As commercial enterprises concerned with profit, drug companies are in the business of selling chemicals that appear to alleviate or eliminate health problems.

To this end, significant revenue is invested each year by drug companies to promote their products to the medical profession and the public, understandably with the emphasis on the perceived benefits and not on the risks associated with exposure to the drug.

In Australia, which in 1993 was reported as being on a "drug binge", an estimated $10,000 of financial incentives was invested in each doctor annually. More recently, country doctors in the USA have been reported as being in receipt of $10,000 annually from pharmaceutical companies, by way of incentives in the form of cash, trips and entertainment. Research has shown that this does indeed influence their judgement.

The profuse and sometimes indiscriminate prescribing of drugs greatly increases the likelihood of unnecessary suffering for patients and their families due to unforeseen side effects. This risk is unlikely to be recognised unless and until we accept that systems designed to protect the public cannot be 100% effective. Medical research conducted before a drug is made available for widespread use, cannot encompass every variable. The time is ripe, in this Green era, for consumers and practitioners to ask whether all the drugs prescribed are necessary and can be relied upon to have benefits that outweigh the risks involved in taking them.

Since the initial clinical experimentation of penicillin in 1941 involving one man with a life-threatening infection, many industrialized societies have now reached a situation over the past half century where synthetically modified penicillin with greater potency is taken for comparatively minor ailments such as coughs, colds, sore throats and tonsillitis. Penicillins have been readily accepted as having life-saving properties without adequate study to determine whether these minor conditions may in fact be aggravated or even caused by penicillins. The list of 'side-effects' (which I consider would be more accurately described as toxic effects) of penicillins, can affect the body both internally and externally. For example, dermatitis (eczema) and blood disorders can appear in the short-term. However, it is highly probable that there are similar and other serious health problems that may only become apparent many months after a single or repeated exposure. It is due to the time-lag between exposure and the onset of symptoms that result in this failure of recognition of association.

From that short-term clinical trial of penicillin on one adult patient in 1941, individuals of all ages in many populations may now be said to be unwittingly taking part in what is no more than an undesigned, unmonitored long-term trial frequently involving multiple exposure to one or more drugs.

The faith that the medical profession and the public demonstrate in prescribed drugs, due in part to the elaborate marketing strategies of pharmaceutical corporations, is ill-deserved. Drugs can save a life, that is indisputable, but there must be recognition that drugs are also capable of poisoning an individual and shortening life.

For centuries, minerals and plants have been used as a source of chemicals for medicinal preparations, and cases of their toxic effects

have been documented for just as long. Although it may now seem improbable that earlier in the twentieth century we were using opium and morphine, two highly toxic and addictive drugs, in preparations even for babies, we seem not to have learnt our lesson. Consequently, our children are still being exposed to a variety of drugs before, during and after birth, without sufficient questioning of their toxic effects.

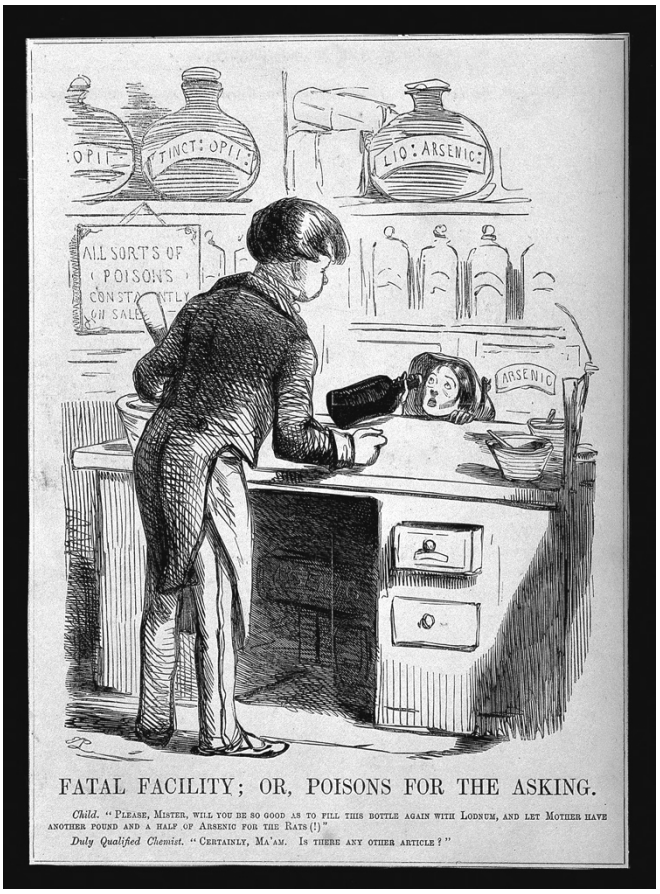


Fig. 1.4 ‘Poisons for the Asking’. Pharmacist dispenses arsenic to a child. (Reproduced with permission from the Wellcome Library).

Drug Legislation and Clinical Trials

The legislative aspects of the testing and use of pharmaceutical products is also a cause for concern. For years, men and women exposed themselves to drugs without legislative protection. Even in the developed world today, legislation may only be introduced following injury to health and/or loss of life from headline-grabbing drug disasters. Indeed, some drugs introduced since the implementation of the Medicines Act in 1968 in the UK, following in the wake of the thalidomide disaster, are typically still not tested for adverse effects which may become apparent only after several courses of treatment, with health problems occurring many months, or even years later. That this situation should persist, in spite of the potential of drugs to exert such adverse effects, which has already been demonstrated and documented in both human and animal studies, must be a cause for alarm.

The design of drug trials too, has sometimes been revealed to be inappropriate for the intended use of the drug. For example, the most vulnerable sectors of the population: foetuses, babies, children and the elderly, are typically not the subject of clinical trials. Also, the follow-up period following exposure to the drug is often very short, of the order of days in some instances, with comparisons frequently being made with a group on another drug for the same condition. Some studies on the efficacy of a drug involving the use of a placebo, a substance given as medicine that has no intrinsic value, have revealed that a significant proportion of the placebo patients recover from their illness even in the *absence* of drug therapy.

As tragedies with drugs such as thalidomide, which resulted in the birth of deformed babies, and Opren which killed arthritic patients have shown, scientists and the medical profession are *not* infallible. Indeed, in many areas of research there is often controversy resulting

from conflicting results. In medicine, it may take many years before the real dangers to health following exposure to a particular drug are recognised and accepted. Although the thalidomide and Opren tragedies may now seem unique, remote, and unlikely to be repeated in today's technological era, the standards of clinical trials that exist today are insufficiently demanding to prevent the recurrence of drug related injuries.

Drugs and the Medical Profession

Fig. 1.6 “MERCURY and his ADVOCATES DEFEATED, or VEGETABLE INTRENCHMENT.” Cartoon depicting doctors protesting at the successful sales of a natural liquid that cured health problems. This was Isaac Swainson’s Velnos Syrup. (Reproduced with permission from the Wellcome Library).

Fig. 1.5 Centuries ago people recognised that medicinal preparations killed patients. This extract from a play shows a butcher threatening a doctor for killing his wife with medicines. (Reproduced with permission from the Wellcome Library).

Pressure for a doctor to prescribe a drug often comes directly from parents and patients, as in industrialized societies we expect not to have to endure the inconvenience of even minor illnesses or discomfort and to be able to remedy any life-threatening conditions. Today, pills are seen by many as a panacea. We have grown to rely on drugs to provide us with a readily available and usually inexpensive means of quickly alleviating suffering and sometimes inconvenience. But perhaps we should stop to consider the evolution

of medical practices and the use of chemicals in medicine, before we blindly entrust our minds and bodies to foreign chemical agents, about which relatively little is known.

The practice of wiping the wounds of several surgical patients with the *same* sponge that was commonplace during the nineteenth century appals us now and is considered to be totally unacceptable, but it may well be analogous to some of the prescribing practices in use today.

Patients and the medical profession in industrialized societies, trained to receive and prescribe drugs respectively for the majority of illnesses, have developed an increasing prejudice in favour of drug use and appear to condone the absence of warnings of the possible toxic effects of the drugs in many prescription medicines dispensed at present. We may have been more honest during the earlier part of the twentieth century, when some medicine bottles carried the warning 'POISON'. In fact, the Australian drug and poisons schedule states in the section Principles of Scheduling: "Poisons for therapeutic use (drugs) are included in Schedules 2, 3 4 and 8..."!

As old habits die hard, particularly in medicine, doctors are unlikely to change their prescribing habits until there are concrete reasons to do so. Unfortunately by then, countless other unsuspecting patients may have fallen victim to drug exposure. British records show that in the past, the medical profession was outraged by the successful sales of an alternative natural cure that was not prescribed by the profession (Fig. 1.6).

Medical Research

Our present knowledge of the adverse effects that drugs may have is probably the equivalent to that of technology in the Dark Ages.

It is a truism that what is not looked for is rarely discovered except by chance. Whilst the majority of medical research, funded and therefore influenced to a large extent by pharmaceutical corporations, concentrates on understanding the mechanism of disease processes and ways of combating them, usually with the use of pharmaceutical products, advances in understanding the origin of disease will inevitably take second place.

For example, diabetes and asthma, two of the most frequently occurring chronic diseases of childhood and of epidemic proportions in adults in many countries, are known in some instances to be drug related. But to my knowledge, no research has been conducted to examine whether the present epidemic that exists in many Western societies may have more to do with drug exposure than is currently recognised. The information required to answer these questions is out there, principally in the vast volume of patient records in hospitals and doctor's surgeries. These sources are a *gold-mine,* and can provide data to relate the drugs prescribed to patients with the diseases and health problems which they may have suffered after exposure. What is now required, is direct interest by patients, parents, doctors and politicians in what that material contains.

2

A Brief History of the Uses of Medicine

"Géronte (patient): It seems to me you are locating them wrongly: the heart is on the left and the liver is on the right.

Sganarelle (doctor): Yes, in the old days that was so, but we have changed all that, and we now practice medicine by a completely new method."

Moliere: "Le médicin malgré lui" *(Doctor in spite of himself)*

In recent years, we have been made aware of the way in which we have polluted our bodies, through the increasing emphasis on the contamination of our environment. The range of pollutants is wide: from high lead levels in school playgrounds, radioactive discharge from power stations, heavy metals from chemical plants, raised nitrate levels in our drinking water from agricultural fertilizers, pesticides sprayed on crops, to food additives that are deliberately introduced in the manufacture of processed food to give it a longer shelf-life or to render it more palatable.

We now realize that chemical pollutants can no longer be ignored. Whilst technology and medicine have helped to provide phenomenal improvements to the quality of life during the past century, the downside is that we have also radically altered and in some cases irreparably damaged our environment, upon which we are dependent for survival. Part of this thoughtless destruction has been the result of chemical pollution. Fertilizers, pesticides, unpurified liquid discharge from industrial sites, food stabilizers and additives all contain chemicals which

enter the environment and food chain or are directly consumed. What about our medicines? These too are *chemicals* to which we directly expose ourselves and about which we know very little, in terms of their adverse effects on our health.

We must realize that we may be irreparably damaging our health and that of forthcoming generations, by exposing ourselves and our children, often unnecessarily, to prescription and over-the-counter drugs. For the majority of us, prescription drugs may be seen as providing the possibility of improved health and longevity. Our faith in the drugs we take is bolstered by the fact they are authorized by government legislation, which is ostensibly intended to protect the population, and prescribed by doctors, who are seen as healers. But these drugs have lethal toxic effects when given in certain concentrations, which will vary according to the individual. In view of the known side-effects which exist for every drug, it is perhaps surprising and of concern that many children and adults are often exposed to such hazards for relatively *minor* conditions that do not threaten life.

Despite medicinal compounds having been in use for hundreds of years, with many appearing in ancient herbal publications, the first British pharmacopoeia produced by the Royal College of Physicians did not appear until 1618. Just as the British National Formulary the principal drug reference book for doctors in the UK today is revised twice yearly to publicize the removal and addition of drugs, together with any alteration in the recommended dosage, the original pharmacopoeias were also regularly updated. The information they contained was obtained by *trial and error* and their updating was dependent on further information becoming available as more of the population was exposed to various drugs.

A British medicine chest from 1745 could contain some 158 preparations; including balsams, elixirs, extracts, gums, oils, powders, salts, spirits, tinctures and ointments. Many of the preparations were derived from plants such as saffron, anise, clove, cinnamon, ginger, cinchona bark and lavender. Table 2.1 lists some of the chemicals used in medicine that were freely available even into the early years of the twentieth century. Some were often administered by the woman of the house in mixtures based on her own recipes.

Arsenic

Arsenic tri-oxide and arsenic tri-iodide were formerly used internally as solutions or externally as ointments in the treatment of various skin diseases. Symptoms of poisoning included *constriction of the throat, severe gastric pain, vomiting, profuse watery or bloody diarrhoea, muscle aching and weakness, sore mouth and throat, inflammation of the conjunctiva, convulsions*, *coma and death*. Patients often develop intense *thirst* and *muscle cramps*. Arsenic is *toxic to the bone marrow* and produces a wide range of *blood disorders* including *leucopenia, thrombocytopenia* and various other *anaemias*. The therapeutic use of inorganic arsenical preparations is no longer recommended.

Mercury

Mercury forms the basic constituent of several medicinal preparations and among its adverse effects are *nausea, vomiting, diarrhoea, bloody diarrhoea, kidney damage, mental deterioration, dermatitis, loosening of teeth* and it is *toxic to the respiratory system*. Children have in the past been given mercury in teething powders and ointments. It may take years to eliminate mercury from the brain. The hazards associated with mercury generally outweigh any therapeutic benefit and its clinical use has largely been abandoned.

Strychnine

Strychnine is an alkaloid obtained from seeds of the species Strychnos. It is used in several preparations to stimulate the central nervous system and was formerly used as a bitter and analeptic. Signs of poisoning can include *tremors, twitching, kidney failure,* stiffness of the face and legs, painful *convulsions* in which the body becomes arched backwards with the arms and legs extended and the feet turned inward, the jaw is rigidly clamped and contraction of the facial muscles produces a characteristic grinning expression. Few patients survive more than five episodes of convulsions, death usually occurring due to *respiratory arrest.* Fatalities have occurred with doses of 10mg or less. It is now mainly used as a rodenticide or as a fox or mole poison.

Morphine

Side-effects may include *nausea, vomiting, constipation, drowsiness, confusion, difficulty in micturition, dry mouth, sweating, palpitations, urticaria* and *pruritis, anaphylaxis, hypotension, respiratory depression and deepening coma.* It was freely available in the UK in the early 1900s in Mrs Winslow's Soothing Syrup for babies who were teething. It has also been used for acute gastritis and vomiting of pregnancy. The euphoric activity of morphine and similar compounds has fed to their abuse. As morphine was the only effective pain killer before aspirin, many became addicted.

Opium

Opium is obtained from the unripe capsules of the plant Papaver Somniferum, and contains some 9% morphine amongst other alkaloids. It has analgesic and narcotic actions due mainly to its morphine content. Its adverse effects are as for morphine.

Table 2.1 Drugs freely available during the early twentieth century.

As may be seen from some of the exhibits in the Wellcome Museum of the History of Medicine, London, some of the preparations available at the beginning of the twentieth century carried the warning POISON. However, since potent health-damaging prescription and over-the-counter drugs are also available *today,* are we perhaps being deceived by the absence of a poison warning on today's medicines?

In 1941, a new substance called penicillin was introduced into medicine. Having displayed marvellous antibacterial properties during a trial involving a policeman in Oxford, who was suffering from a severe life-threatening infection, it was very quickly put into widespread use partly due to the demands of the Allied forces during the Second World War. Although a British discovery, initially it was principally manufactured in the USA and within years, *tons* of the drug had been consumed.

Later, with increasing chemical knowledge, the plants, moulds and fungi from which many medicinal chemicals with antibiotic properties were extracted, were subjected to chemical analyses in an effort to identity their major therapeutic constituents. The next logical progression was to make these compounds artificially rather than extract them from organic matter, usually a more costly process. Having made the chemical in a laboratory, chemists were then given the task of synthesizing the same basic chemical with subtle differences, in the hope that a drug with even greater efficacious properties would be created.

Fig. 2.1 Glass pharmacy jar of strychnine nitrate used in medicines.

Fig. 2.2 Workers engaged in the production of arsenic for medicinal purposes. (Reproduced with permission from the Wellcome Library).

In today's highly competitive and commercialised marketplace, where new drugs may be patented, thereby giving the manufacturers a monopoly over the compound for some 10-15 years, continuous efforts and resources are deployed into research and development by drug companies to create new compounds. Many of the compounds however, often with identical *basic* chemical structures have similar properties. These are consequently known as Me-Too drugs and have been known to provoke criticism as to whether they are really necessary. The creation of a similar product however, can provide a pharmaceutical company with an opportunity to employ a different marketing slant designed to capture a share of the market currently enjoyed by its rivals.

Pharmaceutical companies, producing products which often alleviate suffering and save lives, are nevertheless commercial enterprises whose goal is to create profit. If even half the cost of developing a new drug was used to try to discover the cause of the disease which the drug is designed to cure; there would surely be less demand for pharmaceutical products. Clearly this would not be commercially attractive to the drug companies. Today, many types of household appliances and non-pharmaceutical products are subject to safety tests and often have to meet certain safety standards in an attempt to reduce injury to consumers. What of our medicines and drugs?

Some forty to fifty years ago, there were very few demands made on a company prior to the introduction of a new drug to the marketplace. An information officer from a major drug company in the UK commented to me: *"In those days, the drug simply came on to the market"*. However soon after the introduction of penicillin, for example, it was discovered it was not without side-effects.

> "Allergic reactions to penicillin were recognised as a serious problem since 1949, and its use became more restrained. Other forms of penicillin have been developed since the 1960s and other antibiotics have been extracted from different moulds. Unwanted effects, and the increase in resistant bacteria, have led to attempts to control the use of antibiotics more effectively."
> **(Exhibition Case, The Wellcome Museum of the History of Medicine, Science Museum, London, 1992.)**

Some thirty years later however, information from the Department of Healh in the UK, reveals that the number of prescriptions for many antibiotics has escalated. Statistics from many other countries show similar increases. In addition, with the introduction of formulations for children, antibiotic therapy has become commonplace with even babies and infants being routinely prescribed drugs for conditions that would in the past have remained untreated *without* any injury to health. Our experience of penicillins and many other antibiotics, is limited to approximately fifty years. This is a relatively short period when we consider the time it has often taken in the past for the medical profession to recognise and accept there is a problem with a drug.

Many drugs, even after centuries of use in some cases, have come to be recognised for their serious toxic potential and consequently have been withdrawn from use. In the UK, during the latter half of the twentieth century, hundreds of drugs have either been withdrawn or have had their product license revoked. Unfortunately, due to the Official Secrets Act, the reasons for the withdrawal of a drug may not be made public, with the result that many individuals may have been victims of harmful drugs without realizing it. It often takes mankind many years to realize the real dangers and flaws in

some of his discoveries and creations. It seems very possible, that time will show we have been too facile in our acceptance of penicillin and other drugs as beneficial agents, as long-term side-effects become apparent.

In the 17th century, opium could be bought over the counter and was taken as a remedy principally for *headaches.* We have progressed since that time in our understanding of the dangers of drug use, but perhaps too slowly in comparison to the rate of growth of the pharmaceutical industry.

In the UK, the Committee on the Safety of Medicines (CSM) established in 1972 following the Medicines Act of 1968, in the wake of the thalidomide disaster, now 'controls' the use of medicines and is responsible for monitoring adverse drug reactions. The CSM has been criticized however, for being somewhat ineffectual because of weaknesses in the system. For example, judgments are made by the Committee based on information concerning toxicity of a drug provided by the drug company. Members of the CSM have at the same time, also acted as consultants paid by drug companies, despite the obvious conflict of interest! However the ultimate responsibility for reporting adverse drug reactions once the drug enters clinical use, lies with doctors, who can only make such a report if an adverse reaction is suspected. Unfortunately, as may be seen from clinical records presented in later chapters, adverse reactions are frequently unrecognized.

Unless sufficiently alert to the possibility of untoward reactions to drugs in their patients, doctors may be prone to miss even the most common side-effects, especially when the drug has been on the market for many years. Probable penicillin rashes for example, from my research experience have been diagnosed as being of unknown origin; possibly

measles or German measles. The more difficult adverse drug reaction to detect is obviously one which is *insidious* and which requires several exposures before any clinically detectable symptom is apparent. If the time-lag between exposure and side-effect is more than a few days, it is *very* unlikely to be detected. Additionally, if it usually requires many exposures, perhaps one of the last things a doctor would suspect is malignancy in a drug that seems to have been satisfactorily prescribed to many other patients, some of whom have had repeated courses.

The fact that patients may present with a disease process as a result of former drug exposure some years after drug therapy, makes it even more unlikely that a correlation between the drug and the disease will be suspected. Especially if there are already *theories* regarding agents responsible for a disease. Doctors are unlikely to detect something that they are not on the lookout for. In the UK, eighty percent of doctors have never made an adverse drug-reaction report, and not unnaturally, most would not even be on the lookout for adverse reactions from drugs prescribed by them for many years. Sadly, it may only be when babies, with lower body mass and immature organs and sometimes less efficient drug excretion rates, are given drugs which are apparently beneficial to adults, that their potentially disastrous consequences may become evident.

This naturally calls into question the design of clinical trials based on the monitoring of patients who use the drug in the days following its introduction for clinical use. An information officer of a major pharmaceutical company told me that in the UK, before the existence of the CSM, drugs were not controlled by *any* legislation and were simply made available for sale. Drugs that had been in use for many years at the time before the introduction of the CSM were usually granted a 'Product License of Right' *without* any additional tests,

unless there had been substantial reports of serious side-effects. Most drugs therefore received approval without any further testing.

Although clinical trials today might be expected to have stringent requirements, they have been known to be poorly designed. As will be discussed later, these studies often do not sufficiently embrace the various possibilities for economic reasons and perhaps because this might result in the reporting of a higher incidence of adverse reactions, which would be unwelcome to the drug manufacturers. For example, photosensitivity, (an abnormal degree of sensitivity of the skin to sunlight) which may occur following exposure to one of many drugs and may cause painful blistering of the skin, would not be detected as an adverse reaction, if during clinical trials the drug is primarily given to older, less mobile patients during the autumn and winter months, in areas where there is little sunshine. Some recent victims of photosensitivity following drug exposure in the UK have been forced to lead nocturnal lifestyles to avoid sunlight.

As visitors walk round the exhibits of The Wellcome Museum of the History of Medicine, in the Science Museum, London, the Orthopaedics Exhibit Case T27, is a somber reminder of just *one* of the casualties of drug exposure. It is to be hoped that in years to come, we will not see an additional showcase beside T27, containing inhalers and nebulizers used in the treatment of asthma, and a range of syringes, blood and urine test strips, glucometers, insulin pumps and implants that have been developed over the years for use by diabetics.

Appliances for 'Thalidomide' Victims

In 1960-61 a number of children whose mothers had been given the drug Thalidomide were born with congenital deformities. The children had phocomelia

> (the hands or feet attached directly to the trunk) and amelia (the absence of limbs). Extensive research has been carried out to develop orthopaedic appliances for these children.
> **(Exhibit Case T27, Wellcome Museum of the History of Medicine, Science Museum, London, 1992).**

Imagining a similar showcase might enable one to appreciate the self-perpetuation of the ‘sickness’ industry. That is, iatrogenic disease creates a multi-billion dollar industry by creating a demand for doctors, nurses, hospitals, health insurance, drugs, laboratory tests, imaging tests such as X-rays, CT and MRI, medical consumables and so on. Each of these has an impact on the economy. If doctors were instead paid for having healthy patients, it is likely we would have a healthier society, instead of one manipulated by market forces.

3

Drug Therapy and Health

"On the appearance of any new drug an interesting cycle of events may often be observed. A trickle of favourable reports develops into a stream, and the drug then becomes fashionable. Then the stream of favourable reports dries, and accidents claim attention. The drug falls into relative disrepute, and its use may even be abandoned..."

British Medical Journal, 1956.

No one likes bad news, but we can learn from mistakes. Scientists are sometimes tempted to report findings that will support their concepts or hypotheses, but one can often learn more and make more important discoveries by attaching at least as much importance to those results which are unexpected and do not support the hypothesis being tested. Physicians too must not allow their current understanding of a disease to prejudice them against new suggestions of disease causation, particularly when the cause has not been unequivocally established.

Most drugs have probably been responsible for damaging health or shortening life at some time. As the population in many industrialized countries, especially children, has become increasingly exposed to chemicals used in medicine since the Second World War, we should not overlook the possibility that some of our growing health problems are the result of earlier drug exposure.

Diabetes for example, has been considered (without much scientific basis) for many years to be predominantly an inherited disorder. But how can one then explain the tremendous increases in incidence in children in many industrialized countries such as the UK, USA and Australia during the past 20 years? This explosive increase is most unlikely to be due entirely to hereditary factors. In the words of a mother with two diabetic children and no family history of diabetes: *"it must be something we're doing to ourselves"*.

There is substantial evidence to show that some drugs and chemicals can cause diabetes. Unfortunately, to my knowledge, the exposure of diabetics to drugs in the years between conception and the diagnosis of diabetes has never been examined in depth, to identify the full range of drugs which can cause diabetes. Perhaps this has something to do with the medical profession's reluctance to question its practices, and typically to consider any disorder to be a problem that stems from the constitution of the patient.

For example, people who experienced difficulty in withdrawing from tranquillizers were for decades incorrectly considered to be dependent-prone. The problem was perceived as being caused not by the drug, but by the patient. As a result of this, countless lives were destroyed as patients became addicted to these drugs, many of them receiving increasing doses and combinations of drugs in an attempt to subdue the physical and psychotic side-effects.

Typically, whenever it has been suggested that a particular drug may have some unforeseen serious side-effects, there has always been a strong lobby by the drug companies and medical profession to refute the claim. This is understandable, since no reasonable person, least of all a doctor, would wish to be instrumental in causing a health

problem. But iatrogenic diseases and health problems have been in existence for centuries and continue to be a problem.

Apart from diabetes in children, there are also alarming increases in other childhood health problems in many countries. In the UK, there has been a tremendous increase in the incidence of childhood cancers this century, and roughly a two-fold increase in childhood disorders such as deafness (temporary and permanent) during the 1980's - 1990's. Children in the UK during the 1990's were *ten* times more likely to become asthmatic than children ten years previously. Similar steep increases have been seen in the USA, New Zealand and other westernised countries. Unfortunately, attention appears to be focused on the management of these problems, rather than on efforts to discover the underlying causes. Asthma is considered unpreventable, despite the fact that the recent and dramatic increases in its incidence are consistent with the theory that *environmental factors* are implicated.

It seems to me, that certain health conditions are still too easily accepted as being generally inherited or virally induced, without adequate proof. Both patients and doctors tend to reach out for a ready-to-hand reason to explain why a particular patient should be afflicted. Where environmental agents have been targeted as causative in the onset of childhood diabetes, no suggestions as to specific sources have been forthcoming. Although some families may be considered to be genetically susceptible to a disease, exposure to an environmental agent may be required as a trigger. Conversely, individuals who are not genetically susceptible are not necessarily without risk of the disease. With this in mind, it is important to realize that not everyone who ingests the same dose of a toxic substance will exhibit the same adverse effects in the same magnitude.

Nevertheless, given the substance in the required concentration, *all* will be affected in some adverse manner.

We should realize that if a drug kills one person in 10,000, a doctor in the UK for example, with a general practitioner's limited practice population of 2,000 patients is statistically very unlikely to come across such a case. In Western Australia, which has at least three times as many doctors for the same number of patients as the UK, a doctor would be even less likely to anticipate lethal side-effects from a drug that is being prescribed.

The fact that clinical trials have not exposed any potential problems with a drug is not a guarantee of its safety. An obvious flaw in a clinical trial is that the number of 'volunteers', often recruited by financial enticement, is usually relatively small and composed of young adults, a section of the population in which the harmful effects of any drug are less likely to be exposed. This is despite the fact that the drug may eventually be given to babies and the elderly. In 2003, I was told that some individuals staying at hostels in Edinburgh, Scotland, were currently earning about £1000 for participating in pharmaceutical trials lasting 2-4 weeks.

Added to the complex variables which may cause an individual to suffer adverse effects, is that it may take several courses of the drug or a time-lag of many years, before the body finally shows signs of any disease. This is well illustrated by lung cancer caused by smoking, as many smokers only show clinical signs of disease many years *after* ceasing to smoke.

Exposure to antibiotics is known to cause asthma in 'occupational' situations such as the pharmaceutical industry. This is recognised by the British Government which provides financial compensation for

victims. It is my opinion that it is highly probable that individuals who take medicines containing antibiotics, are also at risk. Considering the varied and serious side-effects of antibiotics, perhaps our current epidemics of adult and childhood health problems should be expected in the wake of our increasing exposure to antibiotics, particularly amongst the young.

One's initial response to suggestions that the safety of drugs is suspect might be "*But these drugs have been tested and any dangers would have been discovered*". Unfortunately, if one examines the standards of clinical trials and legislation expecting to be assured of protection from any untoward effects, one would be dreadfully disappointed. Often the numbers involved in clinical trials are small and the design of the trials is such that the drug will be shown in a favourable light. Another shortcoming is that volunteers are frequently only kept under surveillance for a very brief period often after a single course. Consequently, any adverse effects appearing after the study period will not be detected. In defence of the existing legislation regulating clinical trials, one member of the CSM concerned with adverse reactions to antibiotics, expressed his view to me that "clinical trials with immense variables are impossible to regulate".

Often, the toxic effects of many substances may only become apparent once the body has been sufficiently exposed to the chemical. In other words, the effects may only become apparent once the individual has had sufficient exposure causing significant damage resulting in clinically apparent symptoms. Despite the profusion of prescribing that has existed for some groups of drugs such as antibiotics, I know of no research which examines the long-term effects of *multiple* exposures over several years, with a follow-up period of many years after the last exposure. This can mean only one thing: we cannot rule out the possibility that these drugs will adversely

affect our health in either the short or long-term. The fact is a disease process or health problem, related to the drug exposure, may reveal itself much later.

Too much secrecy has shrouded the medical profession for too long and there is a lack of mechanisms by which it can be made accountable. Doctors will argue their patients' privacy is paramount and that knowledge of certain facts would only confuse or worry the patient or aggravate the patient's condition, although most patients would like to be told about their treatment and are quite capable of understanding basic medical facts. It may not be unfair to say, that in some cases, patients who question their treatment are regarded as impertinent.

I know of a doctor in the UK who insisted that hormone replacement therapy which her patient had been receiving for some five years, could not be in any way responsible for her depression. If the patient had been given the opportunity to lean across her doctor's desk and look up the side-effects of her drug in the British National Formulary (BNF), she would have read the following:

> *Side-effects:* nausea and vomiting, weight gain, breast enlargement and tenderness, withdrawal bleeding, sodium retention with oedema and hypertension, changes of liver function, jaundice, thrombosis, rashes and chloasma, *depression,* endometrial carcinoma in postmenopausal women.

Even if the chances that depression would occur were remote, the patient should have been made aware that it *might* occur. The doctor's denial of any possible link between the drug and her patient's depression caused unnecessary self-doubt in an already emotionally fragile patient and meant that she continued the sedative,

anti-psychotic drug therapy which she had been prescribed for her depression. Later, through independent counselling, she was made aware of the possible reasons for her current physical and emotional symptoms and her new doctor was only too ready to reduce her dose of the hormone with the intention of eventually stopping the therapy altogether. The patient had apparently been receiving a higher dosage than necessary, for which there was no explanation.

As patients are exposing themselves to risks through taking drugs, surely they should be given more information about the products they are taking. The granting of *informed consent* by a patient to receive treatment raises the issue of a patient's right to be informed. In the UK, only recently have patients been granted legal access to their medical records, and even then, only to records since autumn 1991, unless their doctor agrees to release earlier records.

In Australia, despite Government usually being responsible for at least 85% of the cost of a consultation with a doctor through the Medicare system, there is at present no legal right of access by patients to their medical records. Surely, as it is the patient's own health and treatment which the records discuss, automatic access to *complete* medical records is a basic right and essential in the advent of suspected drug injury.

A receptive mind, that does not dismiss new ideas without adequate cause is essential to scientific progress. Unfortunately, in today's profit-oriented society of corporations and professional bodies, receptive minds seem to be found predominantly amongst the consumers and independent, often self-financed organisations who despite their limited resources, will bring their concerns to the attention of the public in an attempt to change things for the better.

Professional bodies of long-standing are understandably very sensitive to criticism and reluctant to change. Medical practices have altered radically over the centuries, but still the time taken to investigate current procedures and implement change has resulted in unnecessary damage to health and even loss of life. There is insufficient publicity concerning drug trials. Also, research which attempts to investigate possibly harmful procedures or drugs, is usually conducted without the public being aware this is taking place.

When an expectant mother is assured by her doctor that the drug that she takes during pregnancy is safe, she is often being misled. For most drugs, it is frequently stated in pharmacopoeias that either the affect on the foetus has not been investigated or that no report of adverse effects has been received. This however, can result in the unfortunate and probably inaccurate perception that the drug constitutes no risk to the unborn foetus.

Drugs resulting in dreadful consequences such as the birth of malformed babies as in the case of thalidomide will inevitably be exposed. However, less likely to be detected are drugs which have no outward effects on the newborn, but which may result in a disease several years after birth. If it has long been accepted, even without hard evidence, that a disease is inherited then possible drug involvement is even less likely to ever be suspected. Further difficulties in identifying harmful drugs may arise if the effects occur only when the drug is taken at a particular stage during pregnancy, as in the case of thalidomide. Thalidomide was a prime example of how timing of exposure to a drug can be crucial: it sometimes produced deformities when taken between the third and eighth week, but if a woman took a single dose on the fortieth day of her pregnancy, the baby was almost guaranteed to be deformed.

In summary, consumers who expose themselves and/or their children to medicinal preparations would do well to remember that:

Prescription and over-the-counter medicines and health remedies, whether synthetic or naturally occurring hormones or compounds, are chemical entities, and exposure to them always confers an element of risk.

Potent drugs are often prescribed unnecessarily for minor ailments many of which would clear up of their own accord. The human body's immune defence system is usually the best line of defence against infection and drugs can have a damaging effect on it. Consequently, not only may a drug be taken unnecessarily, but it may make the body more susceptible to and less capable of combating future infection. There have been reports that HIV and meningitis sufferers have had multiple exposures to antibiotics prior to diagnosis.

There is also the possibility that although drug therapy may alleviate a condition in the short-term, a body organ may be damaged in the process leading to a recurrence of the same condition at a later date. This in turn, could trigger a further prescription of the drug by the unsuspecting doctor.
The past couple of generations of children in industrialized countries have experienced a tremendous and repeated exposure to chemicals in the form of medicines, particularly antibiotics, the effect of which has never been studied.

Some drugs used during pregnancy and labour have never been tested for the long-term effects they may have on the mother or her baby, despite assurances usually being given as to their absolute safety.

Some clinical trials may have a bias in their design which enables the drug to be reported in a favourable light. Many trials have been known to have been inappropriately designed, with volunteers taking part frequently not being representative of the age group most likely to be exposed to the drug.

In essence, we should realize that drugs come and go, and drug testing is continuous. New and sometimes unwelcome information about authorised drugs in current use is still being collected from patients. Concerns during the 1990's regarding the safety of vitamin K injections in newborn babies; the possibility of Creutzfeldt-Jakob disease (CJD, which causes sudden onset dementia and death, with an incubation period of up to 25 years) occurring in infertile patients who were treated with human pituitary hormones gathered from human corpses between 1967 - 1985; breast implants affecting women *and* their breast-fed babies, and exposure to benomyl (a pesticide used in the UK, which is suspected as the cause of children being born without any eyes), should instil in us the realisation that any chemicals used on a routine basis, may later be discovered to have serious adverse effects on our health.

4

Toxic Effects of Selected Drugs in Common Use

This is the age of safe surgery and of dangerous medicine.

Medici TC and Fonatana A, Zurich, 1977

The aim of this chapter is to emphasize that drugs are chemicals, and to highlight the toxic effects of some commonly prescribed drugs in the developed world today. Following exposure to a drug, one is not only at risk of adverse effects of the drug itself, but also of *other* chemicals which may be formed from the drug, due to chemical reactions which take place within the body.

The drugs reviewed in this chapter (Table 4.1) are those which are commonly bought or prescribed for children and adults and are referred to in later chapters. Chemical names are given together with the trade name by which the drug may be more commonly known. The chemical structures of the drugs shown should be regarded as pictorial representations which are *not* essential to the understanding of their action or the information in this book. They have been included to illustrate the similarity of some drugs which in part accounts for their similar toxic effects.

The science of chemistry is basic to our understanding of life and like most other sciences has developed its own shorthand. For example, oxygen that we depend on for survival consists of two oxygen atoms bound together and is written in chemical shorthand as

0_2. Water, which consists of two hydrogen atoms bonded to an oxygen atom, is written as H_2O. In brief, in chemical structural formulae, C stands for an atom of carbon, H for hydrogen, 0 for oxygen, S for sulphur, and R, R_1 and R_2 for groups of atoms which are unspecified. The hexagonal ring with an inner circle is the symbol for benzene which may also be written as C_6H_6.

Chemical Name	**Trade Name**
Acetaminophen	Paracetamol
Amoxycillin	Amoxil
Ampicillin	Penbritin
Acetylsalicylic acid	Aspirin
Beclomethasone	Becotide
Cefaclor	Distaclor
Cephadroxil	Baxan
Cephalexin	Keflex, Ceporex
Chloramphenicol	Choloromycetin
Co-trimoxazole	Septrin, Bactrim
Dicyclomine hydrochloride	Merbentyl
Erythromycin	Erythroped
Promethazine hydrochloride	Phenergan
Salbutamol	Ventolin

Table 4.1 Drugs reviewed in this chapter.

ACETAMINOPHEN (Paracetamol)

Acetaminophen is commonly known as paracetamol (Fig. 4.1).

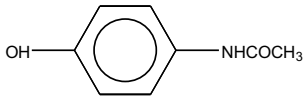


Figure 4.1 Chemical structural formula of acetaminophen.

History

Paracetamol belongs to the so-called coal tar analgesics. It is similar in structure to acetanilide (Fig. 4.2) which was introduced into medicine in 1886. However, after the discovery of its excessive toxicity, the search began for similar compounds which were less toxic. One of the apparently more successful compounds was phenacetin (Fig. 4.3), until it was implicated in analgesic-abuse neuropathy. Acetaminophen, another member of this group of drugs was introduced into medicine in 1893, but only gained popularity after 1949 when it was recognised as the active metabolite of phenacetin and acetanilide.

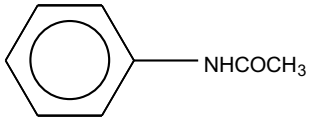


Figure 4.2 Chemical structural formulae of acetanilide.

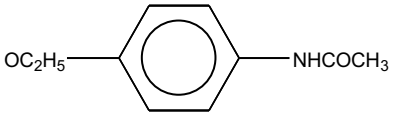


Figure 4.3 Chemical structural formula of phenacetin.

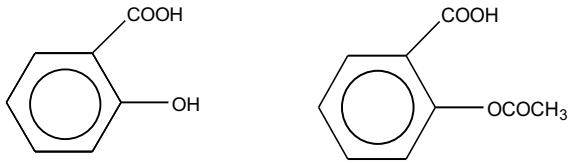
Side-effects

Side-effects of paracetamol are listed as being rare and mild but can include rashes, blood disorders, acute pancreatitis, liver damage following overdosage; young adolescents reported to have taken doses within the recommended levels are known to have died. Toxic levels can sometimes arise when the drug is taken during periods of reduced exertion, as the body may be less efficient at detoxifying chemicals which consequently allows them to reach higher concentrations in the blood. As with other drugs, the long-term effects of repeated exposures have never yet been studied. Such studies

would seem to be appropriate in an age when adults, children and babies may frequently consume paracetamol for pain relief.

ACETYLSALICYLIC ACID (Aspirin)

Acetylsalicylic acid commonly known as aspirin may be made from salicylic acid (Fig. 4.4).



Salicylic acid Acetylsalicylic acid

Figure 4.4 Chemical structural formulae of salicylic acid and acetylsalicylic acid.

History

Salicylic acid which is found in the oil from wintergreen and other plants can be chemically modified to produce acetylsalicylic acid, commonly known as aspirin which was first introduced in 1899. By the early years of the twentieth century, its antipyretic, anti-inflammatory and analgesic actions were known because of information obtained from patients taking the drug.

Side-effects

Salicylic acid is so irritating that it can only be used externally. Its ability to destroy epithelial cells renders it useful for the treatment of warts, corns and fungal infections, since it causes tissue cells to swell, soften and desquamate. Aspirin is a derivative of salicylic acid that may be used systemically. However it can adversely affect the gastrointestinal system causing nausea and vomiting, gastric

ulceration, irritation, erosion or bleeding and exacerbation of peptic ulcer symptoms (heartburn, dyspepsia). It may also adversely affect the liver and kidney and prolong the clotting time of blood.

Despite the number of years that aspirin has been available, it has only been in recent years due to fears of links with a rare disease known as Reye's syndrome (involving severe hepatic injury and encephalopathy) the use of aspirin in children under twelve years of age is no longer recommended. This is in stark contrast to former years when it was probably the most popular analgesic for children.

The labelling of aspirin as a possible risk for the development of Reye's Syndrome, which in one study revealed a 33-40% fatality when taken by children during influenza or chickenpox, was first proposed in 1981 by the Centres for Disease Control, USA. However, no such labelling appeared until 1986, during which time it has been estimated that 1470 deaths of children in the USA, which were avoidable, had occurred.

AMOXYCILLIN (Amoxil)

Amoxycillin (Fig. 4.5) is an antibiotic with the basic penicillin structure shown in Fig. 4.6.

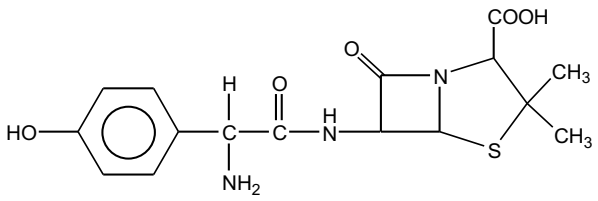


Figure 4.5 Chemical structural formula of amoxycillin.

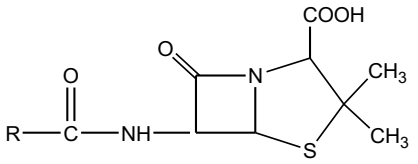


Figure 4.6 Chemical structural formula of the *basic* penicillin nucleus. R is chemical short-hand for a group of unspecified atoms.

History

Amoxycillin, an extremely popular antibiotic, was synthesized by chemists looking to alter the structure of penicillin in an attempt to create other penicillins which would perhaps be more effective, or have wider therapeutic scope. Modifications to the basic penicillin to create amoxycillin, were found to make the drug less susceptible to cleavage by enzymes and to confer upon it different antibacterial and pharmacological properties. For example, amoxycillin administered orally is far better absorbed than most other penicillins, and as a result reaches approximately *twice* the concentration in the blood stream and other body fluids than an equivalent dose of some other penicillin such as ampicillin.

Amoxycillin was launched in the UK in 1972. Amoxil for children is produced by Bencard, a subsidiary of SmithKline Beecham formed following the amalgamation of Smith Kline (an American company) and the British owned Beechams. Sales of the drug since its launch have escalated and amoxycillin is today one of the most commonly prescribed antibiotics for adults and children.

Side-effects

Due to their basic structural similarity, different penicillins have *similar* side-effects which can include:

Skin rashes of all types: scarlatiniform, urticarial, vesicular, morbiliform, bullous eruptions. Contact dermatitis has been observed in pharmacists, nurses and physicians who prepare penicillin solutions. More severe reactions are exfoliative dermatitis and exudative multiforme.

"The most serious hypersensitivity reactions are angioedema and *anaphylaxis.* Angioedema with marked swelling of the lips, tongue, face, and periorbital tissues, frequently accompanied by *asthmatic* breathing and 'giant hives' has been observed after *topical, oral,* or *systemic* administration of penicillins of *various* types."
(Goodman and Gilman's, The Pharmacological Basis of Therapeutics)

About 1:100,000 patients treated with penicillins die from anaphylaxis. It has been estimated there are at least 300 deaths per year in the UK due to this complication of therapy. Death has even been known to occur following the installation of a very small quantity between skin layers, for the purpose of testing for the presence of hypersensitivity.

The clinical pictures of anaphylaxis that develop vary in severity; the most dramatic is sudden, *severe hypotension* and *rapid death.* In other cases, *bronchoconstriction* with severe *asthma,* or *abdominal pain, nausea* and *vomiting,* or *extreme weakness* and fall in blood pressure, or *diarrhoea* and purpuric *skin eruptions* can occur.

Serum sickness varies from mild *fever, rash,* and *leucopenia* to severe arthralgia or *arthritis,* purpura, lymphadenopathy, splenomegaly, mental changes, ECG abnormalities

suggestive of myocarditis, generalized oedema, albuminuria and haematuria. This reaction may not occur until one or two weeks *after* the administration of the drug has been stopped. Reversible *neutropenia* and *arrestation of bone marrow maturation* may occur.

Fever may be the only evidence of reaction to a penicillin.

Eosinophilia and *interstitial nephritis* with blood, albumin, renal cell and other casts appearing in the urine; biopsy has revealed tubular *damage to the kidney.*

These clinical symptoms should be recalled when reading later chapters which show individual drug exposure profiles of children.

Amoxycillin is more rapidly and completely absorbed from the gastrointestinal tract than ampicillin. Peak concentration in plasma is *22.5 times* greater than for ampicillin after oral administration of the same dose. Food does not interfere with absorption. While the half-life of amoxycillin in plasma is similar to ampicillin, effective concentrations of orally administered amoxycillin are detectable in plasma for twice as long as with ampicillin, again because of the more complete absorption.

AMPICILLIN

The structure of ampicillin (Fig. 4.7) as can be seen by comparison with Fig. 4.5 is identical to amoxycillin apart from the lack of an oxygen and hydrogen atom which forms an alcohol (OH group) on the benzene ring.

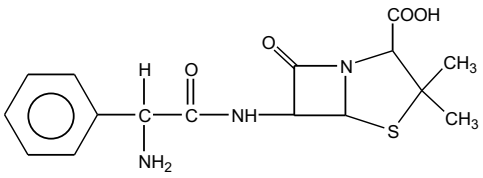


Figure 4.7 Chemical structural formula of ampicillin.

History

Ampicillin was launched in 1961 and is prescribed for conditions similar to those for which amoxycillin is used. Ampicillin for children, which may take the form of sweetened syrup, has been marketed under the name Penbritin by the former British company Beechams who created the drug. However, since the 1980's, prescriptions for amoxycillin for children in most countries have outstripped those for ampicillin.

Side-effects

These are virtually identical to those for amoxycillin. Since the drug is a semi-synthetic penicillin, with the basic structure of a penicillin, it has many side-effects typical of a penicillin. However, the consumption of food prior to the ingestion of ampicillin results in less complete absorption. Conditions such as severe renal impairment can alter the way ampicillin behaves in the body and markedly prolong its persistence in the blood, thereby increasing the possibility of side-effects.

The British National Formulary states that if a patient presents with a rash following the use of ampicillin, the drug should be *discontinued*. From research experience, I have found this instruction is frequently not followed. Furthermore, a patient presenting with a rash may be prescribed another drug such as a steroid cream like hydrocortisone, or an oral antihistamine such as Piriton. The former is

capable of impairing the skin's ability to fight infection and the latter is an extremely powerful drug which can make children drowsy and accident-prone, side-effects of which their parents are not always warned. Chapters 7, 8 & 9 discuss further potential side-effects of antibiotics.

BECLOMETHASONE DIPROPIONATE (Becotide)

Beclomethasone dipropionate (Fig. 4.8) is a synthetic corticosteroid, the actions of which are not fully understood. It is thought they provide relief by reducing bronchial mucosal inflammatory reactions such as oedema and hyper secretion of mucous.

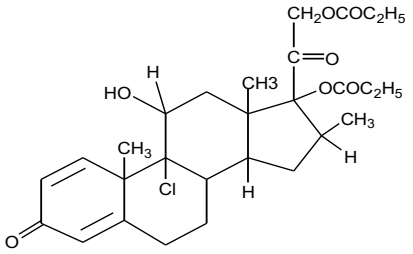


Figure 4.8 Chemical structural formula of Beclomethasone dipropionate.

Side-effects

Hoarseness, nausea, candidiasis of mouth or throat, headache, earache, light-headedness, pruritis, paresthesis, urticaria, angioedema, *bronchospasm, wheezing,* muscle weakness, pancreatitis, dysphonia, bone changes, immunosuppression, possible mental disturbances such as euphoria and depression. Although it is not known if beclomethasone crosses the placenta in humans, the drug crosses the placenta in animals since teratogenic and embryocidal effects have occurred following subcutaneous administration of the drug. Beclomethasone dipropionate is one

example of a drug which can cause side-effects *similar* to those symptoms for which it is being administered. Consequently any bronchospasm and wheezing resulting from use of the drug will very likely result in further exposure to the drug.

The American Hospital Formulary Service pharmacopoeia states that the drug should only be used during pregnancy when the potential benefits justify the possible risks to the foetus and that it should be used with caution in nursing women since it is not known whether the drug is distributed in breast-milk. It is not known whether beclomethasone affects fertility in humans. However, other corticosteroids are known to be distributed into milk and may cause the suppression of growth in breast-fed infants.

CEPHALOSPORINS (Cephalexin, Cefaclor, Cefadroxil)

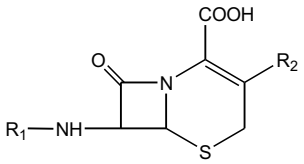


Figure 4.9 Basic chemical structural formula of a cephalosporin.

Cephalosporins appear to inhibit bacterial cell-wall synthesis in a manner similar to penicillin, and as can be seen from Fig. 4.9, share some structural similarity with penicillin (Fig. 4.6). The difference between a basic penicillin and cephalosporin is that the imidazole ring is replaced by a six-membered benzene ring.

History

The first source of the cephalosporins, a fungus, was isolated from the sea near a sewer outlet off the Sardinian coast in 1948. Three cephalosporins which are amongst some of the most commonly

used are cephalexin, cefaclor and cefadroxil (Figs. 4.10, 4.11 and 4.12). Cephalexin and cefadroxil may be regarded as structurally analogous to ampicillin and amoxycillin respectively, since they have the same chemical substitution at R' (see Fig. 4.9) on the molecule.

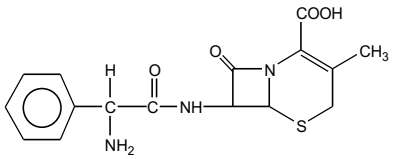


Figure 4.10 Chemical structural formula of cephalexin.

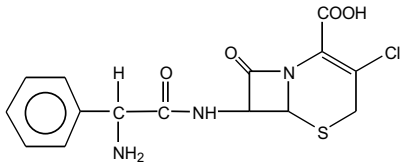


Figure 4.11 Chemical structural formula of cefaclor.

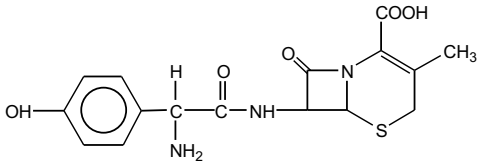


Figure 4.12 Chemical structural formula of cefadroxil.

Side-effects

'Hypersensitivity' reactions are the most common and there is no evidence to suggest that any single cephalosporin is more or less likely to cause such sensitization. The reactions appear to be identical to those caused by the penicillins, and it is thought this may be related to the beta-lactam structure common to both groups of antibiotics.

As with penicillins, patients often exhibit maculopapular *rashes* with or without *fever*, *urticaria*, *anaphylaxis* or *bronchospasm.* Due to

the similarity in structure of the penicillins and cephalosporins, patients who are 'allergic' to one class of agents may show cross-reactivity when a drug of the other class is administered.

Cephalosporins, as with penicillins, have also been reported to cause bone marrow depression and be implicated as agents capable of damaging the kidney. To my mind, this begs the question of whether these drugs and other antibiotics might in some cases, be implicated in the onset of leukaemia or renal failure, particularly if they were administered to babies or infants.

CHLORAMPHENICOL (Chloromycetin)

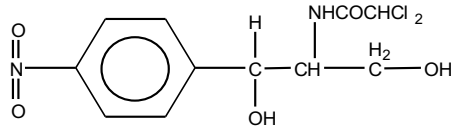


Figure 4.13 Chemical structure of chloramphenicol.

History

Chloramphenicol is an antibiotic produced by an organism that was first isolated in 1947 from a soil sample collected in Venezuela. Later that same year, it was successfully used to treat typhus in Bolivia and Malaysia. As early as 1948, it was being produced in sufficient quantity for general clinical use and was found to be of value in the therapy of a variety of infections. By 1950 however, it became evident that the drug could cause serious and fatal blood dyscrasias. The history of this drug is a prime example of how only some fifty years ago, patients were used as 'guinea-pigs' to test the efficacy of drugs which were very rapidly put into widespread use following their discovery.

Side-effects

The British National Formulary specifically states that repeated courses and prolonged treatment should be avoided. Blood disorders that may result from exposure to the drug include aplastic anaemia, which may terminate in leukaemia, nausea, fever, vomiting, peripheral neuritis, erythema, diarrhoea, optic neuritis and Gray baby syndrome in very young babies. The most important adverse effect of chloramphenicol is on the bone marrow, which can lead to a reduction in the number of white cells in the blood which are responsible for fighting infection, or blood platelets involved in the clotting of blood. The incidence is *not* related to dose, but seems to occur more commonly in individuals who are exposed to the drug on more than one occasion. The British National Formulary (Number 22) states: 'chloramphenicol is a potent, potentially toxic, broad-spectrum antibiotic which should be reserved for the treatment of *life-threatening* infections'.

Chloramphenicol is also available as eye-drops and eye ointment. The side-effects reported in the BNF are transient stinging and rare reports of aplastic anaemia. In view of the serious side-effects, I am of the opinion that we should question the use of chloramphenicol in babies who suffer from mild conjunctivitis or sticky eyes. Bathing with cotton-wool balls moistened with warm water, although more tedious, may be as beneficial and potentially less harmful. As chloramphenicol is an antibiotic, it will not be effective if the problem is not caused by a bacterial infection. Use of this chemical in the eye provides easy access for the chemical into the blood.

I have noted that sticky eyes in babies sometimes follow chemical exposure in-utero or during birth. If this is part of the body's response to certain foreign chemicals, the use of chloramphenicol is inappropriate; clearly it would be better to remove one drug from the

system rather than introduce another. It is worth noting that toxins such as arsenic (see chapter 2) and other drugs can cause conjunctivitis.

CO-TRIMOXAZOLE (Septrin)

Septrin is composed of two drugs sulphamethoxazole and trimethoprim (Fig. 4.14).

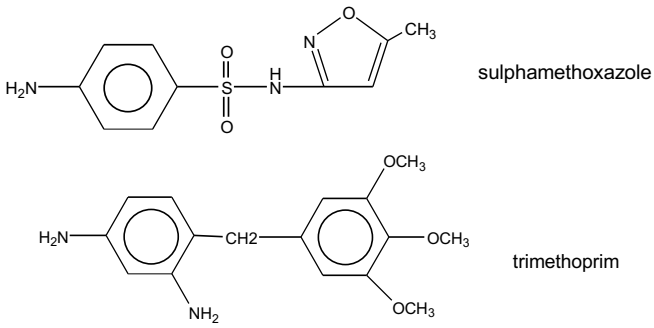


Figure 4.14 Chemical structural formulae of sulphamethoxazole and trimethoprim.

History

Trimethoprim was created around the late 1940s as an antibacterial agent and was later also found to have anti-malarial properties. Sulphamethoxazole was created following a German patent issued in 1932 to two workers at the I.G. Farbenindustrie (a factory producing dyes) for Prontosil and several other azo dyes containing a sulphonamide group, after the discovery that mice with infections could be protected with this chemical. Azo dyes are chemicals used by the food industry and are present in many confectionery and food items. They form a class of extremely *toxic* chemicals capable of causing cancers in unprotected workers in dyeing industries and have been linked to childhood behavioural problems and *asthma* attacks.

Sulphamethoxazole in combination with trimethoprim was introduced in the mid 1970s. The BNF states that the indications for the use of co-trimoxazole are invasive salmonellosis, typhoid fever, bone and joint infections due to haemophilus influenzae, urinary tract infections, sinusitis, exacerbations of chronic bronchitis, gonorrhoea in penicillin allergic patients.

Side-effects

The side-effects associated with either of these drugs are numerous and potentially fatal. Side-effects of nausea, vomiting and diarrhoea are relatively common following the ingestion of sulphamethoxazole which comes from a class of drugs known as sulphonamides; notorious for their toxic effects. Other reactions which may occur include rashes, photosensitivity, exfoliative dermatitis, dermatitis, systemic lupus erythematosus (SLE) and kidney failure. Some blood disorders that may occur include aplastic anaemia, thrombocytopenia, leucopenia, and eosinophilia. Other side-effects include toxic reactions to the liver, myocarditis, pancreatitis, anaphylaxis, fever, optic neuropathy, headache, insomnia, peripheral neuritis and vertigo.

Side-effects associated with trimethoprim include pruritis, skin rash, fever, nausea and vomiting. Adverse effects on the gastrointestinal tract, liver and nervous system have also been reported. Under the Swedish drug damage scheme, compensation is most often paid to victims of adverse reactions to the sulphonamide group of drugs. In view of the side-effects, it is perhaps surprising to learn that in the UK in 1988, an estimated 825,000 prescriptions for *paediatric* formulations of co-trimoxazole were dispensed. Since SLE, (often considered an autoimmune disease of unknown origin) may be drug induced, it is my opinion there may be many cases attributable to

exposure to sulphamethoxazole alone or in combination with other drugs.

DICYCLOMINE HYDROCHLORIDE (Merbentyl)

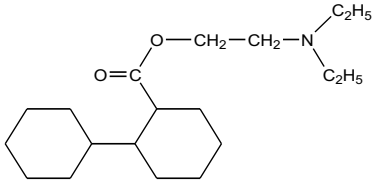


Figure 4.15 Chemical structural formula of dicyclomine hydrochloride.

History

Merbentyl syrup which contains dicyclomine hydrochloride, was approved for use in the UK in 1983, and is used in the treatment of functional disturbances of gastrointestinal motility such as irritable bowel syndrome. However, the American Hospital Formulary states that it has limited efficacy in the treatment of these disorders and should be used only if other measures such as diet, counselling or amelioration of the environmental factors have been of little or no benefit.

Side-effects

Goodman and Gilman's 'The Pharmacological Basis of Therapeutics' states that dicyclomine hydrochloride is one of a group of drugs for which clinical use has been disappointing. Its side-effects include dry mouth with difficulty in swallowing and thirst, dilation of the pupils with sensitivity to light, increased intra-ocular pressure, flushing, dry skin, bradycardia followed by tachycardia, palpitations and arrhythmias, difficulty with micturition, constipation, fever, rashes and confusional states.

Manufacturers of Infacol-C Colic Syrup which contains Dicyclomine hydrochloride, state on the accompanying instructional leaflet available in Singapore, *'administration of dicyclomine has been associated with rare reports, mostly in children under two months of age, of breathing difficulties including breathlessness and apnoea as well as convulsions, variable pulse rate, muscle hypotonia and loss of consciousness.'*

Despite controversy as to its culpability, Debendox, a drug prescribed for morning sickness during pregnancy, was withdrawn from the market in the USA and Australia during the 1970s after increasing litigation following claims that it was responsible for foetal abnormalities. Since Merbentyl like Debendox, contains dicyclomine hydrochloride, it is alarming that Merbentyl is available for infants before appropriate and exhaustive clinical trials have been conducted to exclude any risk of long-term side-effects.

ERYTHROMYCIN (Erythroped)

Erythromycin (present in preparations for children such as Erythroped) has a complex, unusual structure as shown in Fig. 4.16.

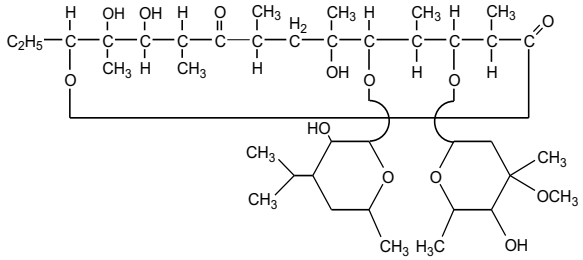


Figure 4.16 Chemical structural formula of erythromycin.

History

Erythromycin is an antibiotic which was discovered in 1952 as a product of bacteria obtained from a soil sample in the Philippine

archipelago. Traditionally used in orally administered preparations for chest and throat infections, it has recently become available for topical application in the treatment of acne.

Side-effects

Reactions to erythromycin may include fever, skin eruptions and raised levels of eosinophils. It has been reported that one rare side-effect, cholestatic hepatitis, may begin after 10-20 days of treatment and is characterized by nausea, vomiting and abdominal cramps. Hypertrophic pyloric stenosis, a thickening of the normal tissue of the pyloric orifice of the stomach, which may cause projectile vomiting, was reported in 1976 in infants during administration of one form of erythromycin. Intravenous administration of the drug results in much higher concentrations in the blood than for doses of similar concentration given by mouth. Temporary *hearing impairment* has also been reported following intravenous administration. Erythromycin crosses the placental barrier and concentrations in foetal plasma are 5%-20% of those in the maternal circulation.

Erythromycin is useful for a variety of infections, but is currently reported to be the preferred drug for only a few. Some of the infections for which it may be used include pneumonia, Legionnaires disease, diphtheria, pertussis, pharyngitis, scarlet fever, tetanus, syphilis and gonorrhoea. Considering these infections, it is surprising that Erythroped which is erythromycin in suspension is commonly prescribed for children in many countries.

In view of the numerous side-effects which may be observed in individuals whilst they are taking erythromycin, it is likely many patients who develop side-effects several weeks after a course of the drug do not relate their side-effects to their earlier exposure to the drug. Since the introduction of topical erythromycin for acne, there

has been a report that skin contact with the drug (which had crystallized around the neck of the bottle), caused a burning sensation below the skin and dermatitis which resulted in blistering and peeling of the skin. These symptoms were reported to have occurred after very few exposures many weeks after the last exposure. It could however be linked to exposure to the drug, because the affected area on the thumb resembled an arc which related to the area which came into contact with the neck of the bottle and lower end of the cap, around which the erythromycin had crystallized. Following discontinuation of its use, the dermatitis resolved itself after several months although sub-epidermal scarring persisted some eighteen months later.

Since contact with skin, an *external* protective surface of the body with erythromycin, is capable of provoking such a reaction, it should be of no surprise to find that the drug is capable of causing internal damage, causing vomiting and diarrhoea some weeks after the final exposure. There is thus a possibility that permanent damage to the delicate lining of the gastrointestinal tract, which may only become apparent months later, can also occur.

PROMETHAZINE HYDROCHLORIDE (Phenergan)

Phenergan contains the chemical promethazine hydrochloride (Fig. 4.17) and has the basic structure of a phenothiazine (Fig. 4.18). Phenothiazines are *antipsychotic* drugs that affect the brain and may alter behaviour.

History

Phenergan was discovered during the 1940s and has been available since the completion of animal toxicity studies later during the *same* year. It is used for the relief of symptoms associated with urticaria, hay fever and for travel sickness since it is a sedative.

Side-effects

Adverse effects include dryness of the mouth, blurring of vision, dizziness, nightmares, confusion, disorientation and abnormal movements. Lassitude, fatigue, incoordination, tinnitus, insomnia, excitation, nervousness, hysteria, tremors, seizures and euphoria have also been reported.

Those familiar with the extreme reactions that may occur in patients undergoing withdrawal of psychotic drugs are aware of the necessity for gradual withdrawal of these chemicals to reduce the severity of withdrawal symptoms, which may be more severe and of longer duration than the symptoms for which the drug was prescribed. It is therefore not surprising to hear of infants who have been given the drug for a week, presenting with behavioural problems such as screaming, continuous crying and insomnia when the drug therapy ends following several days of continuous use.

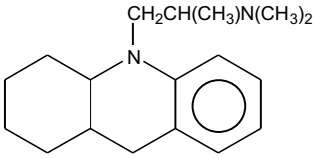


Figure 4.17 Chemical structural formula of Promethazine hydrochloride.

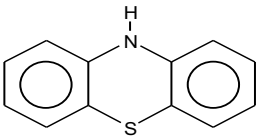


Figure 4.18 Basic chemical structural formula of a phenothiazine.

In adults, overdosage of promethazine may result in deep sleep, coma, seizures and cardio-respiratory symptoms. In the UK in 1992, some 200 parents whose children became comatose following the administration of Phenergan were pursuing compensation for

damages. To compound the problem, Phenergan is currently available from pharmacists in the UK and Australia without a prescription and with scant information concerning side-effects. In conversation with one mother, I learnt of the death of her child which occurred whilst the child was taking Phenergan. The death was attributed to SIDS (Sudden Infant Death Syndrome). If this drug can result in coma, can we be certain that SIDS was the true cause of death? In Australia, packaging of Phenergan now carries a warning that it is not suitable for children under the age of two years. SIDS has also been blamed for the deaths of a number of infants and young children who received usual dosages of trimeprazine tartrate, a phenothiazine-derivative antihistamine.

SALBUTAMOL (Ventolin)

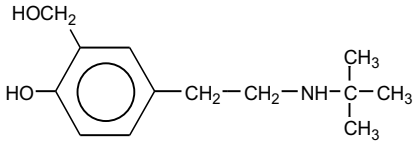


Figure 4.19 Chemical structural formula of salbutamol.

History

Salbutamol (Fig. 4.19) is used in the treatment of asthma and other conditions associated with reversible airways obstruction and for the prevention of pre-term labour. Ventolin, which contains salbutamol, was licensed in the UK in 1968.

Side-effects

Salbutamol may cause fine tremor of skeletal muscle (particularly the hands), palpitations, muscle cramps, hypokalaemia, urticaria, angioedema, slight tachycardia, cardiac arrhythmias, tenseness, headaches and peripheral vasodilation.

In 1991 a member of a European drug company which does not produce salbutamol, was reported as saying that he suspected it may be responsible for unexpected heart attacks in young asthmatics. Another concern is that fluorinated hydrocarbons, themselves potentially damaging chemicals, have been used as propellants in aerosols of salbutamol.

Since salbutamol is used to try to prevent pre-term labour, perhaps we should ask ourselves what effect the drug may have on the menstrual cycle and pregnancy of a female asthmatic who has been inhaling the drug since childhood. Recently, medical advice advocates restrained use of bronchodilators since it has come to be recognised, that by expanding the airways, more of the dust or offending agents which can cause an asthmatic attack are able to enter the body and cause yet more irritation.

DISCUSSION

Before exposing ourselves to a drug that was available before the Medicines Act of 1968 in the UK, we would be well advised to recognise the minimal controls which existed at that time to prevent a harmful drug from entering the market. Some thirty to forty years ago, clinical trials were based on little more than monitoring the patient for recovery from illness, ignoring any reactions that were not serious or immediately apparent. The numbers of patients usually involved in each individual study, often represented nothing more than a handful of plankton taken from the ocean.

Unfortunately, in the UK, unlike the USA, results of clinical trials are regulatory documents and are not available for public scrutiny. But it seems likely that children studied in trials of amoxycillin after its introduction for clinical use, often numbered a mere 50 to 100 children. Often the children were monitored only for side-effects

during their hospital stay. Consequently, any reactions to the drug appearing a week to several months later, would very likely go unreported. Also, even if the drug killed 1 out of 10,000 children, this would be unlikely to be detected in a study of 50 or 100 children.

The failure to monitor the health of children in a clinical trial, for at least 12 months after their exposure to the drug, is also disturbing and a flaw of these studies. Also, perhaps more importantly in today's climate of profuse prescribing, no study has ever been made to look at the health of children who are *repeatedly* exposed to amoxycillin or a variety of drugs and antibiotics. Recently, it has been reported that '80% of victims of chronic fatigue syndrome have a history of chronic antibiotic exposure'.

One can better appreciate the importance of this, if one has seen cases where antibiotics have been prescribed on three consecutive occasions during a ten week period (for examples see chapters 7 and 8). Many doctors can't fail to be aghast at such treatment, but repetitive prescribing of antibiotics within short periods is by no means uncommon. Some doctors and a medical director of one pharmaceutical company to whom I have spoken, admit that antibiotics are over prescribed. Of just as great a concern, is the fact that they are also *inappropriately* prescribed ie. they are given for conditions (eg. viral) that will not improve under administration of an antibiotic; conditions that are not sufficiently serious to warrant the use of *any* drug; and conditions that frequently have not been positively diagnosed.

This is a situation where patients, parents and doctors can all be at fault. Consumer awareness and understanding of the nature of chemicals that are bought at the pharmacists counter is virtually *negligible.* Instead, those at the receiving end perhaps look upon

pharmaceutical products as a torch in the dark, gaining security and comfort from something presented in smart packages, which issue from respected and admired professions.

Additionally, many are the times when the physician is faced with a persistent mother demanding an antibiotic, possibly arising from previous experience of a seemingly favourable outcome following a prescription for a drug or an antibiotic. Faced with some forty patients a day, doctors may not be possessed with the energy and patience needed to try to convince their patients that by not prescribing the drug they want, they are speaking out of concern for them.

It is no wonder then, that doctors are persuaded and encouraged to prescribe these toxic chemicals, not only by their patients in some cases but also by prolific publicity and marketing campaigns from the drug companies. In developed countries, paraphernalia from the drug companies often threatens to engulf the doctor's desk in a sea of sticky notepads, calendars, laminated charts, stethoscopes and clocks, each emblazoned with the name of the drug they are designed to promote.

Additionally, there may be other indirect financial benefits on offer to medical practices which are receptive to drug companies (the degree of this persuasive marketing varies between countries). This may result for example in the surgery gaining computing equipment, cheaper drugs (for doctors who dispense their own drugs) and free trips to attend conferences where there may be a speaker who has a favourable report on the company’s latest drug.

In the USA during 2002, pharmaceutical companies with an army of 80,000 drug representatives spent almost $100 million a *day* trying to make sure doctors prescribe their latest most expensive medicines.

5

Drug Use during Pregnancy and Labour

> **"With every medical treatment there are risks, and a lot of those risks are unknown at the time."**
> Professor Wilfred Butt, UK, 1993 (Pioneer of pituitary hormone therapy now thought to be responsible for deaths from Creutzfeldt-Jakob *'Mad Cow'* Disease)

As noted earlier, medicinal drugs usually have unpleasant and damaging side-effects when taken in sufficient quantity. The amount required and the side-effects which arise will vary according to the individual's sensitivity to the drug, body weight, number of previous exposures to the same drug, site of injection of a drug, and present and past exposure to other drugs. There are also other factors including the time of day the drug is taken, whether or not it is taken with other drugs, taken before or after food, and the nutritional status of the individual, to list but a few.

In more recent years, the medical profession has come to recognise that certain drugs should not be used during pregnancy. However, for most of the drugs available on the market, there is no data regarding possible side-effects and the drug companies tend to issue disclaimers stating that safe use during pregnancy has not been established. Unfortunately, this caveat is usually unknown to the layperson and it is often on the basis of such a negative statement, that a doctor will assure a pregnant woman that a drug is safe to take. In addition, in many countries, many over-the-counter (OTC) remedies for coughs and hay-fever which contain potent chemicals such as

pseudoephedrine and antihistamines, carry no warnings for pregnant women and provide insufficient information about adverse effects.

Perhaps the mere fact that drug studies involving pregnant women have not been done, speaks for itself. Chemicals such as alcohol and those present in tobacco smoke, of which there are some 4000, are undeniably implicated in certain childhood medical syndromes and birth defects. Consequently, the possibility undoubtedly exists that other chemicals will exert undesirable effects on the foetus. After all, since a myriad of chemical reactions are taking place in the growing foetus, the chances that the presence of a foreign chemical may disturb at least one of them, are high.

An important factor appropriate to drug exposure during pregnancy is body weight. If, for example, a mother weighing 50kgs takes a drug that crosses the placenta undiminished, her foetus, when it has a weight of less than 100g, has an exposure to the drug *500* times greater per kg of body tissue than its mother. The dose of the drug which has been administered to the mother is in a concentration which is designed to treat the mother, with minimal likelihood of adverse side effects. But the foetus, at its very delicate and vulnerable stage of development, has also to be taken into consideration.

Investigation into the history of obstetric practices will show that they have varied enormously throughout the years. During the seventeenth century, women were covered with a sheet during labour so that their bodies could not be seen by male-midwives, who were sometimes known to crawl in along the floor to reach the bed. In those days, in the case of a difficult labour where forceps (which were invented in the 1600s) were to be used, only a member of the Barber Surgeon Guild could be employed. This was because forceps were

classified as surgical instruments and only those in the Guild were authorised to use them.

During the twentieth century in Australia, when birthing stools were in vogue, women giving birth were sometimes placed in an upright position with the aid of the birthing stool for delivery of their baby. Obstetric practices have changed considerably during the twentieth century, with childbirth today being more likely to be chemically controlled. Drugs are used to prevent pre-term labour, to induce labour, and painkilling drugs assist the birth. Undoubtedly many drugs given during labour have been instrumental in reducing mortality and labour pains. However, who among us has not heard of childbirth being induced when it might possibly have been avoided?

In 1808, a publication described the use of a chemical as a remedy for quickening childbirth. This marked the official introduction of ergot for medicinal use. Ergot is a very powerful chemical. If the dose was too large it would cause nausea and vomiting and in most cases it exhibited its effects very suddenly, such that the physician was advised to be completely ready for the delivery before administering it. In 1808, John Stearns wrote: *"Since I have adopted the use of this powder I have seldom found a case that detained me more than three hours"!*

Even before 600 B.C., the effect of ergot on pregnant women had been observed. Ergot which comes from a fungus, was described as causing "pregnant women to drop the womb and die in childbed", after they had been exposed to it as a result of eating contaminated grain. During the centuries that followed, ergot came to be recognised as a *poison* that could cause gangrene of the feet, legs, hands and arms. In severe cases, the tissue became dry and black and it was known to

mummify limbs which would separate from the body without loss of blood.

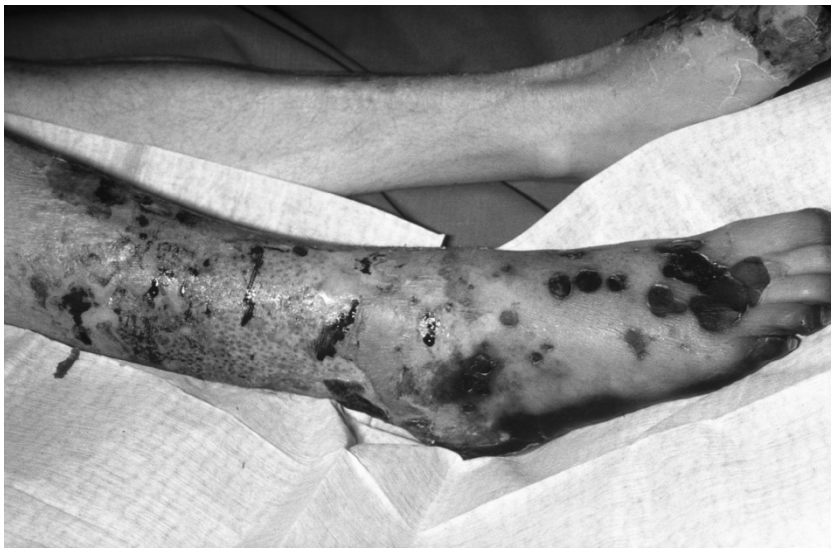


Plate. 5.1 Gangrene caused by ergot poisoning. (Reproduced with permission from the Wellcome Library).

Ergots continued to be used by midwives and doctors during the nineteenth century to stimulate uterine contractions. Exhibition cabinet S4 in the Wellcome Museum of the History of Medicine, Science Museum, London (1992), contains a display of a bottle of ergot, which bears the warning 'POISON'. Purification of *ergometrine* from ergot led to more predictable results as dosing became more controlled. Today, ergometrine is *commonly* used to control postpartum haemorrhage. As will be discovered in later chapters, ergometrine is a drug that I consider may be implicated in the onset of diabetes.

It has been said, *"Curiously, it is often poisons in small doses which make the best medicine"*! However, a chemical which is toxic at

a particular concentration could understandably cause less severe but none-the-less harmful effects at lower concentrations. Adverse effects which are perhaps more subtle or take longer to become apparent. The following drugs are some of those most frequently used during labour in many industrialized countries today.

PETHIDINE

Pethidine (Fig. 5.1) is an opioid (narcotic) analgesic, comes from the same class of compounds as morphine, heroin and codeine, and shares the toxic potentials of the opiate agonists. It was introduced in 1939 and has the actions and uses of morphine, and may be used to relieve pain during labour. In an adult, side-effects can include depression of respiration and even cessation of respiration, nausea, vomiting and hypotension when in an upright position.

Although the analgesic effects last for only 2-4 hours in an adult, it usually takes up to three days for most of the pethidine to be excreted and can take up to *six* days to be completely eliminated from a newborn baby. This illustrates well the difference that can exist between an adult and neonate where drug exposure is concerned.

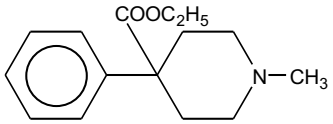


Figure 5.1 Chemical structural formula of pethidine.

Not surprisingly, babies who have been exposed through their mothers to pethidine during labour, show a higher incidence of respiratory problems such as delayed respiration, decreased respiratory minute volume (ie. shallow breathing), or decreased oxygen saturation (ie. their blood carries less oxygen than normal)

and are more likely to require resuscitation. Pethidine is however used with considerable frequency in many developed countries.

The effect of pethidine on the newborn baby has been shown to vary according to the time between administration of the drug and delivery. In one study, respiratory depression was present in 6 of 24 infants (ie. 25%) delivered 1 to 3 hours after injection, and in *all* 5 infants (ie. 100%) who were delivered 3 to 6 hours after injection. Respiratory depression was also found during the first and second days of life in infants whose mothers had received pethidine; the depression was greatest with the highest dose of pethidine (75mg to 150mg within 4 hours of delivery). Apart from pethidine crossing the placenta, it also distributes into breast milk and 60-80% of the drug binds to proteins within the blood. Despite its respiratory effects, I am not aware of any studies which have looked at the incidence of SIDS in babies exposed to pethidine at birth.

Whilst visiting a modern 700 bed hospital in Viana do Castelo in Northern Portugal, I was interested to discover that pethidine is seldom used. This is because it is appreciated that pethidine "is a narcotic which inhibits the suckling reflex of newborn babies". Possibly the all-too-common use of this drug in industrialized societies may have something to do with the difficulty which some mothers have experienced in establishing breast-feeding.

EPIDURAL ANAESTHESIA (Bupivacaine Hydrochloride; Marcain)

Local anaesthetics, of which bupivacaine hydrochloride (Fig. 5.2) is a potent chemical capable of producing prolonged anaesthesia, may be used during labour or for caesarean section. Anaesthetics act by blocking nerve conduction near their site of application, thereby producing a temporary loss of sensation in a limited area of the body. The duration of the anaesthetic ranges from 3-7 hours and the

principal side-effects that can occur include hypotension, bradycardia and cardiac arrest. Effects on the central nervous system include anxiety, restlessness, nervousness, disorientation, confusion, dizziness, blurred vision, tremors, twitching, shivering, euphoria, respiratory depression and seizures. Nausea, vomiting, chills and tinnitus may also occur. It was not until 1986 that bupivacaine was reported to be substantially more cardiotoxic than most other commonly used local anaesthetics.

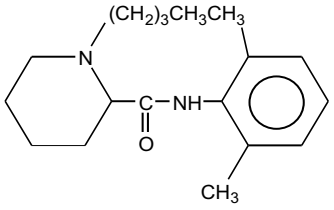


Figure 5.2 Chemical structural formula of bupivacaine hydrochloride.

Even when the concentration of a drug administered to a mother during labour occurs in a higher concentration per unit volume of blood than in the infant, the amount of the drug received by the infant per kilogram of body weight can be significantly greater than that received by the mother. For example, if the concentration of a drug in a baby's blood is only 40% of that experienced by the mother who receives 100mg of the drug, a child weighing 3kgs compared with a mother weighing 60kgs, would have a dose equivalent to 40mg/3kg. The mother would have received 100mg/60kg ie. approximately 1.7mg/kg, whereas the baby will have received approximately 13mg/kg, ie. the child will have experienced almost *eight* times higher dosage relative to body weight.

Not only may the baby receive a much higher dose of the drug per kilogram of body weight, but at a stage when its organs and bodily

systems have not reached maturity, it may often take a baby much longer to remove these chemicals from its bloodstream than its adult mother.

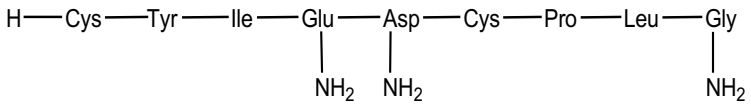
It is therefore possible that some of the problems faced by women, in establishing breast-feeding or with crying newborn babies, has in some cases more to do with the side-effects of the anaesthetic the baby has been exposed to during birth than maternal tension. Unfortunately, once a mother experiences difficulty with establishing breast-feeding, a self-perpetuating cycle of anxiety and loss of confidence may result. These traumas can physically decrease milk production and cause a woman to decide she is unable to provide sufficient milk for her infant. This may cause her to commence formula feeding using inappropriate animal-milk substitutes that are devoid of vital nutrients.

The result may be that the infant, who was disadvantaged from birth in terms of chemical exposure, becomes further disadvantaged as the result of inappropriate nutrition. Whilst the baby food manufacturers may strive to convince us of the excellence of their products, labels on infant formulae milk products correctly state that breast-feeding is best.

OXYTOCIN, SYNTOCINON

Oxytocin (Fig. 5.3) is a modern pharmacological agent that has replaced the ergot alkaloids to modify, initiate and accelerate parturition. It is a naturally occurring hormone which is produced in the pituitary, a small gland suspended from the base of the brain. It is used in the induction of labour as it stimulates uterine contractions thereby promoting the expulsion of the foetus, although the mechanism by which this occurs is not fully understood.

There are severe adverse effects associated with the use of excess oxytocin including rupture of the uterus, tearing of soft tissues, foetal bradycardia and arrhythmias, anaphylactic and other allergic reactions, pelvic haematomas, nausea, vomiting and even foetal or maternal death. Neonatal jaundice has also been reported.



Key to amino acids (small molecules containing an amino {NH_2} and carboxylic acid {COOH} group at opposite ends of the molecule): Asp: asparagine; Ile: isoleucine; Glu: glutamic acid; Pro: proline; Cys: cysteine; Leu: leucine; Gly: glycine; Tyr: tyrosine.

Figure 5.3 Abbreviated chemical structural formula of oxytocin. Actual structures of amino acids have not been shown.

The American Hospital Formulary Service Drug Information publication states that:

“Elective induction of labour merely for physician or patient convenience is not a valid indication for oxytocin use."

Oxytocin may occasionally be used in the management of postpartum haemorrhage, although ergometrine is more likely to be the drug of choice.

A combination of oxytocin and ergometrine (eg. Syntocinon) in a single preparation may sometimes be given either by intramuscular or intravenous injection. Communication by the author with the company which markets oxytocin and ergometrine in the UK elicited the

response that despite an extensive search of their databases, they could not, unfortunately, find reports of any studies which looked at the long-term health of children exposed to oxytocin (see chapter 7).

ERGOMETRINE

Ergometrine (Fig. 5.4) is an amine alkaloid derived from ergot, which comes from a fungus which grows on rye and other grains. Ergometrine maleate is used in the prevention and treatment of post-partum haemorrhage.

Adverse effects that have been reported following the use of ergometrine include headache, dizziness, tinnitus, abdominal pain, nausea, vomiting, hypertension, chest pain, palpitation, dyspnoea, and bradycardia. Ergometrine shows fewer tendencies to produce gangrene than ergotamine, but ergotism has been reported and symptoms of acute poisoning are similar. Babies, who have *accidentally* been injected with ergometrine instead of vitamin K after birth, have experienced convulsions, respiratory failure, water intoxication and acute renal failure.

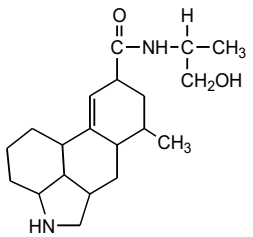


Figure 5.4 Chemical structural formula of ergometrine.

Despite the rapidity with which ergometrine is destroyed and eliminated from the adult body, it is possible that elimination from newborn babies may be prolonged. Since ergometrine has been detected in breast milk, it is likely that babies who are breast-fed

immediately after delivery by mothers, who have been given ergometrine, are also exposed to the drug.

DISCUSSION

Most infants who are exposed to drugs during labour are not monitored for more than a brief period following birth, since with medical intervention, they appear to recover completely. However, in light of recent awareness of the possible damaging effects that drugs taken during pregnancy may have on the foetus, perhaps we should remain sceptical about the safety of babies exposed to drugs at this most fragile stage of development, until there are studies which show conclusively that they are non-damaging in the long-term.

Pethidine which was introduced in 1939 (at a time when drugs were often brought into general clinical use after apparently successful experimentation in only a few individuals) is unlikely to have been adequately studied for its effects on infants. Studies in more recent years of infants exposed to pethidine typically are based on less than 100 babies. Consequently, any potentially life-threatening toxic effect of the drug which may affect 1 out of 1000 babies has a poor chance of being discovered. It is possible this drug, which may cause death by inhibiting the breathing reflex, is a risk factor for Sudden Infant Death Syndrome (SIDS) in which infants appear to stop breathing for no apparent reason. Since 'side-effects' of a drug often only become apparent several weeks or months after exposure, it is possible that a side-effect which most commonly occurs immediately after exposure to the drug, will manifest itself at a later date, perhaps upon exposure to some other trigger agent such as antibiotics which also carry a risk of life-threatening anaphylaxis.

During 1990, SIDS claimed the lives of 3,319 infants under the age of one year in England and Wales and was the most common

cause of death between 2 weeks and 1 year of age, with the peak incidence occurring between 2 to 4 months of age.

Another extremely important but perhaps insufficiently appreciated potential source of chemical exposure to babies, lies in the breast-milk of mothers who have been in receipt of drugs during and after labour. From my experience, it must be doubted that babies who have been administered antibiotics immediately after birth, have had their dose modified to allow for the concentration of the drug that they are also receiving from the breast-milk of their mother if she should also be on a course of antibiotics. I have encountered cases where children have been given three different types of antibiotics at birth and were breastfed while their mother was being administered antibiotics intravenously. When the child then presents at the doctor's surgery within a month after birth suffering from eczema or some other condition which may last for the whole of his or her childhood, or longer, there is at present insufficient information available to satisfy ourselves that these conditions were not the result of drug exposure at a very early age.

The fact that skin rashes are the most common side-effect following exposure to antibiotics in children and adults deserves careful attention. Whilst skin problems may not be life-threatening, they can necessitate constant care and attention and may require the daily application of creams, oils and bandages. No one with any appreciation of suffering could fail to be stirred by the sight of a young child covered with red lesions that were such a source of irritation they were being scratched until they bled. And the pain visible on the child's face as it is smothered with a steroid cream, causing a burning sensation, and then swaddled with bandages in an attempt to treat the problem.

Whilst medical science has resulted in impressive advances during the past fifty years, we should not become overawed to the extent that we cease to question. Where drug therapy is concerned, the duration for which a drug has been available, should not be taken as a guide to supposed safety. In fact, the earlier the introduction of a drug, the less stringent the requirement is likely to have been for investigations of possible toxicity.

A further source of concern is the availability of potent chemicals without a prescription, in the form of natural health remedies. Among those concerned about this unrestricted availability, is the Royal Pharmaceutical Society, London, which has tried to urge Government to place restrictions on these remedies, as the public is predominantly unaware of their possible toxic effects.

However, 'alternative' products should not be regulated to the extent that vitamins, minerals and herbs are no longer easily available or affordable. Unfortunately, over-regulation now appears to be occurring on a global scale, despite *prescription medicines* being responsible for hundreds of thousands of deaths each year.

Since herbal remedies do not make any health claims, they are not classified as medicines and are consequently not subject to any sales restrictions. Some of these products, such as *Natracalm* or *Kalms* which are advertised as remedies which enable one to cope with the stresses of life, contain potent chemicals. These products contain extracts from a plant known as Passiflora Incarnata, and therefore contain *alkaloids,* a class of chemicals to which strychnine, the ergots and ergometrine belong. One mother, who took a few courses of such a preparation whilst she was pregnant, bore a baby with a raised strawberry coloured birthmark 5-6cms in diameter, which later became diabetic at one year of age.

Ephedrine found in preparations of Ephedra, another herbal remedy, is also an alkaloid and a powerful stimulator of one of the two divisions of the autonomic nervous systems. It has numerous side-effects and is otherwise a *prescription-only* medicine. The inconsistency of the availability of drugs only by prescription, when manufactured by pharmaceutical companies, and yet available indirectly in preparations from health shops, is totally unacceptable. In addition, most of these herbal remedies carry no health warnings as to possible adverse reactions or of any possible risk during pregnancy.

As for drugs such as oxytocin and ergometrine, as far as I am aware, no studies have been conducted to eliminate the possibility they may be a factor in the onset of developmental or health problems in children. In conclusion, mothers would be well advised to reflect on the fact that routine commercially based clinical trials of drugs are not perfect in design. And in the case of *most* drugs currently in use during pregnancy and labour today, there have not been any studies to examine the *long-term* effects that these drugs may have on the health of *either* mother or child.

6

Drugs and Chemicals that can cause Diabetes

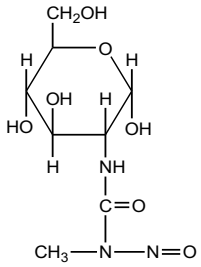
Magic substances like antibodies, which affect exclusively the harmful agent, will not be so easily found in the series of the artificially produced chemical substances. It must be regarded as in the *highest degree* probable that substances of this kind, foreign to the body, will be attracted also by the ORGANS, and that, since we shall be dealing with a range of substances, all with pronounced activities, these are not unlikely to injure the organism as a whole, or some part of it.
Paul Erlich (Chemist noted for his achievements in synthesizing new drugs), 1906.

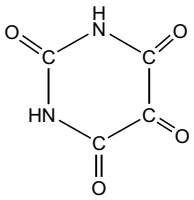
The purpose of this chapter is to make the reader aware that some drugs and chemicals are *known* to be capable of causing diabetes. Cases of chemicals and drugs causing temporary or permanent insulin-dependent diabetes are well documented in medical literature[1-15]. Unfortunately, such cases do not commonly come to the attention of physicians and most patients are quite unaware of the dangers.

Two of the best known chemicals capable of damaging the pancreatic beta cells which are responsible for the production of insulin, are the antibiotic streptozocin and the chemical alloxan (Fig. 6.1). These drugs are routinely used in animal experiments to study diabetes. Vacor (Fig. 6.2), a rat poison, has also been reported to cause insulin-dependent diabetes in humans who survived the exposure.

There is some structural similarity between the chemicals streptozotocin, alloxan and Vacor: in each, there is at least one oxygen atom joined by two bonds to a carbon atom (C=O), which forms a carbonyl group, which is flanked on each side by a nitrogen (N) atom. This is interesting since carbonyl groups and nitrogen atoms are often reactive species due to their excess of negative charge. That is, they are electron rich sources that very often have an affinity for positively charged species such as zinc ions (Zn^{2+}). Therefore, they behave like magnets attracting oppositely charged species. Since insulin is stored in the pancreas in combination with zinc, the pancreas has the highest concentration of zinc in the body and could conceivably present a source for chemical attack.

Additionally, doubly bonded oxygen groups are also potential sources for the formation of free radical species, which are destructive agents that have been implicated in the onset of cancer.





Streptozotocin Alloxan

Figure 6.1 Chemical structures of streptozocin and alloxan.

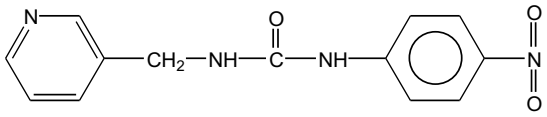


Figure 6.2 Vacor (RH-787 rodenticide).

Other chemicals known to be capable of causing diabetes in humans include the drugs dapsone (Fig. 6.3) used in the treatment of leprosy, and pentamidine isethionate (Fig. 6.4), an antiprotozoal agent used in the treatment of pneumonia in AIDS patients. Dapsone and pentamidine bear little resemblance to the drugs shown in Figures 6.1 and 6.2, except that dapsone also contains electronegatively charged oxygen atoms which in this instance are doubly bonded to sulphur (forming a sulphonyl, S=0 group) instead of carbon. Both drugs have electronegative terminal amino (NH_2) groups attached either to or in close proximity to a benzene ring.

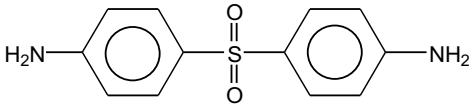


Figure 6.3 Chemical structure of dapsone.

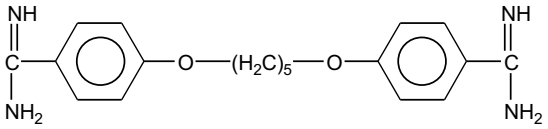


Figure 6.4 Chemical structure of pentamidine isethionate

Comparison of dapsone and pentamidine with two other drugs frusemide (Fig. 6.5) and chlorthiazide (Fig. 6.6) (both diuretics reportedly associated with the onset of diabetes) reveals that these drugs also share some structural similarities. In frusemide, we again see the electronegative sulphonyl (S=O) group and a terminal amino (NH_2) group; while chlorthiazide exhibits two SO_2 groups and a terminal NH_2. These groups are not commonly found in drugs. For example, in the American Hospital Formulary Drug Information publication 1991, which lists some 1000 drugs, less than 5% have an amino group bound either to a benzene ring or to a carbon atom

attached to a benzene ring. Sulphonyl groups however, are common to thiazide diuretics and the sulphonamide group of drugs.

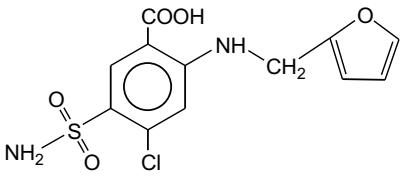


Figure 6.5 Chemical structural formula of frusemide.

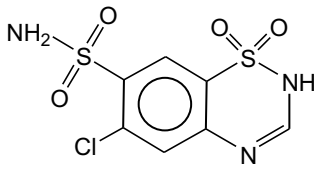


Figure 6.6 Chemical structural formula of chlorthiazide.

Alarmingly, in Australia, diuretics such as hydrochlorthiazide (identical to chlorthiazide apart for an additional hydrogen atom) may be given to young women for the treatment of pre-menstrual water retention. Additionally, statistics for the Pharmaceutical Benefits Scheme 1992-93 show that diuretics were the eleventh most frequently prescribed drugs in Australia. If drugs such as thiazides are diabetogenic, it would not be surprising to find that the incidence of diabetes is increasing in adults.

It is not always understood that a substance with a simple chemical structure, is not necessarily one of low toxicity. However, a drug with a complex structure is more likely to have reactive groups. For example, aniline (Fig. 6.7), which is simply an amino group attached to a benzene ring, is an extremely toxic chemical. It received publicity in 1981 when it was detected in rapeseed oil sold in Spain as

pure olive oil, having killed over 100 people. Aniline is used to denature rapeseed oil for industrial purposes.

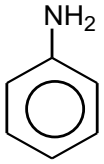


Fig. 6.7 Chemical structural formula of aniline.

There have also been reports that some antihypertensives (drugs used to control high blood pressure) may also cause diabetes. One of these is nifedipine (Fig. 6.8). Again, although the overall structure of this drug is not like any of the other drugs previously mentioned, it also has several electronegative doubly-bonded oxygen groups including a NO_2 group bound to a benzene ring as found in Vacor (Fig. 6.2). Thus it can be seen that nifedipine shares some structural similarity with a chemical known to be diabetogenic.

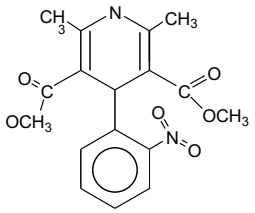


Figure 6.8 Chemical structural formula of nifedipine (Adelats).

In summary, the chemicals and drugs presently known or suspected as being associated with a risk of diabetes, would appear to have primary amine (NH_2), a carbonyl (C=O) group close to a nitrogen or an oxygen, $S0_2$ or NO_2 groups. Primary amines and oxygen atoms bound to carbon, sulphur or nitrogen, being reactive species due to their negatively charged centres, will bind to zinc under the right conditions by a process known as chelation. The pancreas, a

rich source of zinc, could therefore present a potential target for attack by zinc-seeking chemicals.

It has been suggested[14] that chemicals which can cause diabetes may do so by interaction with zinc in the insulin secreting beta-cells of the pancreas. This suggestion is supported by the fact that diabetes arising from chemical exposure is accompanied by a loss of histochemically detectable zinc from the pancreatic beta-cells[15], and zinc injected into animals before exposure to the diabetogenic chemical, protects animals against diabetes[16,17].

It has also been reported[18] that penicillin interacts with zinc. It is conceivable therefore, that a chemical such as penicillin circulating in the blood stream could be attracted to the beta-cells of the pancreas which contain zinc. This could result in the displacement of insulin bound to zinc and chelation of penicillin to zinc, thereby changing the acidity within the cells as new different bonds are formed. This in turn could cause the insulin-zinc aggregates to dissolve, leading to a marked increase in osmotic pressure and rupturing of the cells.

It is possible therefore, that such chemical changes within the pancreatic beta-cells which produce insulin, may activate the body's immune defence system which detects foreign agents. This would result in the formation of antibodies directed against the pancreatic beta-cells in an attempt to bind the beta-cells and destroy them, as they are now seen as foreign to the body. This may account, at least in part, for the presence of islet-cell antibodies in the blood of many newly diagnosed diabetics.

If this were the case, the agent responsible for causing the diabetes would be the chemical which ruptured the cells of the pancreas, and not the antibodies, as the cells of the pancreas were

already damaged. This is an important distinction, since following the discovery of islet cell antibodies, current scientific theories about the origin of diabetes centre on it being an autoimmune disorder causing, for some unknown reason, the body to manufacture antibodies directed against the beta-cells of the pancreas, which destroy the cell's ability to produce insulin. This scenario implies that it is the patient's constitution which is at fault.

Diabetes in humans and animals which is caused by chemicals is often referred to as chemical or drug-induced diabetes. However, as far as I am aware, there have not been any suggestions that diabetes per se may in fact be a disorder resulting from chemical or drug exposure. Perhaps this is partly due to compartmentalisation in medical research, with doctors investigating the clinical aspects of a disease whilst scientists are working with blood or animal models. It is also likely to be because our appreciation of the damage drugs can do is still clouded by the continuing emphasis in drug marketing on the seemingly beneficial effects. Since chemicals and drugs can both cause diabetes, there is every likelihood that insulin and non-insulin dependent diabetes today in Western societies, which in many countries has reached epidemic proportions, is predominantly the result of chemical exposure through prescription drugs.

One drug which appears to be potentially diabetogenic due to its similarity in structure to alloxan (see chapter 7) is the barbiturate phenobarbitone (Fig. 6.11). Chemical modifications (Fig. 6.10) of alloxan (Fig. 6.9) are also diabetogenic in some animal models. All three chemicals therefore, which share some structural similarity, can cause diabetes in animals. Phenobarbitone (Fig. 6.11) and other barbiturates used in human medicine also bear some resemblance to alloxan. Moreover, to my knowledge they have never been investigated for any potential diabetogenic effect. (For ease of

comparison, these chemical structures are illustrated on the next page).

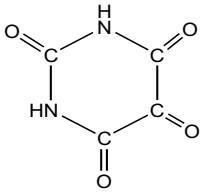


Figure 6.9 Chemical structural formula of alloxan

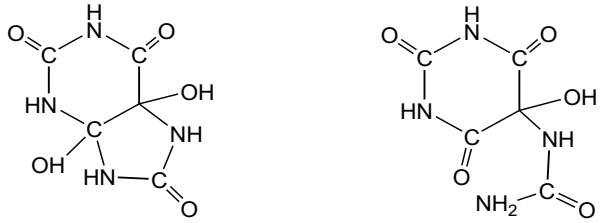


Figure 6.10 Chemical structural formulae of two derivatives of alloxan.

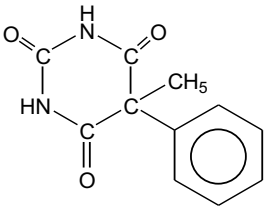


Figure 6.11 Chemical structural formula of phenobarbitone.

Table 6.1 shown below lists *some* of the drugs I believe need to be investigated for their potential to cause diabetes. Further discussion of some of these drugs will be found in chapters 7 and 8.

Antibiotics:

Penicillins (eg. amoxycillin)

Cephalosporins (structural similarity to penicillin).

Erythromycin

Tranquillizers:

Barbiturates (structurally similar to alloxan).

Benzodiazepines

Other drugs:

Syntocinon (synthetic hormone used to induce labour, contains ergometrine).

Ergometrine (used to stop postpartum bleeding).

Paracetamol (analgesic)

Table 6.1 Drugs considered by the author to be potentially diabetogenic.

7

Where *does* Diabetes come from?

> **Overall the genetic and epidemiological publications *consistently* show that at least 60% and perhaps over 95% of diabetes in children would be prevented if the agents could be identified and the prevalence of these factors reduced.**
> Diabetes Epidemiology Research International, 1987

Theories on the origin of diabetes

Before first commencing research involving diabetics in 1984, I thought that diabetes was no more than a problem encountered by elderly persons who were unable to eat sugar. However, from research undertaken during 1984-86 which required taking blood from diabetics to examine a protein called alpha-2-macroglobulin, it soon became apparent that this was not the case. From that time onwards, I was to learn about the physical, emotional and psychological problems suffered by many diabetics during their lifetime. This information related to adults and teenagers, and one can only speculate as to the effects on those diagnosed as babies and children, where the health ramifications are likely to be magnified.

The causes of diabetes, which has now reached epidemic proportions in industrialized countries, remain unknown. However, historically and without solid scientific justification, diabetes was and still is considered to some extent, to be an inherited disorder. There have been various suggestions made throughout the years about the origin of diabetes. It was after all, a condition that was first documented hundreds of years ago. Theories regarding the cause of

the disease have included stress or shock (eg. the death of a relative) and in more recent times, an association with an infectious agent, possibly a virus.

The possible involvement of a virus has been considered, since the peak onset in children often occurs during the winter months and some children reportedly suffered from an upper respiratory tract infection shortly before, or around the time of diagnosis. Following the publication of a report that a virus had been isolated from the pancreas of one child with diabetes, the early 1980s saw a shift in research emphasis towards viral infections as the principal environmental agent of the disease.

Suggestions that particular genetic components are implicated have also been made. Individuals with certain genes are considered to be more susceptible to diabetes, as approximately 95% of Caucasian diabetics have one or both of these components. However, 50-60% of the *normal* Caucasian population also has one or both of these components, yet only 0.25-0.35% of the population develops diabetes. Additionally, some 90% of brothers and sisters of diabetic children who are also genetically vulnerable do not develop diabetes. A study of monozygotic diabetic twins in 1979 revealed that only about 50% of twins both developed diabetes. If particular genetic components were *entirely* responsible for causing diabetes, *both* twins would have been diabetic.

Current theory and research are based on the assumption that diabetes is a genetic disorder. Since the detection of islet cell antibodies in the blood of many newly diagnosed diabetics, the disease is now considered to be an immunogenetic disorder. That is, the body is genetically programmed to produce these antibodies

which are considered responsible for destroying cells within the pancreas, thereby rendering it incapable of producing insulin.

However, there are many determinants other than genetics capable of influencing health within a family. For example, different generations of the same family may be exposed to tobacco smoke and suffer from lung cancer, but due to our present knowledge about the chemicals that smoke contains, chemicals rather than genes are considered responsible for causing the cancer. The genetic constitution of individuals and their lifestyles may be significant only in terms of the *degree* of exposure required before the individual becomes affected.

The results of epidemiological studies show tremendous variation in the incidence of diabetes in children internationally (Figs. 7.1 and 7.2). In Hokkaido, Japan, about 2 out of every 100,000 children have diabetes, compared with approximately 30/100,000 in Finland. In the USA the range is approximately 9-21 per 100,000 children; the average incidence rate in the UK is 7.7 per 100,000. In the USA and Western Europe, the current incidence rate for diabetes is second only to asthma among severe chronic diseases of childhood, with considerable geographical variation. In terms of total numbers, in the United Kingdom some 1600 children under the age of 15 years were diagnosed during 1988, whilst it is estimated that in the USA, some 22,000 children under the age of 15 years developed diabetes during the three years 1978-1980.

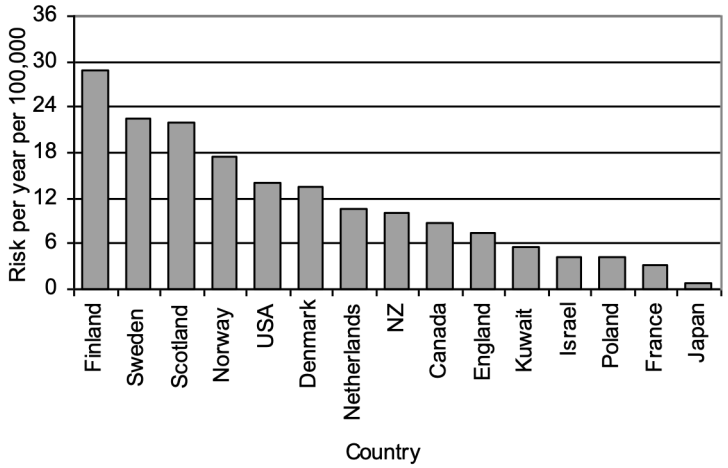


Fig 7.1 Incidence of diabetes in under 15 year olds internationally. (Diabetes Epidemiology Research International, 1985).

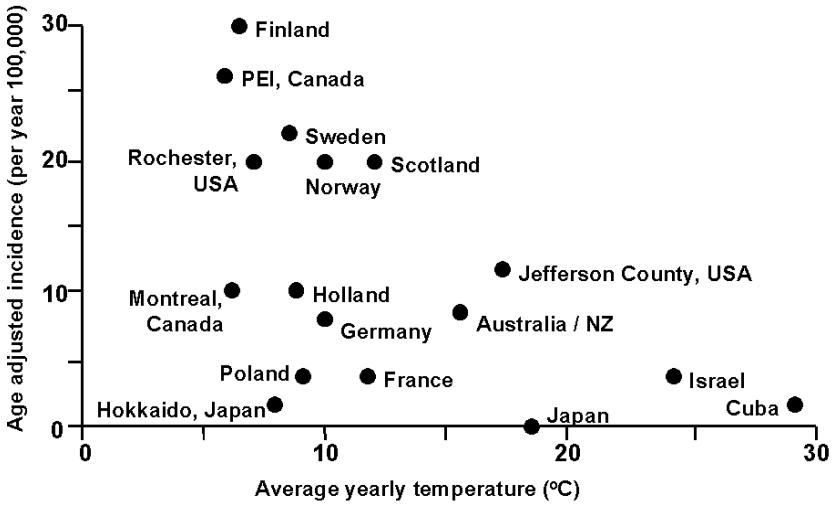


Figure 7.2 Correlation between age-adjusted incidence of diabetes under age 15 years in various areas and average yearly temperature. (Diabetes Epidemiology Research International Group, 1988[5]).

Another thing which points towards environmental agents as being causative is that Japanese children in the USA have four times as great a risk of becoming diabetic as Japanese children in Japan. Jewish and French children in Canada are two to three times more likely to suffer from diabetes than children living in their native country. This suggests it is some factor or factors in the country of residence which confers a degree of risk on the inhabitant, rather than the genetic make-up of the person. Since a person, moving from a country with low incidence to one with a higher incidence is more likely to become diabetic.

Studies of the incidence of diabetes in children in the UK appear to show that there has been a dramatic increase during the past 40 years. Two sets of data shown in Figs. 7.3 and 7.4 show similar upward trends although no firm conclusions can be reached from a comparison of the two sets of data, since the sampling methods for each study varied. However, the number of diabetic children under 5 years diagnosed during 1988(7) was 404, twice as many as were diagnosed during 1976. These figures are from a reporting scheme in operation by the British Paediatric Association and are considered to have ascertained the number of children diagnosed as diabetic with a high level of accuracy. Recent studies have confirmed these dramatic increases.

These statistics suggest the presence of some factor(s) in the environment to which the population has been increasingly exposed, particularly since the 1940's.

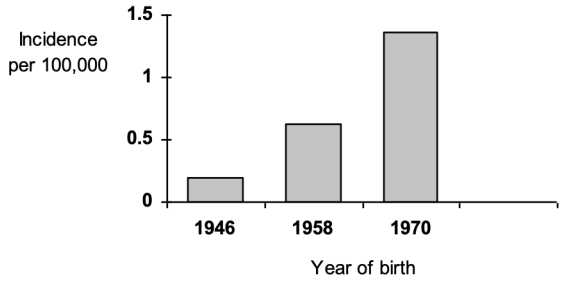


Fig. 7.3 Incidence of diabetes in children in the UK.

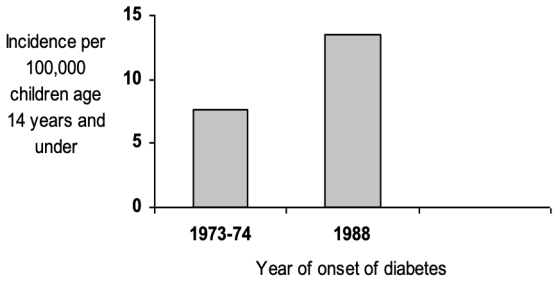


Fig. 7.4 Incidence of diabetes in children in the UK (7 & 8).

The author's research experience of diabetes

During my early research experience of adult diabetics which involved taking blood samples, each patient was asked whether or not they had ever been a regular smoker. This was because I thought the protein I was investigating, may alter structurally under the influence of inhaled tobacco smoke. Hence I wished to separate diabetics into smoking and non-smoking groups.

Interestingly, the research showed that half of the male diabetic patients had stopped smoking between the time diabetes was diagnosed and the time of being bled. A review of the dates when they had ceased smoking indicated that their cessation of smoking

was not due to any policy by the clinic to discourage the habit. This raised the question of whether the earlier smoking habits of these men had anything to do with the onset of diabetes and whether, more generally, if the increase in diabetics might not be related to the increase in smoking after the two World Wars because Government made cigarettes freely available to those in military service.

The possible implication of tobacco smoke inhalation in the onset of diabetes is strengthened by a report concerning diabetes in children in Iceland, and the destruction of insulin-secreting cells of the pancreas in the progeny of mice fed smoked/cured mutton during pregnancy. The study from Iceland reported that the peak incidence of the onset of diabetes occurred in children born during the month of October, and linked early foetal growth to New Year festivities, which in Iceland traditionally involve the consumption of smoked mutton for several weeks. The suggestion was that pregnant women consuming smoked mutton during the early part of pregnancy carried a greater risk of bearing children who were likely to become diabetic.

The fact that men who are heavy smokers produce sperm with chromosomal aberrations, also suggests the possibility that paternal smoking habits preconception could result in an increase in the probability of diabetic offspring. Maternal smoking during pregnancy could also be a factor in the development of the disease.

Since smoked meats and tobacco smoke are rich sources of nitrosamines (chemically reactive species that have been implicated in cancer) the possibility exists that these might also be linked to diabetes. The hypothesis that tobacco smoke may be implicated in diabetes remained unexplored until August 1991, when I undertook a pilot study (essentially a head count) to look at the number of diabetics diagnosed before the age of 23 who were smokers at

diagnosis, or had parents who smoked, and whether the diabetics were breast or formula-fed as babies. Questions on infant-feeding practices were included since there had been unconfirmed reports that babies who were breast-fed, were less likely to become diabetic. It seemed possible that the other studies (which reported that breast-feeding did not protect against diabetes) may have had a high proportion of breast-feeding mothers who had smoked during pregnancy.

The pilot study was designed to explore the possibility of pancreatic damage resulting from exposure to tobacco smoke; chromosomal damage to the sperm of male smokers; damage to the foetus as a result of maternal smoking during pregnancy; and the possible implication of formula-feeding. Since questions concerning maternal tobacco smoke exposure were essentially about *chemical* exposure during pregnancy, a ‘control’ question to determine whether the mother had taken any medicines during pregnancy was also included.

As the study expanded from adult patients attending a hospital Outpatients Department, to include children attending a children's hospital, and adults and children attending a different hospital in the UK, I was surprised to discover that many children had been diagnosed as diabetic before the age of ten years.

The age at onset of diabetes obtained from young adults studied earlier (1984-5), generally showed an age at onset of ten years whereas many children attending the children's hospital had been diagnosed before the age of ten. There are several possible reasons for this: in the past, some very young children might have died before being diagnosed, or might have been referred to teaching hospitals in London, more experienced in the treatment of young children.

However, a consultant at one hospital, where diabetic children were being studied, assured me that during his 15 years of experience at that hospital no child had died from diabetes or because of diabetes not having been diagnosed. This led me to amalgamate all data obtained for diabetics diagnosed before 23 years of age and to compare the age at which they were diagnosed with the *year* of onset. Figure 7.5 incorporating these data, show the decline in the *average* age at onset with each successive decade.

Figure 7.6 shows the plot of the proportion of children against the age at which they became diabetic, for all children attending a hospital in the UK in the early 1990s. The variation in incidence was unexpected, since most epidemiological studies of diabetes in children had shown a gradual increase through the ages, with a peak incidence at 10-13 years. This unusual variation is interesting, since the decline in incidence between birth and 4 years suggested to me there may be an agent responsible for causing diabetes, which children had been subjected to, either in-utero or around the time of birth.

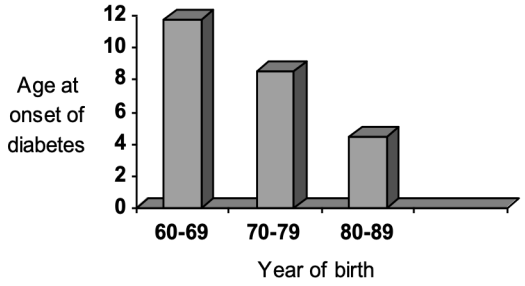


Figure 7.5 Bar graph showing decline in age at onset of diabetes during 1960-1989 in a group of patients less than 23 years of age.

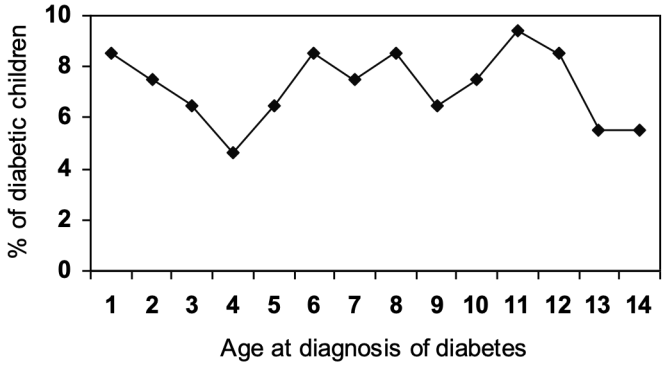


Figure 7.6 Graph showing percentage incidence of diabetes according to age (total number of children in sample = 107) for a population of diabetic children attending a hospital in the UK.

In summary, interviews with some 170 mothers of diabetic children from different groups during the pilot study resulted in the following observations:

Many children had suffered from recurring tonsillitis during childhood - 8 out of 13 of those studied during 1984-5 reported tonsillitis as a serious problem.

Many children suffered from asthma either before or since diagnosis.

Some children suffered from recurrent ear problems and hearing loss.

Some mothers had taken certain drugs to prevent miscarriage, morning sickness, or antibiotics to treat infections during pregnancy or after delivery.

Some children had suffered from prolonged eczema or recurrent exfoliative dermatitis.

Many children had been breast-fed for more than a few weeks.

There was nothing outstanding about the proportion of smoking mothers or fathers.

Some children had always been sickly when compared to other children from the same family, and others had apparently been perfectly healthy before they were diagnosed.

Several mothers felt that their child had shown signs of sub-clinical diabetes for 2-4 years before diagnosis, as they had been very thirsty children, tired easily, experienced 'funny' spells, showed a disinclination to eat, or failed to gain weight.

When asked about significant events during labour, a small number of mothers reported having been induced or administered epidurals. It was observed that in general, children whose mothers had taken drugs during pregnancy or labour (excluding pethidine) generally became diabetic at a lower average age. And the greater the degree of chemical exposure during pregnancy, labour or soon after birth either directly or via breast-milk, the lower the age at onset of diabetes. When mothers of the 20 children who had been diagnosed as diabetic before 3 years were re-questioned and specifically asked whether they had been, administered drugs during labour, 10 were found to have experienced induction, epidurals or both.

Although I had not previously considered the possibility that drugs in use today may cause diabetes, assuming this would have been discovered and the drugs withdrawn from use, it now seemed possible there could be other drugs in common use today that could

cause diabetes. Following reference to medical and drug handbooks, I discovered that children who suffered from tonsillitis or ear problems were very likely to have been exposed to antibiotics. Also, that eczema and exfoliative dermatitis are side-effects of exposure to antibiotics. Asthmatics and sickly children were also probably more likely to visit the doctor and be prescribed drugs. It was at this stage that I began to consider the possibility that drug exposure was the common factor.

Further studies were undertaken to look at the drug exposure of the diabetic child in-utero, during birth and from birth to diagnosis of the disease.

1. RESULTS OF STUDIES TO LOOK AT THE HEALTH OF DIABETIC CHILDREN PRE-DIAGNOSIS OF DIABETES

(a) Results of a study of diabetic children diagnosed before 12 years and attending a hospital in the UK.

Table 7.1 shows the drug exposure profile of 35 diabetic children pre-diagnosis of diabetes and attending a hospital in the UK, whose parents agreed to participate in the study involving the examination of their child's medical records. It was explained to some parents who had not participated in the earlier pilot study, that the study was investigating the health of their child pre-diagnosis of diabetes.

It is unlikely that the group of parents responding would have been biased towards children with in-utero, birth or childhood drug exposure, as parents did not know that drugs were under investigation. Table 7.2 shows the percentage of children who were exposed to drugs in-utero, at birth or around the time of birth and the average age at onset of diabetes.

Table 7.2 does not include those children who were exposed to drugs that were administered to either mother or baby after delivery, for reasons other than postpartum bleeding (eg. antibiotics for baby due to meconium aspiration). The seemingly high incidence of chemical exposure in this group of children may be explained by a greater proportion of mothers of such children agreeing to the examination of their child's health records. However, since many children who were not involved in this part of the study but had participated in the pilot-study examining the mode of infant feeding, had also been induced, this is unlikely to be the case. The percentage of children in the study who were induced was 32% (excluding the child born overseas) compared with a rate of 18% for the S.E. Thames region[9] in 1989.

	Drug exposure	**No drug exposure**
Number of children (%)	**65**	35
Average age at onset (years)	**4.9**	6.5

Table 7.2 Number of children and average age at onset of diabetes in those who were reported to have been exposed to drugs in-utero or at birth (excluding pethidine since this is commonly administered in the UK).

Despite the fact that not all diabetic children attending the hospital were in the study and that the value of the data relies on accurate reporting by mothers, if anything, the proportion of children who were exposed to drugs either in-utero or during labour, is likely to be under-represented. Since it is possible the mother had forgotten about a single course of drugs she may have taken during pregnancy or been administered during labour. The proportion of mothers in this group

who smoked for more than the first 6 weeks of pregnancy was 21% and the portion of fathers who were smokers at the time of conception was 38%.

(b) Results of studies of diabetic children diagnosed before either 3 or 4 years and attending a hospital in the UK.

Tables 7.3a and 7.4 show the drug exposure profiles of children diagnosed before the age of either three or four and attending a hospital in the UK. In one region, all parents agreed to participate in the study; in the other, some 80% of patients were studied. Percentage capture of patients is important in epidemiological studies, as the higher the percentage, the less chance of bias in the study. Age was the only selection criterion used and within these two groups of patients, some 58% had a history of in-utero or drug exposure (*excluding pethidine*) during labour.

Table 7.3b shows the drug exposure profile of a child diagnosed at 6 years. This child's parents were approached about the study, as their child was thought to have been under 4 years at diagnosis. As this was the only child who did not fit the age criteria, but whose parents had agreed to the study, I decided to examine the health records. This record not only shows the kind of profligate prescribing that can exist but also, if antibiotics are implicated in the onset of diabetes, that it may take many exposures to these drugs before there has been sufficient damage for diabetes to become clinically apparent.

(c) Results of studies of diabetic children diagnosed before 3 years obtained from various regions in the UK.

Tables 7.5 and 7.6a show the drug exposure profiles of children diagnosed diabetic before the age of three, obtained from local diabetic groups and *The Daily Telegraph* newspaper readers in the UK, respectively. In the first group, parents were informed that the study was to look at the health of diabetic children pre-diagnosis, with no mention of drug exposure being evaluated. *The Daily Telegraph* respondents had read that I was looking at a possible link between diabetes and drug exposure, although the publication incorrectly stated that *rarely* prescribed drugs were being considered and no mention was made that in-utero exposure was being considered. Although sample numbers are small, *both* groups had a high proportion (69%) of children who had experienced drug exposure either in-utero or during labour.

Table 7.6b which summarizes the drug exposure of a child diagnosed as diabetic at eleven years, reveals very little history of drug exposure after birth. However, the child's drug exposure from conception reveals a pattern similar to that of some other diabetic children in the study, in that antibiotic exposure was experienced in-utero, and oxytocin and/or ergometrine was administered to the mother during or after labour. If antibiotics and oxytocin and/or ergometrine (drugs routinely used to control postpartum bleeding) are implicated in the onset of diabetes, these records show that it may take many years before clinical diabetes becomes apparent.

All children who took part in the study have been included in the result tables shown. Health records of mothers were not examined and it is quite likely there are some drugs these mothers were exposed to during labour which have not been listed. Following advice

of the MRC Epidemiological Unit, Southampton, UK no information regarding vaccinations was obtained. Their opinion was that this was unnecessary as most children of this era had been vaccinated.

That diabetes could manifest itself many years after exposure to potentially diabetogenic chemicals is highly likely if drugs were administered to a child at a very young age and caused the destruction of only a proportion of the insulin producing cells of the pancreas. The disease would manifest itself when the demand for insulin increased with age, to a level which required more insulin than the pancreas was able to produce. The younger the age at which exposure to potentially diabetogenic drugs takes place, the greater the potential for damage since organs are immature (and may therefore take longer to remove toxic chemicals from the body) and smaller in size.

Before clinically recognisable diabetes may be diagnosed, children are very likely to have been suffering from diabetes in a sub-clinical manner. This, like non-insulin dependent diabetes in adults, may only be diagnosed following an oral glucose tolerance test. During this time, it is likely that many children may suffer from fatigue, irritability, cold and flu-like symptoms, visual problems, headaches or fungal infections as their average blood glucose levels would be above normal.

Tables 7.7-7.11 summarize the results of tables 7.1 and 7.3-7.6 with respect to the drug exposure of diabetic children in-utero or during labour.

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
DB001	12 yrs	None	None	Breast 1wk	Amoxil x3 Ampicillin x3 Erythromycin x1 Septrin x5 Penicillin-V x5	None
DB002	10 yrs	None	None	Uncertain	Amoxil x 1 Ampicillin x3 Erythromycin x4 Penicillin-V x1 Septrin x5	None
DB003	8 yrs	Not known	Not known	Uncertain	Amoxil x10 Septrin x2	None
DB004	3 yrs	None	**Epidural**	Breast 4mths	Amoxil x1	None
DB005	8 yrs	Incomplete	Records			
DB006	3 yrs	**Daraprim to protect from malaria**	**Induction tried 2wks before birth**	Breast 6wks	**Daraprim** (antimalarial) Amoxil x1 Ampicillin x1	None
DB007	1 yrs	None	**Induced Epidural**	Breast 11mths	No record of antibiotics having been given	Great-grandfather
DB008	2 yrs	Not known	None	Uncertain	Erythroped	Great-grandfather

Child was born with an undeveloped kidney and later diagnosed with celiac disease concurrently with diabetes.

Table 7.1 Diabetics diagnosed before 13 years of age and attending a hospital in the UK.

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
DB009	1yr	None	None	Breast 6mths	Amoxil x3 (first at 3.5mths). Phenergan Promethazine	Mother' s uncle and cousin
DB010	9yrs	None	None	Breast 1yr	Erythromycin x4 (first at 7yrs) Phenergan	None
DB011	11yrs	**Steroid injections at 3mths** due to a threatened miscarriage	**Induced**	Breast 2mths	Amoxil x4 Erythromycin x2 Penicillin-V x6 Phenergan x4 Septrin x4	Brother (at 16yrs having had 21 courses of antibiotics)
DB012	12yrs	None	None	Breast 2wks	Erythromycin x2 (first at 6mths) Penicillin-V x2 Septrin	None
Very few prescriptions for antibiotics recorded and none in the year of diagnosis despite mother reporting on questionnaire that for a bad throat in the year diabetes was diagnosed, the ' usual' penicillin was prescribed.						
DB013	6yrs	None	**Injection for removal of placenta**	Breast 3wks	No record of antibiotics being prescribed	Grandmother at 50-60yrs
Ergometrine is a drug that would be used to assist removal of a placenta after delivery.						
DB014	8yrs	**Intal** (sodium cromoglycate) couple of times	**Induced**	Breast 4mths	Amoxil x11 (first at 8 mths). Cephalosporins x2 Erythroped x3 Penicillin-V	First cousin

Table 7.1 *(continued)* **Diabetics diagnosed before 13 years of age and attending a hospital in the UK.**

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
DB015	5yrs	None	**Induced Anti-emetic** to prevent vomiting	Breast 8 mths	Ampicillin x3 (first at 1yr 6mths)	None
Child has been treated for delayed speech and language development.						
DB016	4yrs	**Phenytoin Phenobarbitone** (tranquillizers)	None	Formula	Ampicillin (11 days before diagnosis)	Grand-mother at 40yrs
Baby reported by paediatrician after birth to be constantly sleeping; drank a lot from 2-3 yrs onwards.						
DB017	10yrs	**Oedema tablets** at 6wks.Thyroidectomy at 3wks. 2 blood transfusions. **Thyroxine**	None	Formula	Amoxil Ampicillin x4 Septrin x3 Fluocloxacillin	None
DB018	6yrs	None	None	Breast 1mth	Mother had rubella vaccination and steroid birth-control injection at 1 wk post-partum. Child: Amoxil x3, Ampicillin x3, Erythromycin x2, Pen-Vx2 Phenergan x2, Septrin x2	None
Mother described baby as being unsettled immediately from birth, as crying a lot at night and hard to handle until 2yrs 6mths.						

Table 7.1 *(continued)* **Diabetics diagnosed before 13 years of age and attending a hospital in the UK.**

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
DB019	4yrs	None	**Induced**	Breast 3wks	Amoxil x3 Erythromycin x3 Pen-V	None
DB020	6yrs	None	Not known	Uncertain	Amoxil x2 Erythromycin x6 Pen-V x4	Not known
DB021	6yrs	**Antibiotic at 32/40 for chest infection (Pen-V)**	**Syntocinon Epidural x2 Syntometrine Ergometrine** on 9th post-natal day	Breast 9mths	Amoxil x2 (first at 4yrs) Augmentin Merbentyl x2 Pen-V Septrin x1	Mother at 40yrs Grand-mother
DB022	8yrs	None	None	Breast 5mths	Amoxil x2 Erythromycin x4 Phenergan x2	Uncle in 20s
DB023	1yr	None	**Ergometrine**	Formula	Amoxil at 6.5mths	Grand-mother
Mother reported that no drugs were used during labour, but the child' s health records revealed that ergometrine had been given. The mother said she did not take any drugs during pregnancy because ' they can deform the baby' .						
DB024	2yrs	**Liquid for heartburn**	**Drip** (to induce?)	Formula	Amoxil x2 (first at 7mths) Ampicillin	None
Mother reports this as being the worst delivery she had ever had, with reference to the drip, she said they ' turned it up to get it over with' .						

Table 7.1 *(continued)* **Diabetics diagnosed before 13 years of age and attending a hospital in the UK.**

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
DB025	1yr	**Antibiotic for ear infection**	**Epidural Injection to bring back contractions** (induced)	Breast 8days	Amoxil (at 1yr 7mths)	Grand-father
DB026	2yrs	**Drugs for bladder infection at 3-6mths.** Paracetamol	None	Breast 6wks	Amoxil Cephalozporinz x3 Erythromycin Salbutamol x2	None
DB027	3yrs	**Blood pressure problems** (not known if treated)	None	Formula	Cephalosporin	None
DB028	1yr	None	**Induced Epidural *kept in for 2 days and topped up***	Breast 2mths	Ampicillin at 5mths	None
DB029	2yrs	None	**None** (born at home)	Uncertain	Pen-V (at 4mths) Amoxil x3 (in first yr) Cephalosporin x1	Not known
DB030	6yrs	None	**Induced by drip**	Breast 1wk	Medical records for 1st yr missing. Piriton	Aunt

Child was second baby out of identical twins, and was jaundicd during the neonatal period. Being the second of the twins being born, exposure to the induction drug would have been greater.

Table 7.1 *(continued)* **Diabetics diagnosed before 13 years of age and attending a hospital in the UK.**

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
DB031	10yrs	None	**Induction attempted with Prostin pessary and injection. Drugs to stop bleeding** (ergometrine?)	Breast 1wk	Penicillin, gentamycin & cloxacillin intravenously at 8 wks. Amoxil x7	None
DB032	8yrs	None	**Induced Epidural**	Breast 4wks	Erythromycin x2 Merbentyl	None
Due to diarrhoea 36hrs after the first course of Amoxil was started, it was stopped. However, it was prescribed again 3yrs later.						
DB033	4yrs	None	**Induced**	Formula	Amoxil x2 Septrin Penidural Erythromycin x2	None
DB034	4yrs	**Lorazepam** (benzodiazepine tranquillizer)	**Induced Epidural**	Formula	At boarding school No records seen	None
DB035	2yrs	Not known Born overseas	**Induced Epidural**	Uncertain	Incomplete records Born overseas	None
DB036	10yrs	**Penicillin drug at 8wks** for throat infection	Not known Normal delivery	Formula	Amoxil x4 (first at 1yr 1mth)	Grandmother

Table 7.1 *(continued)* **Diabetics diagnosed before 13 years of age and attending a hospital in the UK.**

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
P001	3yrs	None	**Induced**	Breast 4mths	Amoxil x2	Father at 20yrs
Father suffered from febrile convulsions from 2-8 yrs, tonsillitis (tonsils removed at 8yrs) and frequent colds pre-diagnosis.						
P002	3yrs	Not known	None	Formula	Erythromycin at 6wks Septrin	None
P003	2yrs	None	Don' t know Forceps delivery	Formula	Penicillin & flucloxacillin at 2wks for burns. Amoxil at 18mths	None
P004	1yr	None	**Induced. Drug in drip following blood loss during delivery** (ergometrine?)	Formula	Chloral at birth to sedate baby	None
P005	3yrs	Not known	**Induced Epidural**	Breast 5wks	Ampicillin at 2.5yrs Erythromycin ?Phenergan	None
P006	2yrs	**Amoxycillin at 6mths for 10 days**	**Epidural**	Formula	Mycostatin oral at 2wks. Amoxil at 3.5mths, 7mths, 8mths then for coughs and colds	None
All medication received in the USA, only dates for first 3 exposures of Amoxil provided.						

Table 7.3a Drug exposures of children diagnosed with diabetes before 4 years of age and attending a hospital in the UK.

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
P007	2yrs	None	None	Formula	Apart from vaccination records, no records found pre-diagnosis	None
P008	2yrs	None	None	Formula	Amoxil	Father at 24yrs
P009	1yr	Occasional paracetamol	None	Breast 4mths	None (records appear complete)	Great-grandmother
P010	1yr	None	**Injection to dilate cervix** (oxytocin?)	Breast 9wks	Amoxil Erythroped	Sister
P011	2yrs	**Possible anti-histamine for hayfever**	**Induced Epidural**	Breast 10mths	Amoxil x2 from 1.5yrs	None

Table 7.3a *(continued)***Drug exposures of children diagnosed with diabetes before 4 years of age and attending a hospital in the UK.**

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
P012	6yrs	**Rosemary leaf tablets** (available from health food shops)	None	Breast 3wks	**Amoxil** at 4wks, 5wks, 3mths, 5mths, 9mths, and a further 5 courses. **Erythroped** at 5mths, 10mths, and a further 5 courses.**Ampicillin** x2, Maxolon, Phenergan, Merbentyl **Keflex**, **Bactrim** (*Total of 21 courses of antibiotics taken)*	None

Table 7.3b Drug history of child from the UK diagnosed as diabetic at 6yrs of age.

S001	1yr	None	None	Formula	Doctor refused access to records	None
S002	2yrs	None	**Drip at start of labour**	Formula	Ampicillin at 5mths and 8mths. No records from 8mths to 2yrs 3mths	Mother' s cousins
S003	2yrs	None	**Epidural x2**	Breast 6mths	Amoxil at 5mths. Otosporin ear drops. Phenergan for travel	Grandad' s uncle
S004	1yr	**Oxazepam** (benzodiazepine tranquillizer at 5mths)	None	Formula	Pen-V, Septrin, Lomotil, Phenergan x2, Ceporex, Ventolin, Erythromycin	Uncle 2nd cousin Great aunt

Baby operated on at 1mth of age for pyloric stenosis with the removal of a benigh tumour. Benzodiazepines can cause foetal harm when administered to pregnant women.

Table 7.4 Diabetics diagnosed before 3 years of age and attending a hospital in the UK.

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
S005	2yrs	None	**Epidural**	Formula	Amoxil 1mth prior to diagnosis	None
S006	2yrs	**Amoxil probably x2 for sinus problems**	None	Formula	**Intravenous antibiotics at birth.** Amoxil x2	None
S007	1yr	None	**Epidural**	Breast 2wks	**Mother on antibiotics after birth. Baby also on antibiotics after birth.** ***No*** drugs from GP despite 10 visits.	None
The author considers this case to contain extremely valuable data as drugs were given only during labour and immediately after birth.						
S008	1yr	None	Not known	Breast 2yrs	**Mother on antibiotic 1 mth after birth** (still breastfeeding). Amoxil x5, first at 3mths	Father at 21yrs Great-grandfather

Table 7.4*(continued)* **Diabetics diagnosed before 3 years of age and attending a hospital in the UK.**

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
L001	1yr	Not known	**Induced**	Breast 5mths	None	Uncle
This baby had an apgar score of 3 when born and was respirated for 2 minutes.						
L002	1yr	**Natracalm (herbal remedy** for stress, contains alkaloids, sedative)	None	Breast 10mths	Amoxil x3 (first at 1mth, last course 3days prior to diagnosis). Mother took paracetamol every 4hrs for 1wk after delivery. Vallergan	Grand-mother
This baby was born with a 5cm raised strawberry birth-mark which was extremely prominent at 3yrs.						
L003	1yr	None	**Syntometrine** after delivery (contains **oxytocin and ergometrine)**	Breast 13mths	Amoxil x1 at 3wks	Grandfather
L004	1yr	None	None	Breast 9mths	**Mother on antibiotic for mastitis at 1-2 wks post-partum.** Possible penicillin 6mths pre-diagnosis	Not known
L005	1yr	None	**Induced with Syntocinon**	Breast 6mths	Possible course of antibiotics x1 in USA age 1yr	None
L006	9mths	**Antibiotics x1 for chest problem**	**Induced**	Breast 4mths	Amoxil at 7mths	None

Table 7.5 Diabetics obtained from local diabetic groups in the UK. The only selection criteria used was the onset of diabetes before 3 years of age.

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
T1	2yrs	**Asacol 1200mg daily for ulcerative colitis**	None	Breast 7mths	Asacol and Prednisolone from breast milk? Steroid injection in knee due to JRA at 2yrs. Ibuprofen and naprosyn	None
This child was also diagnosed with Juvenile Rheumatoid (JRA) at 2 years of age. It is the author's opinion that Asacol may be implicated in the onset of this child's JRA.						
T2	16mths	**Progesterone injections weekly to prevent miscarriage**	**Epidural**	Breast 6wks	**Mother took penicillin drugs after delivery** for retained placenta. Amoxil at 10mths for cold	Cousin at 10yrs
T3	10mths	**Antibiotic – for oral infection at 8wks**	None	Breast 9mths	**Antibiotic in breast milk** due to mother's mastitis at 2wks. Nystatin Amoxil	None
T4	2yrs	**Septrin for 1 wk**	**Induced**	Breast 7mths	Amoxil x4 for throat and upper respiratory tract infections	None
T5	12mths	**Maxolon for gastroenteritis**	None	Breast 8mths	None	None

Table 7.6a *The Daily Telegraph* respondents with diabetic children diagnosed before 3years of age.

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
T6	1yr	**Paracetamol** daily – average x2 per day for headaches from nocturnal grinding of teeth	None	Breast	**Paracetamol** from breast milk? Average 2 per day taken by mother while breast-feeding	None
T7	2yrs	None	None	Breast 1wk	Ampicillin Erythroped Salbutamol Septrin Vallergan	None
T8	1yr	None	None	Breast 6wks	Child 6wks premature swallowe mucus – treated with nasal ephedrine and ?eyen? *for 5 days after birth.* Amoxil x3 (last course just before diagnosis) Penicillin Ventolin x2	None

Table 7.6a *The Daily Telegraph* respondents with diabetic children diagnosed before 3years of age

Code	Age at onset	Drugs during pregnancy	Drugs during labour	Neonatal feeding	Drugs taken by child pre-diagnosis	Family history of diabetes
T9	2yrs	None	Not known	Formula	Penicillin at 3.5mths Bactrim (co-trimoxazole) at 10mths. Distaclor (cefaclor)	Niece at 20yrs
T10	2yrs	None	**Induced**	Breast 4 days	Ampliclox Amoxil Erythromycin x2 aged 2yrs	None

Table 7.6a *(continued)* ***The Daily Telegraph*** **respondents with diabetic children diagnosed before 3 years of age.**

T11	11yrs	**Antibiotic for sinusitis**	**Epidural Drugs for 2 haemorrhages**	Breast 4 wks	Amoxil Erythroped Merbentyl	None

Ergometrine is the drug likely to have been administered for post-partum haemorrhage. In view of this child having been prescribed only two courses o antibiotics pre-diagnosis, it is the authors opinion that a child exposed to antibiotics in-utero and /or drugs such as ergometrine during labour is possibly at higher risk of diabetes.

Table 7.6b ***The Daily Telegraph*** **respondent with a child diagnosed with diabetes at 11 years of age.**

Code	Family History	Drugs taken by mother during pregnancy, labour or immediately after delivery if breast-feeding
DB001	None	None
DB002	None	None
DB003	None	None
DB004	None	**Epidural**
DB005		Records incomplete
DB006	None	**Induction** tried 2 wks before birth
DB007	Great grandfather	**Induced. Epidural**
DB008	Great grandfather Cousin	None
DB009	Cousin	None
DB010	None	None
DB011	Brother	**Induced**. **Steroid injections** during pregnancy to prevent miscarriage
DB012	None	None
DB013	Grandmother	**Injection for removal of placenta**
DB014	Cousin	**Intal during pregnancy. Induced**
DB015	None	**Induced. Drug to prevent vomiting**
DB016	Grandmother	**Phenobarbitone and Phenytoin** during pregnancy
DB017	None	**Drug for oedema (diuretic?) and thyroxine** during pregnancy
DB018	None	None
DB019	None	**Induced**
DB020		Records incomplete

Table 7.7 Summary of in-utero and birth drug exposure (excluding pethidine) of diabetic children attending a hospital in the UK.

Code	Family history	Drugs taken by mother during pregnancy, labour or immediately after delivery if breast-feeding
DB021	Mother	**Induced. Syntometrine. Penicillin-V for respiratory infection.**
DB022	Uncle	**None**
DB023	Grandmother	**Ergometrine**
DB024	None	**Induced.** Liquid for heartburn
DB025	Grandfather	**Antibiotic for ear infection**. **Epidural. Injection to induce.**
DB026	None	**Antibiotic for bladder infection. Paracetamol**
DB027	None	None
DB028	None	**Induced. Epidural**
DB029		None
DB030	Aunt	**Induced**
DB031	None	**Induced with pessary and injection. Drugs to stop bleeding** (?ergometrine)
DB032	None	**Induced. Epidural**
DB033	None	**Induced**
DB034	None	**Induced. Epidural. Lorazepam** (benzodiazepine tranquillizer)
DB035	None	**Induced. Epidural**
DB036	Grandmother	**'Penicillin'** drug at 8 wks for throat infection during pregnancy

Table 7.7 *(continued)* Summary of in-utero and birth drug exposure (excluding pethidine) of diabetics attending a hospital in the UK.

Code	Family history	Drugs taken by mother during pregnancy, labour or immediately after delivery if breast-feeding
P001	Father	**Induced**
P002	None	Don't know
P003	None	Don't know
P004	None	**Induced. Intravenous drug** following haemorrhaging (?ergometrine)
P005	None	**Epidural**
P006	None	**Amoxycillin** for 10 days during pregnancy. **Epidural.**
P007	None	None
P008	Father	None
P009	Sister	None
P010	Sister	**Injection to dilate cervix.** (?oxytocin)
P011	None	**Induced. Epidural.** Possibly antihistamines.

Table 7.8 Summary of in-utero and birth drug exposure of children diagnosed as diabetic before the age of four and attending a UK hospital.

Code	Family history	Drugs taken by mother during pregnancy, labour or immediately after delivery if breast-feeding
S001	None	None
S002	Distant	**Drip at start of labour**
S003	Distant	**Epidural x2**
S004	Distant	**Serenid (tranquillizer**) during pregnancy
P005	Distant	**Epidural**
S006	None	**Amoxycillin** (probably x2 for sinusitis)
S007	None	**Epidural**
S008	Father	None

Table 7.9 Summary of in-utero and birth drug exposure of children diagnosed as diabetic before the age of three and attending a UK hospital.

Code	Family history	Drugs taken by mother during pregnancy, labour or immediately after delivery if breast-feeding
T1	None	**Asacol 1200mg daily for ulcerative colitis**
T2	Cousin	**Progesterone injections weekly to prevent miscarriage**
T3	None	**Antibiotic for oral infection at 8wks**
T4	None	**Septrin. Induced**
T5	None	**Maxolon for gastroenteritis**
T6	None	**Paracetamol on average 1000mg *daily*.**
T7	None	None
T8	None	None
T9	Niece	None
T10	None	**Induced**

Table 7.10 Summary of in-utero and birth drug exposure of respondents of the *The Daily Telegraph,* England with children diagnosed as diabetic before the age of three.

Code	Family history	Drugs taken by mother during pregnancy, labour or immediately after delivery if breast-feeding
L001	Uncle	**Induced**
L002	Grandmother	**Natracalm** (herbal remedy containing alkaloids)
L003	Grandfather	**Syntometrine** (oxytocin and ergometrine)
L004	None	None
L005	None	**Induced** (Syntocinon)
L006	None	**Antibiotics for chest infection. Induced**

Table 7.11 Summary of the in-utero and birth drug exposure of children diagnosed as diabetic before the age of three and attending local diabetic groups in the UK.

Tables 7.12 – 7.20 provide full health profiles of some of the diabetic children studied. All names used are fictitious and prescriptions for antibiotics appear in bold print. These records will enable readers to see how diabetic children often suffer from common complaints such as coughs, tonsillitis and otitis media pre-diagnosis of diabetes and how further and sometimes new health problems often occur within a few weeks of a prescription for an antibiotic.

Case A1: Alexis born 1983
Diagnosed as diabetic at 8yrs; induced at birth; breast-fed for 4 months; neither parent had ever smoked. There is no family history of diabetes.

Date	Prescription	Condition treated
1983		Health visitor to call
1983		Eczema
1983	**Amoxil**	Otitis media. In pain
1983		Ears ok
1983	**Amoxil**	Earache, R ear red, L discharge
1984	**Amoxil**	Cough, cold, sticky eye
1984	Chloromycetin	
1984		Chest clear
1984	**Pen-V**	Sub-acute tonsillitis. L ear drum red
1984	**Amoxil**	R otitis media
1984		Viral URTI
1984	**Amoxil**	Has been away, using Amoxil for 4days. *Rash?* Rubella? Continue Amoxil
1984		Rash when hot. Allergic eczema?
1984	**Erythroped**	Chest clear
1986	**Amoxil**	Bad earache. Slight worry about hearing
1986		Pain?
1986	Lactulose	Still constipated
1987	Chloromycetin	Conjunctivitis. Gland L neck
1987	**Cephorex**	Tonsillitis. L otitis media
1987	**Distaclor**	Laryngitis. Croup
1987	Dimotane	Hoarseness? Ear drum red
1987	**Erythroped**	L otitis media
1987	**Amoxil**	R otitis media
1987	**Amoxil** Dimotane	Tonsillitis. Bilateral sub-acute otitis media.
1988		Inward gait
1988		Headache 2 days ago. ?associated with vomiting. On examination very well
1988	**Amoxil**	L otitis media

1989	**Amoxil**	
	Bactroban	
1990	**Amoxil**	R otitis media
1990	Ventolin	Cough at night ?on exertion
1990		Stop Ventolin. Cough, throat mildly inflamed.
1990	**Pen-V**	Tonsillitis
1990	**Amoxil**	R otitis media. Pharyngitis
		Thirst++. Blood sugar 35.5mmol

Table 7.12 Case A1. Health records of a diabetic child.

Discussion

Alexis received 19 courses of antibiotics before being diagnosed as diabetic at the age of 8 years. This child, who was induced at birth, was brought to the doctors eight months after birth suffering from otitis media. After three courses of Amoxil, she is brought to the doctors with a chest problem. In the month following a prescription for erythromycin, she returns to the doctors suffering from tonsillitis. In July 1984, after four days of being administered Amoxil, she presents with a rash which does not appear to be suspected by the doctor as possibly being related to the use of Amoxil.

During May 1987, Alexis was prescribed a cephalosporin for tonsillitis and otitis media and returns to the doctors two weeks later with laryngitis and croup, for which another cephalosporin was prescribed. Following a course of Amoxil in November 1987, she returns to the doctors in December with tonsillitis. These records show that there was nothing unusual about the health of Alexis before she was diagnosed as diabetic, except that she suffered from conjunctivitis and more frequently occurring episodes of tonsillitis and otitis media which were treated with antibiotics.

Her mother reported that "*from the age of 5, she had a number of episodes, much like a migraine. She would complain of a headache, vomit and then fall asleep. This would happen only two or three times*

a year. In the four months before diagnosis, she was ill with a blocked nose, wheezing and general cold-like symptoms."

Case A2: Douglas born 1980
Diabetic diagnosed at 9 years; mother smoked 10 per day during pregnancy; no drugs reported having been administered during delivery; baby beast-fed solely for one year. There is no family history of diabetes.

Date	Prescription	Condition treated
1981		Area of warts
1981		Diarrhoea and vomiting
1981	Hydrocortisone	Impetigo
1982		Advice
1983		2 stitches removed
1983		Measles
1984		Cough
1984		Seems well
1985		No spasms now
1985	?gel	
1985	?syrup	
1987	Phenergan	
1988		Viral tonsillitis
1988	**Erythromycin**	L otitis media
1988	**Erythromycin**	URTI
1989		Painful heels
1989	**Erythromycin**	
		Viral, red throat
1989		Not purulent
1989	**Erythromycin**	
1989		Excessive thirst, sore throat, sleepy. Admit

Table 7.13 Case A2. Health records of a diabetic child.

Discussion

Douglas visited the doctors infrequently during the first seven years of life. Following the first recorded prescription for an antibiotic, he received four prescriptions for erythromycin during 17 months, and became diabetic three months after the last prescription.

Case A3: Stephanie born 1978

Diagnosed as diabetic at 8 years; neither parent smoked; normal delivery without drugs apart from pethidine; baby breast-fed for 18 months. There is *no* family history of diabetes.

Date	Prescription	Condition treated
1978	Ephedrine nasal drops	Stuffy nose, bringing up feeds
1978	**Amoxil**	Cough, wheezing
1978	Phenergan	
1978	**Amoxil**	Wheezing
1978	Phenergan	
1978		Looks well
1978	**Septrin**	
1979	Phenergan **Amoxil**	Teething
1979	Actified	Cough and pulling ears
1979	**Septrin** Sudafed	Cough
1979	**Amoxil**	Cough, wheezy chest
1979	**Amoxil**	
1979		Better
1979	Actified	Cough
1980	**Amoxil** Actified	Cough, vomiting, thick mucus in throat
1980		?german measles. No glands in neck
1981	**Amoxil**	drum
1982	**Amoxil**	
1983	**Amoxil**	*Viral*. Barking cough, very snuffly. Asymptomatic. Well
1983		(no notes made)
1983		Mumps
1984		Chickenpox
1984	**Flucloxacillin** Phenergan	Infection. ?abscess
1985		Finger
1985	**Amoxil** Phenergan	Cough

Table 7.14 Case A3. Health records of a diabetic child.

Discussion

Stephanie was admitted to hospital in January 1987 after a few weeks of increasing thirst and frequency of urination. Before being diagnosed as diabetic, she received 12 courses of antibiotics. The

first, Amoxil, was given at just four months of age. Amoxil was inappropriately prescribed for a viral condition in 1983.

Could it in fact have been the exposure to pethidine during labour that caused Stephanie to have a stuffy nose, which resulted in Ephedrine a bronchodilator being prescribed? This in turn, although given in the form of nose drops, would find its way into the blood stream and could have acted as a lung irritant causing her to cough and wheeze, particularly as she was only 3 weeks old. The first course of Amoxil at 4 months may have sown the seeds for a repetitive cycle of coughing and wheezing followed by antibiotic prescriptions. These records show that apart from coughs, wheezing and pink eardrums, Stephanie did not suffer from any unusual health problems before diabetes was diagnosed.

Case A4: Mike born 1976
Diagnosed as diabetic at 11 years. Injections and a drip are reported to have been given during labour; the drip was thought to have been given to induce delivery. Mike's mother smoked up to 10 cigarettes per day during pregnancy; his father was a smoker at conception. There is no family history of diabetes.

Date	Prescription	Condition treated
1976		TB contact, X-ray
1976	?	
1978	**Pen-V**	URTI
1978	Hydrocortisone cream	*Allergic rash*
1978	**Erythroped**	Chest
1978	Polytar	
1978	?	
1979	**Erythroped**	Measles. T 102ºF
1979		Scalded
1979	**Septrin**	URTI
1979	**Septrin**	R earache. Sore throat
1980		Ears
1980	**Septrin**	Tonsillitis
1980	**Ampicillin**	Measles
1980	**Ampicillin**	
1980		Pyrexial, mild otitis media
1980	**Amoxil**	L submandular
1980		To continue Amoxil

1980		Stitches removed
1981		Refer ENT *?hearing loss*
1981	Chloramphenicol drops	
1981		*Sleepy, lethargic, fever*
1982	Chloramphenicol drops	
1982		*Rash*. Dermatitis
1983	**Erythroped**	Pain in eyes
1984	**Septrin**	Otitis media
1984		Better
1984	**Septrin**	Sore throat
1984		Rash on face. ?viral ?german measles
1984	Calamine lotion	Chicken pox
1985	**Pen-V**	Dental infection
1985		Cough
1986	**Erythroped**	
1986	**Penbritin**	'Cold', cough
1986		Abdominal pain
1986		Verruca
1987		Nausea, polyuria, polydypsia

Table 7.15 Case A4. Health records of a diabetic child.

Discussion

Mike received 15 courses of antibiotics over a 10 year period. Points of interest include the following: erythromycin prescribed in February 1979 is not known to have any therapeutic value in the treatment of measles; the antibiotic ampicillin was prescribed in May 1980, again for measles. It is possible that the course of Septrin prescribed during March 1980 caused the rash reported in May and diagnosed as measles, which Mike had already suffered from in February 1979. Following another prescription for Septrin in March 1984, the rash Mike returned to the doctors with, just two days later, does not appear to have been considered as a side-effect following exposure to Septrin and is instead queried by his doctor as possibly being due to german measles.

Mike also suffered from lethargy, fever, a rash and painful eyes after using chloramphenicol eye drops in 1981, which could have been caused by the drug (see chapter 5). As other children's records

have already shown, the most common health problems typically preceding diabetes are sore throats, tonsillitis, coughs and ear problems. As many antibiotics are toxic to the ears and lungs, it is not surprising that Mike presents with these complaints.

Case A5: Samantha born 1976
Diagnosed as diabetic at 12 years. Apart from pethidine, no drugs were reported to have been given during labour. Father was a smoker at conception. There is no family history of diabetes.

Date	Prescriptions	Condition treated
1978	**Ampicillin**	
	Phenergan	
1979	**Ampicillin**	Ear infection
1979	**Ampicillin**	Wasp sting. Red face
	Phenergan	
1979	?(unknown)	?Gonorrhoea
1979	**Penicillin**	Infection
1979	**Erythromycin**	Same infection
1980	**Pen-V**	Early otitis media
1980	**Pen-V**	R otitis media
1980	**Septrin**	Tonsillitis
1980		Diarrhoea. Faeces to lab.
1981		Measles
1981	**Pen-V**	Wax++, nodes
1981		Wax++cervical adenoids++ tonsils
1981	**Septrin**	Acute tonsillitis
1981		Throat
1981	**Septrin**	Throat, cervical adenoids+
1981		Pyrexia
1982	**Septrin**	Laryngitis
1982		Rash++ everywhere, vomiting fever, tonsillitis
1982	**Pen-V**	Left otitis media
1982		Ears
1982		Mumps
1982		Sore throat
1982	**Septrin**	R otitis media
1982	**Pen-V**	Wax, L otitis media
1983		Colic, nausea
1983		Abdominal symptoms again
1983		Temp 101 ^{o}F
1983		Pharyngitis
1983	**Penicillin**	Right otitis media
1983	Betnovate	

	cream	
1983		Feeling sick after food. Slight central abdominal pain. Pharyngitis
1983		Pharyngitis
1983		Nausea
1983		Minor gastroenteritis
1983		Chest ok
1984	Synalar gel	
1984		Abdomen ok
1984	Synalar gel	
1984		?chicken pox
1985		Abdomen ok
1985		Viral
1985	**Pen-V**	Ext. otitis
		Feels sick. Tenderness in abdomen.
1985		Abdomen
1986	**Amoxycillin**	Ears wax++, pain
1986		Ear cleared
1986		Wax
1986		Pharyngitis
1987		Pharyngitis, laryngitis
1987		Pharyngitis, cough, sinusitis
1987		Pyrexial T104^{o}F. Diagnosed flu
1987		Pertussis
1987		Pharyngitis
1987		Still laryngitis
1987		Abdomen
1987		Urine ok
1987		Catarrh++, earache
1988	Triludan	Eyes
1988	Triludan	
1988	Karvol	
1989	**Amoxil**	Headaches, sinusitis
1989	Triludan	Hayfever, runny eyes. Has all the symptoms of hay fever
1989		Abdomen
1989	**Amoxil**	SOS call-out. Temperature, headache
1989	Triludan	
1989	Triludan	
1989		Enuresis, polydypsia. Admit

Table 7.16 Case A5. Health records of a diabetic child

Discussion

Samantha suffered from frequent episodes of abdominal pain of unknown origin for many years before diabetes was diagnosed. Within

a few weeks of a course of Septrin in February 1982, she is suffering from a rash, fever, vomiting and tonsillitis. Following a course of penicillin-V during December 1982, she returns to the doctors the following month complaining of colic and nausea. Further complaints of nausea occur during July 1985, again following a course of penicillin-V. As these health records reveal, Samantha's health problems pre-diagnosis of diabetes were *tonsillitis*, *otitis media* and pharyngitis.

Case A6: Emma born 1987
Diagnosed as diabetic at 4 years of age; no family history of diabetes; father a smoker, mother was a smoker but did not smoke during pregnancy. Drugs at birth: Pethidine and induction drip.

Date	Prescriptions	Condition treated
1987	Dioralyte	Gastroenteritis
1987		Slow improvement
1987	Dioralyte	
1987	**Erythroped**	Bilateral otitis media
1988	**Erythroped**	Chesty cough
1988	Xylometazoline	Otitis media
1988	Chloramphenicol drops	
1988	Dioralyte	Vomiting, right otitis media
1988		Ear better
1988		Vomited last night
1988		Viral infection
1988		Rubella type rash
1988	**Amoxil**	Tonsillitis
1989		Chickenpox
1989	Chloromycetin	Conjunctivitis
1989	**Amoxil**	Cough
1989		Chesty
1989		Otitis externa
1990	**Erythromycin**	Infected throat, URTI
1990	**Amoxil**	Otitis media
1991	**Pen-V**	Sore throat. Rash all over. Tonsils swollen. ?scarlatina ?rubella
1991		Improved
1991		Retching, pyrexial, abdominal pain, throat red.
1991		Very thirsty. Admitted to hospital

Table 7.17 Case A6. Health records of a diabetic child.

Discussion

Emma who was *induced* at birth is recorded as having only been prescribed Dioralyte before presenting with otitis media in both ears at 11.5 months, for which she was prescribed Erythroped (erythromycin) for the first time.

Following the first course of erythromycin in December 1987, she returns to the doctors within three weeks complaining of a chesty cough and is given a further prescription of erythromycin. Within two weeks of her second prescription for erythromycin, she returns to the doctors with otitis media.

In March 1990, Emma is prescribed erythromycin for an upper respiratory tract infection; nine days later, she returns to the doctors again suffering from otitis media. Thus twice, on two different occasions, Emma presents with otitis media within *days* of a prescription for erythromycin. As her total exposure to antibiotics increases, Emma suffers from *tonsillitis, conjunctivitis, otitis media* and *rashes* and is finally admitted to hospital suffering from diabetes at the age of four.

Case A7: Mohammed born 1981

Diagnosed as diabetic at 2 years. Neither parent had ever smoked; there was no family history of diabetes. Mohammed was born at home reportedly without any drugs having been used during delivery. He was breast-fed for 4 months.

Date	Prescription	Condition treated
1981		Sticky eyes
1981		Catarrh, cough
1982		Catarrh, cough
1982	**Pen-V**	Visit re: circumcision
1982		Wheezy bronchitis
1982		Reaction at vaccination site
1982	Dimotapp	Snuffly++
1983	**Amoxil**	Persistent diarrhoea
1983	**Amoxil**	Otitis media
1983	**Ceporex**	Earache both ears
1983	**Amoxil**, Actified	L eardrum red

1984	Dioralyte	Vomited last night
1984		2.5 year check. All well
1984		Polyuria and polydypsia for past few weeks. Admit diabetic unit

Table 7.18 Case A7. Health records of a diabetic child.

Discussion

Within 11 days of a prescription for a penicillin at 4.5 months, Mohammed is reported to be suffering for the first time from wheezy bronchitis.

Following his first course of Amoxil in April 1983, Mohammed returns to the doctor 2 weeks later suffering from otitis media for the *first* time, for which he is again prescribed Amoxil. During April 1983, Mohammed who is only *one* year old, receives 3 prescriptions for antibiotics. By June 1983, after 3 courses of antibiotics, he is *still* suffering from problems with his ears. The first course of Amoxil marks the start of a recurring cycle of ear problems and prescriptions for antibiotics which do not seem to help his condition.

Case A8: Ryan born 1987

Diagnosed as diabetic at 22 months. Neither parent had ever smoked; grandfather diagnosed as diabetic at 30 years; baby was solely breast-fed for 5 months; Syntometrine *(oxytocin* and *ergometrine)* was reported as having been administered after delivery.

Date	Prescription	Condition treated
1987		Snuffly for 4 weeks
1987	Dioralyte	SOS call-out. Diarrhoea
1987		Diarrhoea better on Dioralyte. Chest & upper arms rash, spotty for 6 weeks.
1987		Spluttery and wheezy
1988	Fucidin cream	Infected. Chicken pox spots
1988		Vaccination
1988	No prescription	Vomited last night in sleep
1989		Vaccination
1989		URTI (quiet).Tongue bloated
1989	**Amoxil**	Tongue coated

1989	One week history of Polyuria and polydypsia. Admit

Table 7.19 Case A8. Health records of a diabetic child.

Discussion

Ryan's health records show that before the onset of diabetes only *one* course of antibiotics, prescribed three weeks before diabetes was diagnosed, had ever been prescribed. Ryan who was probably exposed to oxytocin and ergometrine from breast-milk is, within seven weeks of birth, reported as being snuffly, suffering from diarrhoea and a rash, and is spluttering and wheezing. The snuffles and rash have been present for several weeks, originating around the time of birth.

As Ryan's mother reported not having taken any drugs during pregnancy, apart from Amoxil which was prescribed days before diabetes was diagnosed, the only drugs that Ryan had been exposed to before diabetes was diagnosed were *oxytocin* and *ergometrine*.

If either or both of these drugs are diabetogenic, children who have been exposed to oxytocin &/or ergometrine at birth, might be expected to become diabetic at a younger age than those exposed to antibiotics during infancy. In addition, *mothers* directly exposed to these drugs during labour may be at increased risk of diabetes in later life (see Table 7.1, DB021).

Case A9: Steve born 1961. Diagnosed as diabetic at 8 years *(antibiotics in bold print)*

Penicillin-V and Phenergan both before 2 years, then:

Prednisone	**Achromycin**	Mysteclin
Robitussin	Prednisone	**Penbritin**
Phenergan	Prednisone	Prednisone
Euglate	**Achromycin**	**Achromycin**
Phenergan	Alupent	**Achromycin**
Alupent	Euglate	Ephedrine
Aminophyllin	Prednisone	Ledermycin
Dimotane	Intal spincaps	Aminophyllin
Alupent	Chloromycetin	Prednisone
Achromycin	**Achromycin**	Prednisone

Codeine	Prednisone	**Achromycin**
Prednisone	**Achromycin**	Aminophyllin
Alupent	**Achromycin**	Alupent
Ephedrine	**Penidural**	**Achromycin**
Achromycin	Strepto?	Prednisone
Alupent	Alupent	Alupent
Wel?	Alupent	Ledermycin
Sample of	Avomine	Robitussin
oxytetracycline		
Robitussin	Euglate	Prednisone
Penidural	Solfex	Alupent
Euglate	Dimotane	**Achromycin**
Achromycin	**Achromycin**	Ephedrine
L-codeine	Alupent	Alupent
Tedral	Phenergan	Alupent
Alupent	**Achromycin**	Ephedrine
Ephedrine	**Achromycin**	Prednisone
Prednisone	Phenergan	Robitussin
Alupent	Ephedrine	Robitussin
Phenergan	Alupent	Aminophyllin
Prednisone	Phenergan	**Achromycin**
Robitussin	**Achromycin**	Alupent
Erythroped	Phenergan	**Achromycin**
Dimotane	Robitussin	**Achromycin**
Ephedrine	Dimotane	Robitussin
Phenergan	Robitussin	Prednisone
Prednisone	**Achromycin**	**Achromycin**
Ephedrine	Prednisone	Robitussin
Aerotrol	Choledyl elixir	**Achromycin**
Alupent	**Achromycin**	Alupent
Robitussin	Adrenaline	**Achromycin**

Key to chemicals present in drugs:

Alupent:	orciprenaline sulphate
Aminophylline:	theophylline and ethylenediamine
Achromycin:	tetracycline hydrochloride
Dimotane:	brompheniramine maleate
Choledyl:	choline theophyllinate
Ledermycin:	demeclocycline hydrochloride

Table 7.20 Drugs prescribed to a child in a rural area in England, UK, before diabetes was diagnosed.

Discussion

Steve became diabetic at a young age in 1970, when diabetes was less common and visits to the doctor and consumption of antibiotics were in general less frequent. Steve's startling case illustrates the prescribing practices experienced by one unfortunate child in England in the 1960s. At least 134 different drugs, 33 of which were antibiotics, were prescribed for Steve before being diagnosed diabetic in 1970. Despite vomiting after first being prescribed Phenergan, it continued to be prescribed. Thereafter, following prescriptions for antibiotics and a variety of other drugs, his symptoms progressed from coughing to wheezing and asthma, green phlegm, barking cough, otitis media and muscle cramps to diabetes. Incidentally, all of these symptoms are side-effects which can be associated with some kind of drug (see chapters 4 & 6).

DISCUSSION OF RESULTS

Despite millions having been spent on research into diabetes, I am unaware of any other study which has investigated the health of diabetic children from conception to diagnosis of diabetes. Questioned about the health profile of diabetic children pre-diagnosis, it is likely that most clinicians would mention the loss of weight immediately pre-diagnosis, increased thirst and micturition and possibly a respiratory infection. Although there is no data available to enable a comparison to be made between the drug exposures during pregnancy of mothers of diabetic children with those of non-diabetic children, I believe the incidence of mothers of diabetic children with a history of drug exposure during pregnancy to be high.

Diabetic children with no in-utero or drug exposure during birth have sometimes been exposed to antibiotics immediately after birth either directly, or indirectly through breast milk, or have been exposed to antibiotics on several occasions during infancy or childhood. Children who are reported as not having been exposed to drugs in-utero, either during pregnancy or labour, and who have allegedly

not been exposed to antibiotics prior to being diagnosed as diabetic are in the minority. It is possible however, some of these children may have been exposed to drugs that their mothers do not recall taking or being administered during labour or delivery.

The profusion of chemical exposure reported prompted me to compare the chemical structures of drugs known or thought to be diabetogenic (see chapter 6) with those reported in this study.

Possible interaction between drugs and zinc present in the pancreas

It has been suggested that some drugs or the chemical entities formed in the body following their ingestion, have an affinity for zinc. Such that when they enter the blood stream and pass through the pancreas, which is a rich source of zinc, the foreign chemical binds to the zinc in the islet cells of the pancreas. This could displace some or all of the six insulin molecules temporarily bound to the zinc. Such an interaction could change the acidity of the cells causing them to rupture as the osmotic pressure within becomes too great.

This would result in irreversible damage to the cells which may result in the activation of the body's immune system as it detects a 'deformed' cell which it regards as 'foreign' (ie. being different in form). This in turn would trigger the formation of antibodies, proteins that are directed to 'foreign' (non-self) agents within the body, which may explain why many newly diagnosed diabetics have islet cell antibodies in their blood.

If this was the case, these islet cell antibodies would simply be formed as a result of pre-existing damage to the pancreas and would not be the agent responsible for destroying the insulin producing function of the pancreas, as is currently thought. If chemicals such as

drugs or their by-products are not responsible for eliciting an immune response which results in the formation of antibodies, the unanswered question of what triggers the immune system to produce these antibodies remains.

However, if some chemicals are capable of destroying the ability of beta cells of the pancreas to secrete insulin, as has been known to occur in persons who have taken the rat poison Vacor (see chapter 6), then it is conceivable the destruction may be gradual with a portion of the pancreas being destroyed with each chemical attack. Also, it would seem logical to suppose that children who had been exposed as foetuses and babies to such an agent, might become diabetic at a younger age than children exposed to the same agent during infancy, and may require one exposure only if it occurred in-utero or soon after birth.

For example, if a foetus of 25 weeks has half of its insulin producing cells destroyed, it would be unlikely to show the clinical symptoms currently associated with diabetes. However, after birth the child may be expected to grow out of its insulin producing capability at an earlier age than a baby who is exposed to the same amount of the toxic chemical after birth. Since a smaller proportion of the pancreas would be affected, as it is larger in size at birth than at 25 weeks of foetal development; and damaged pancreatic cells unlike liver cells are not replaced as they do not have any significant capacity for regrowth. Therefore, as the bodyweight of these infants increases after birth, those with a lower level of insulin producing capability might be expected to exhibit signs of diabetes at an earlier age.

Instances where this may not be the case might arise if the infant, who was exposed to a diabetogenic drug in-utero, consumes smaller feeds and has a lower sugar and higher fibre intake than the child

exposed at birth. If in these instances average glucose levels within the blood were maintained at a lower level, there would be less demand on the pancreas for insulin. It is also worth remembering that the pancreas of a diabetic is still capable of producing other molecules necessary for survival. For example, it produces enzymes such as trypsin and chymotrypsin necessary for the digestion of proteins and hormones such as glucagon. Since only part of the pancreas has been affected, it would seem that any diabetogenic entity may very likely have an affinity for cells containing zinc. This at least would account for the selective destruction of the beta-cells of the pancreas.

Although information about the binding of drugs to zinc is limited, penicillin has also been reported to bind zinc and copper ions (Cu2+) which are positively charged. The drug penicillamine (Fig. 7.9) which is also one of the breakdown products of penicillin is an effective chelator of metal ions including zinc and is used in medicine in chelation therapy for the reduction of toxic levels of zinc salts.

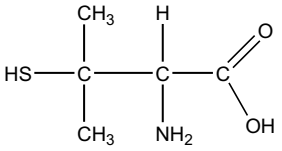


Figure 7.9 Chemical structural formula of peniciliamine.

Whereas erythromycin was reported some 25 years ago as not binding to zinc, it is now known that it can be made to react in an *in-vitro* situation in a 1:1 ratio (Brocades Pharma personal communication). The probability of binding (chelation) between zinc and organic compounds, that is compounds containing carbon, nitrogen and oxygen, is high. This chelation usually occurs between

the negative rich centres of either the *oxygen* or *nitrogen* groups of the chemical and the positively charged zinc (Zn^{2+}) ion. In the case of insulin-zinc complexes that occur naturally in the pancreas, the binding is reversible, enabling insulin to be stored until required.

Whatever the route of destruction of the pancreas' ability to secrete insulin, it is interesting that some of the drugs that diabetic children were exposed to during foetal development share structural similarities with each other. For example, child T1 (Table 7.10) was exposed to Asacol, and child T6 (Table 7.10) to paracetamol. The structure of Asacol (Fig. 7.10) which is the trade name for the chemical mesalazine, has structural similarity to para-aminophenol (Fig. 7.11), a highly toxic chemical that is formed in the body in very small quantities following the breakdown of paracetamol (acetaminophen). Also, Asacol has structural similarity to penicillamine in that it has an amine (NH_2) and carboxyl (COOH) group.

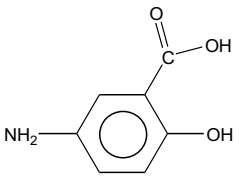


Figure 7.10 Chemical structure of Asacol (mesalazine).

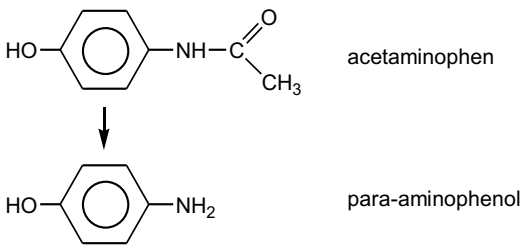


Figure 7.11 Chemical structure of paracetamol (acetaminophen) and para-aminophenol which is a breakdown product formed in the body.

One drug less commonly used today than some 50 years ago which may be diabetogenic to humans, is ephedrine. It has been used in the past to treat asthma and has been prescribed in the UK for babies in the form of nasal drops. One patient I studied had become diabetic at the age of seven, during 1944. This was a time when diabetes in children was rare and fewer children in the UK were probably administered drugs on a regular basis, as this was prior to the introduction of the National Health Service in 1948. This patient had a history of asthmatic attacks which sometimes required hospitalisation and she recalled being administered ephedrine tablets on several occasions. Interestingly ephedrine can, under the right conditions, break down to methylamine and benzoic acid (Fig. 7.12), both of which will complex to zinc under the right conditions. Benzoic acid, a preservative, is used extensively in the food processing industry.

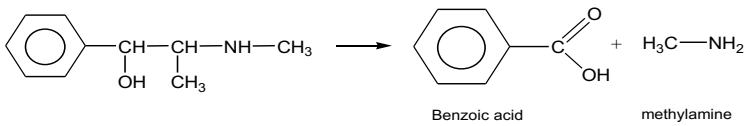


Figure 7.12 Chemical structures of ephedrine, methylamine and benzoic acid.

The use of steroids such as prednisolone (Fig. 7.13) (which comes from a group of chemicals known as glucocorticoids) has also been reported to be associated with the onset of diabetes. Interestingly, conditions in which excessive levels of glucocorticoids are produced also confer a risk of developing diabetes. In view of the structural similarity between prednisolone and beclomethasone dipropionate as found in Becotide (see chapter 4), used in the treatment of asthma, we should ask ourselves whether we can be

certain that appropriate clinical trials have been done to exclude the possibility that beclomethasone is also diabetogenic.

Oxytocin like insulin is composed of many small chemical groups called amino acids and in my opinion is quite likely to be able to bind to zinc as insulin does. In fact, many amino acids including asparagine, tyrosine and glutamic acid, all of which are present in oxytocin, have been shown to bind to zinc. In addition, with growth hormone, we have one example of a naturally occurring hormone being associated with diabetes. Growth hormone like oxytocin, derives from the pituitary gland and has been shown to be diabetogenic in animal models. Indeed, some 20% of patients who suffer from acromegaly or gigantism, (disorders in which the body produces excessive levels of growth hormone) have been reported to be diabetic.

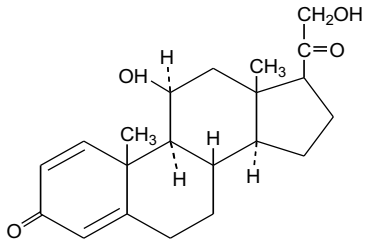


Figure 7.13 Chemical structure of prednisolone.

Oxytocin has not been sufficiently studied to detect any possible long-term adverse effects in children who were exposed at birth. Sandoz, the company which markets oxytocin in the UK, gave the following response to the author when contacted.

> *"Thank you for your telephone call requesting information on Syntocinon (oxytocin).*

> *Unfortunately after an extensive literature search I was unable to find any papers on long term follow up of offspring."*
> (Sandoz Pharmaceuticals, UK., 1992)

In view of this information and the considerable proportion of diabetic children who were found by me to have been induced at birth, the safety of patients exposed to oxytocin should be questioned. Any diabetogenic effect of oxytocin would not be detected even by standards of clinical trials today. In addition, a scientific report published in 1936 revealed that when the anterior portion of rat pituitaries was homogenized and the extract injected into other rats, they became diabetic. Oxytocin derives from the pituitary gland and although present in the posterior part of the pituitary that was not selected for use in the experiments, the two halves of a pituitary are poorly defined and therefore difficult to separate. This could have resulted in contamination of the test material with oxytocin, or alternatively, may mean that one or several of the hormones present in the anterior portion of the pituitary may be diabetogenic.

In the UK, USA and Australia, oxytocin is also sometimes administered in combination with ergometrine, as both drugs are available in a single preparation of Syntometrine which was licensed in the UK in February 1975.

If chemical substances such as drugs are able to react with certain chemicals within the body in such a way that cause the pancreas to lose its ability to produce insulin, then it is very likely that there are many more drugs in use today, lesser known than those discussed in this book, that are also diabetogenic. Since some of the

drugs under discussion in this chapter have only come to the fore as a result of their current widespread and frequent use.

The destruction of only the beta-cells of the pancreas by chemicals with an affinity for zinc, could account for this selective destruction. In support of this, we should remember that the alpha and delta cells of the pancreas, which are *also* present in the islets of Langerhans of the pancreas in which the beta-cells are located, are not destroyed in diabetes. The alpha and delta-cells present in a far lower concentration in the pancreas and sometimes located *next* to the beta-cells retain their ability to produce the hormones glucagon and somatostatin respectively. The pancreas also retains its ability to produce digestive enzymes. It is only the zinc-containing beta-cells within the pancreas that are destroyed.

Non-insulin dependent diabetes (NIDD) (ie. the symptoms are not sufficiently severe to warrant the use of insulin) is, in my opinion, in many cases simply sub-clinical insulin dependent diabetes. Many patients who are not treated with insulin have abnormally high blood glucose levels and often eventually require insulin. One reason why insulin-dependent diabetes (IDD) and NIDD have been considered to be two distinct disorders, is that NIDD is most commonly detected in mature adults and islet cell antibodies are not found in NIDD patients.

However, if chemicals are capable of causing diabetes, with exposure having taken place over many years, antibody levels in NIDD may be low as the onslaught is likely to have been much more gradual. The theory that IDD and NIDD are essentially the same disorder (apart from the *degree* of impairment of the body's insulin producing capacity) is supported by the following findings:

Some 50% of newly diagnosed IDD children do not have detectable islet cell antibody levels.

Some 8% of *non-diabetics* have been found to have islet cell antibodies.

Many NIDD patients eventually require insulin therapy.

NIDD has been found to be as common as IDD in a study of school children in Japan.

To my knowledge there have not as yet, been any studies which enable tobacco smoke exposure to be excluded from the list of potentially diabetogenic chemicals. Exposure to tobacco smoke is known to confer a risk of disease affecting many organs of the body; one of these is *pancreatitis.* If some of the 4000 chemicals present in tobacco smoke are diabetogenic, damage to the pancreas is likely to be gradual, requiring many years of exposure in an adult. Although paternal smoking prior to conception and maternal smoking during pregnancy are often absent from the history of diabetic children, the effect of such exposure may be a risk factor in diabetes in both adults and children and needs to be investigated.

Incidence of diabetes in children in the UK

When considering diabetic children in the same family, the fact that these children will most likely all attend the same doctor must be taken into account. If the family's doctor commonly prescribes antibiotics to babies and children, and if one accepts that antibiotics may be implicated in the onset of diabetes, it would not be surprising to find more than one diabetic child from the same family.

Table 7.21 shows (for 1988[7]) some geographical variation in England in the incidence of diabetes in the under 15 year old age group. East Anglia, a predominantly rural area, has the highest incidence, whereas the four Thames regions, areas of higher population density and pollution, have the lowest. The incidence in East Anglia (17.7/100,000) is more than *double* that of North West Thames (8.0/100,000). This feature of a rural region having a higher incidence of diabetes than an urban region is also repeated in Scotland.

Region	Age-Sex incidence rates (per 100,000)	Author's ranking of incidence
East Anglian	17.7	**High**
Wessex	17.1	**Medium**
Northern	15.8	"
Mersey	15.8	"
Oxford	15.2	"
Yorkshire	14.9	"
North Western	14.6	"
Trent	13.5	"
South Western	13.4	"
West Midlands	13.3	"
SE Thames	13.1	**Low**
SW Thames	12.4	"
NE Thames	11.8	"
NW Thames	8.0	"

Table 7.21 Incidence of diabetes in children under 15 years in England in 1988 (Metcalfe A and Baum[7]).

Table 7.21 shows more than a two-fold variation in incidence between the N.W Thames region and East Anglia. What could account for such variation between area health authorities that are

situated in *close* proximity? Are dispensing practices a factor in the onset of diabetes?

Dispensing medical practices in England

In the UK, doctors are legally allowed to *dispense* their own drugs for patients who meet the criterion of living more than a mile from a pharmacy. Consequently, although very few general practitioners in built-up areas dispense their own drugs, in rural areas the proportion of *dispensing practices* can be quite high.

My study of children in the Cambridgeshire and Wessex Area Health Authorities showed that a high proportion of diabetic children lived in the countryside and not in the towns, where presumably the population density of children would be higher. Thus if all children were at equal risk of diabetes, irrespective of location, one would expect to find more diabetic children in the towns. Quite noticeable, was that some of the dispensing practices appeared to be considerably more affluent, despite being supported by fewer general practitioners, than those in the outer London area.

Some surgeries of recent construction had been purpose-built at considerable cost. It was also noticeable that in some of these practices, antibiotics seemed to be liberally prescribed to babies and children. These small areas studied were located in area health authorities with a high incidence of diabetes. This prompted me to question whether the proportion of dispensing doctors could be related to the incidence of diabetes in children. If drugs such as antibiotics were implicated in any way with the onset of diabetes, and if dispensing doctors prescribed more liberally, perhaps due to financial incentives, one might reasonably expect to find a higher incidence of diabetes in country children.

This led me to investigate the variation in the number of dispensing doctors in the UK. Table 7.22 shows the percentage of dispensing doctors for each regional health authority in England, as at 1st October 1989.

Region	Percentage of dispensing doctors	Author's ranking of percentages
East Anglia	45	High
S. Western	21	Medium
Yorkshire	21	"
Oxford	20	"
Trent	17	"
Wessex	15	"
Northern	14.5	"
W.Midlands	11	"
NE Thames	10	Low
SE Thames	10	"
NW Thames	6	"
SW Thames	6	"
Mersey	4	"
N Western	2.5	"

Table 7.22 Percentage of dispensing doctors in the UK by Area Health Authority as at 1st October 1989 (Data supplied by the Royal College of General Practitioners, London.)

Illustration of data from tables 7.21 and 7.22 according to my ranking of regions of high, medium and low incidence of diabetes in under-15s during 1988, and the proportion of dispensing doctors in the UK as at 1st October 1989 respectively, provides the distributions shown in Figures 7.13 and 7.14.

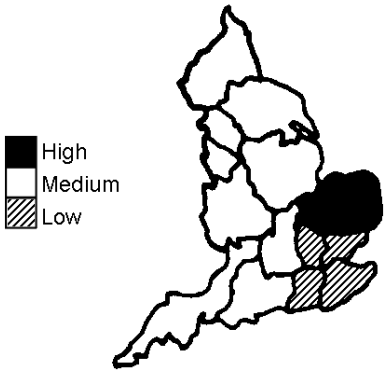


Figure 7.13 Distribution of regions of varying incidence of diabetes in under 15s in England occurring during 1988.

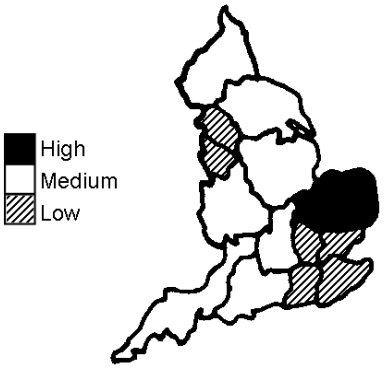


Figure 7.14 Distribution of regions of varying density of dispensing medical practices in England as at 1st October 1989.

Could the partial similarity between the two distributions be anything more than a nasty coincidence? That there should be any sort of correlation between the area of highest incidence of diabetes and the area with the highest proportion of dispensing doctors is suggestive.

The North Western and Mersey regions which have a medium incidence of diabetes and yet a low incidence of dispensing doctors, are incidentally, regions with the *highest* number of prescriptions (excluding data pertaining to prescribing doctors) per person in England for 1981 and 1990 (Office of Population Census and Surveys; no data is available for years in between).

The North Western and Mersey regions are also regions with the greatest *increase* in the number of prescriptions per person in England between 1981 and 1990. The increase in the number of prescriptions per person during 1981-90 for the four Thames regions was approximately 8.7%, in comparison with an average of 25% for the N. Western and Mersey regions.

Additionally, N.W. Thames [the Thames region with the lowest incidence of diabetes in under 15s during 1988 (see Table 7.21)] was the Thames region with the lowest number of prescriptions per person for 1981 and 1990 (5.6 and 5.9 prescriptions respectively). S.E. Thames, (the Thames region with the highest incidence of diabetes), was the Thames region with the highest number of prescriptions per person for 1981 and 1990 (6.3 and 7.0 respectively).

Although these data do not include prescriptions issued by dispensing doctors, the percentage of dispensing doctors in these regions is approximately the same. Interestingly, S.W. Thames which has a low percentage of dispensing doctors (6%) but ranked second highest for incidence of diabetes out of the Thames regions (Table 7.22), was reported in 1985[9] to have the highest rate of *induced* births in England (23.9%), compared with an average of 17.2% for the other three Thames regions.

If *dispensing* doctors were more liberal in their handing out of drugs and the onset of a disease was associated with one or more drugs, one might expect an area with a high proportion of dispensing doctors to have a high incidence of disease, which is indeed the case. One might also expect regions with a higher number of prescriptions per person, to be associated with a higher incidence of diabetes, which is also the case. One would hope that these findings could be attributed to coincidence, but the fact is dispensing drugs can be a lucrative business. For the first 1000 prescriptions dispensed each month by a general practice in the UK in 1992, a fee of £1.70 for each was received. Therefore the weekly turnover from the *dispensing fee* alone by just *one* general practitioner (many practices have more than one doctor) prescribing once daily to some forty patients, would be £340. But the dispensing fee is a minor source of income when compared with the income from the sale of the drugs dispensed. This is because the reimbursement to the surgery by the National Health Service for drug sales may be much higher than the price paid by the surgery for the drug.

Interestingly, a pharmaceutical sales representative told me:

"Country doctors are the worst. When you ask them what samples they would like, they tell you to empty your boot (trunk)!"

This enables a dispensing doctor to obtain free stock which could be used to fill prescriptions for which the NHS may be billed. In the USA in 2003, the pharmaceutical company AstraZeneca pleaded guilty to a felony charge of health care fraud and agreed to pay $355 million to settle criminal and civil accusations that it engaged in a nationwide scheme to illegally market a cancer drug. The government said that doctors across the country had been given grants, salaries, free travel, entertainment and free samples worth hundreds of dollars

each as inducements. The physicians then billed Medicare and other federal health care programs for these drugs.

If drugs were in any way responsible for adversely affecting the health of the population, countries which were heavy consumers of drugs, might exhibit high incidences of diseases. Australia, which has been reported as having the highest incidence of asthma in the world, has the highest consumption of antibiotics per capita, consuming more than the UK or USA. Diabetes in children under 15 years in Western Australia in 1992, reached epidemic proportions affecting 22/100,000 children, despite warm average annual temperatures. Perth, the capital of W.A. in the far south of the State, has an approximate average annual temperature of approximately 19^{o}C. As lower temperatures are associated with an increased incidence of diabetes (see Fig. 7.2), this very high incidence level relative to average annual temperature, might be considered suggestive of another or a stronger factor (eg. the liberal prescribing of antibiotics) influencing the incidence of diabetes in children in W.A.

In 1993, medical fraud and *over-servicing* were estimated to be costing AU$400 million a year. Additionally, Western Australia was in 1994 reported by Dr. Marsden Wagner, consultant to the World Health Organisation, to have the highest rate of birth intervention (eg. induction) in the world.

The suggestion that diabetes is an iatrogenic disease is a nightmarish one. Nevertheless, there is no information available to eliminate the possibility that certain drugs may be implicated in the onset of diabetes. Could the low incidence of diabetes in children (6.8/100,000) in the Republic of Ireland [(7)] have anything to do with the fact that during the 1980s, most families in the Republic had to pay approximately £15 for a consultation with a doctor and pay for

each drug prescribed? I consider it likely that Irish children were at a reduced risk of diabetes as their parents may have been less likely to take their children to the doctor for minor complaints, with the result that Irish children in general, probably incurred fewer exposures to drugs.

Across the border, Northern Ireland which is part of the United Kingdom's National Health System, has a higher incidence of 10.9/ 100,000[7]. The low incidence rate of 2/100,000 in Hokkaido, Japan (see Fig.7.2) may have something to do with the cost of medical services in Japan, and a woman's reluctance to visit a doctor, due to unpleasant experiences during pregnancy and childbirth, when a woman is reportedly treated as a second-class citizen[10].

The concept that drugs can cause diabetes is not new. What is novel, is the suggestion that there are drugs in *common* use which may be partly responsible for the epidemics that we see today in many industrialized countries. The fact that diabetes is a condition known to have been in existence for hundreds of years, does not preclude the possibility that drugs in use today may be implicated in the causation of diabetes. For example, if ephedrine or ergots as discussed earlier are factors in diabetes causation, it would explain the prevalence of the disease over past centuries. Since ephedrine was discovered by the Chinese in ancient times and exposure to and the use of ergots has been documented for centuries. Many extracts of other plants which have been used for medicinal purposes for centuries, are also quite likely to contain chemicals that are diabetogenic.

Valerian, a sedative and sleep aid herbal remedy in common use today, contains the chemical diazepam, which belongs to a class of drugs known as benzodiazepines. Mention of valerian can be found in

drug books from the late 1600s and during 1733-1936, valerian was one of the six most prescribed medicines in European and American medicine. Benzodiazepines however, are also prescription drugs and received media attention due to their addictive properties. Hence, if benzodiazepines are diabetogenic (see table 7.4, S004), it would not be surprising to find diabetes in existence for centuries, especially as these drugs are addictive.

If antibiotics are implicated in the onset of both diabetes and asthma (see chapter 9), it is to be expected that a country such as Finland, which has the highest incidence of diabetes in children (see Figure 7.1) would also have a high incidence of asthma. A report published in 1990 showed a *20-fold* increase in symptoms suggestive of asthma between 1961-89 in young adults attending military service in Finland. Generally, one might expect a greater incidence of diabetes in colder climates (see Fig. 7.2), where children may be expected to suffer more frequently from upper respiratory tract infections, for which they may be prescribed antibiotics. If a high proportion of the adult population are smokers and due to the weather keep their homes closed for most of the time, children would be more likely to suffer from respiratory problems. During 1970-1997 roughly 30% of adult males in Finland smoked.

Finland which has the highest incidence of diabetes in children also commonly prescribed erythromycin until concerns were raised about the prevalence of erythromycin resistant bacteria in the late 1980s. If a drug causing a disease is commonly prescribed, it would be normal to find a high incidence of that disease in the country concerned. In addition, one might find a reduction in the incidence of the disease once prescriptions of the drug sufficiently decreased.

The data shown in Table 7.6a provides details of a child who became arthritic at two years of age and later diabetic. This child was exposed to the drug Asacol in-utero. Another child (Table 7.6a) who was exposed to Paracetamol in-utero on a daily basis and who became diabetic at one year of age should make us question the possibility of congenital birth defects and other health problems, as possibly being caused by drugs taken during pregnancy.

As to why children may be more susceptible to the toxic effects of drugs, the answer may partially lie in the way infants usually take medicine. Many drugs given to young children are in solution which may consequently increase the bioavailability of the drug. This was thought to be one of the reasons why Japan had a higher incidence of SMON (sub-acute myelo-optic neuropathy) disease which was due to the toxic effects of the drug oxyquinoline. Although available since 1934, the drug was not exposed until some 40 years later, during the 1970s, as having *blinded and injured* more than *10,000* people in Japan.

As described earlier in this book, every individual's tolerance to poison will vary, so it should come as no surprise to find individuals who have not been diagnosed as diabetic, despite multiple exposures to possible diabetogenic drugs. However, if the insulin producing capacity of the pancreas is only slightly affected with each exposure, diabetes may develop *many* years later in the face of additional demands for insulin including increased body weight; increased consumption of foods containing sugar; pregnancy, or after the pancreas has been subjected to further chemical insults by diabetogenic chemicals.

8

Drugs and the Health of Children

> **Doctors may give prescriptions for a drug when people go to them, whatever the problem. Studies have shown that about 80% of people who seek medical help have conditions which either would get better if nothing was done or cannot be improved by drug treatment.**
> (Exhibition Case S1, The Wellcome Museum of the History of Medicine, Science Museum, London, 1992)

Perhaps the fact that many children have at some time objected to the taste of medicine, except when it is given in a sweetened or encapsulated form, should jog our conscience and prompt us to question whether ingesting a vile tasting chemical is really such a good thing and whether alternatives that might promote better health exist. For example, keeping children in a smoke-free environment has been shown to reduce the incidence of respiratory problems. A healthy balanced diet based on fresh rather than processed foods, would not only ensure better quality and quantity of nutrients, but would decrease the exposure to harmful dyes, preservatives and antioxidants which are ubiquitous in processed foods.

It is perhaps ironic that whilst we object to eating something that tastes horrible, we are readily ingesting chemicals in the form of

medicines that often taste far worse than most unappetising foodstuffs.

Unfortunately, most of us never get to see the black tar-like broth from which penicillin is extracted and observe those workers involved in its preparation, who don full protective clothing ie. face mask, overalls, gloves and boots. Considering the precautions necessary during the manufacture of penicillins and most other drugs, we have no justification for believing that children who have been increasingly exposed to antibiotics since the 1960s are not at risk from side-effects.

Health records of non-diabetic children

If there are drugs that are diabetogenic and commonly prescribed, what about other non-diabetic children who have been exposed to some of these drugs, sometimes more frequently than diabetic children?

Tables 8.1-8.12 list health records for 12 non-diabetic children from some 90 children that were studied in England, UK. The only selection requirement for these children was that they should be the same sex as the diabetic child being studied from that particular doctor's practice, and that their ages should be comparable. The health of these children was studied for the same period as the diabetic child, ie. from birth until diagnosis of diabetes. They represent only a small proportion of children who have shown some adverse effect following exposure to a prescription medicine.

All names used in the records are fictitious and the sex may have been altered. Prescriptions for antibiotics appear in bold print. Description of the condition treated includes the main reason for the visit to the doctors if documented by the GP. The reader's attention is

drawn to the similar health problems that some children present with following a prescription for an antibiotic. These conditions may be compared with the list of side-effects known to be associated with exposure to an antibiotic (see chapter 4). Details of each child's health history are followed by a brief discussion.

Case B1: Julie born 1980

Date	Prescription	Condition treated
1980	**Keflex**	
1981	**Septrin**	URTI (upper respiratory tract infection)
1981	Piriton syrup given by chemist for hayfever	*Mother* wants antibiotic. None given
1981	**Pen-V**	URTI. Cough++
1981	Emergency call-out	Grizzly and refusing to eat or drink.
1981	**Bactrim**	
1982	**Bactrim**	
1982	**Keflex**	URTI. Cough ++. Catarrh+
1982	**Amoxil**	Wheezy
1982	**Penbritin**	URTI
1983	**Keflex**	Chesty cough. Vomiting
1983	**Amoxil**	URTI
1983	**Erythroped**	Chesty
1983	**Amoxil**	Emergency call out
1983	Hydrocortisone cream	
1983	**Erythroped**	Emergency call out
	Maxolon	Vomiting. URTI. Off food
1983	**Keflex**	Emergency call-out Pharyngitis
1983	Hydrocortisone cream	
1983	Vallergan syrup	Allergic rash. ?cause
1984	**Keflex**	Emergency call-out. URTI
1984	**Keflex**	Coughing. URTI
1984	**Cephalex**, Alupent	
1984	**Keflex**	
1984		Cough
1984	**Erythroped**	Bronchitis
1984	Diprosone cream	
1984	Vallergan	
1984	**Ceporex**	Bronchitis
1985	**Ceporex**	Chesty cough
	Diprosone cream	Eczema on back
1985	**Amoxil**	*Wheezy* chest
1985	**Amoxil**	*Wheezy* bronchitis
1985	Triludan syrup	Hayfever
1985	**Keflex**	*Asthmatic*
	Ventolin	
1985	**Distaclor,** Ventolin	
1985	**Amoxil,** Ventolin	URTI
1985	**Amoxil**	URTI
1985	Hydrocortisone	6months facial itching

	cream	
1986	Fucidin cream	Impetigo
1986	**Ceporex**	URTI
1986	**Keflex**, Ventolin	Asthmatic wheeze
1986	Ventolin	Asthmatic
1986	Ventolin	
1986	Ventolin	
1986	**Erythroped**	Chicken-pox

Table 8.1 Case B1. Health records of a non-diabetic child.

Discussion

Before the age of 6.5 years, Julie had received 14 courses of cephalosporins, 7 courses of Amoxil, 3 courses of erythromycin and 5 courses of other antibiotics, making a total of 30 courses of antibiotics. This is an average of one course of antibiotics *every 2.6 months.* By one year of age, Julie had received two courses of antibiotics; it was only after exposure to antibiotics and an antihistamine (Piriton) for hayfever that she is brought to the doctors complaining of a cough. The use of Piriton should be questioned since it is unusual for a baby of one year to be suffering from hayfever. As her exposure to antibiotics increases, Julie is reported to be suffering from catarrh, *wheezing* and *chest complaints,* until she is finally diagnosed as asthmatic. Julie's first prescriptions for hydrocortisone cream in August and November 1983 are received immediately following a prescription for an antibiotic.

In Dec 1985, Julie is reported to have suffered from 6 months of facial itching during which time she received 4 courses of antibiotics, all of which can have side-effects affecting the skin and cause an intense sensation of itching (pruritis).

Case B2: Alex born 1980. *Premature baby*.

Date	**Prescription**	**Condition treated**
1980	Nystatin oral susp	Oral thrush
1980	Nystatin	
1980	Merbentyl	Colicky. Grizzly
1980	Merbentyl	
1980	Merbentyl	

1980	Merbentyl	Sleeping much better
1980	Merbentyl	
1980	**Amoxil**	Persistent catarrh
1980	Merbentyl	
1980	**Amoxil**	Screaming 24hrs. Pulling knees up. Otitis media
1980	Phenergan	Still very unsettled. Screams
1980		Screaming++. No obvious cause
1980	Phenergan	
1980	**Keflex**	URTI
1980	**Amoxil**	Ears inflamed again
1981	**Erythroped**	Throat still inflamed
1981		Cough at night
1981		Miserable. Throat pus++
1981	**Amoxil**	Diarrhoea and vomiting, really miserable, crying+++, ears red
1981	**Bactrim**	Ears still inflamed
1981		URTI. ?pulling ears
1981		Screams++
1981		Fell
1981	**Amoxil**	Sticky eyes, screams, otitis media
1981	**Amoxil**	Screaming. URTI
1981	**Bactrim**	
1981		Bump on head
1981		Small lesion on foot
1981	**Bactrim**	Feverish, screaming. Ears red
1982		URTI
1982		Catarrh
1982		Fell down stairs
1982		Diarrhoea & vomiting. Tired
1983	**Amoxil**	Cough, cold
1983		Coryza
1983		Vomiting
1983		Bilateral otitis media
1984		3 sutures removed from head
1984		Intermittent earache? reduced hearing
1984		*Mother says hearing poor*
1984	Mucodyne	
1984	**Erythroped**	Spasmodic barking cough
1985		Enuresis

Table 8.2 Case B2. Health records of a non-diabetic child.

Discussion

Alex had his first course of antibiotics before two months of age and received two courses in one month. Before Alex was three

months old, he was taking Merbentyl a potent sedative, so it is no wonder that he was reported to be sleeping better in May 1980! Otitis media was first reported after a course of Amoxil; a course of Amoxil in April 1981 did not appear to alleviate the problem of inflamed ears. After several courses of antibiotics, hearing difficulties were reported. After Alex's first course of erythromycin in Feb 1981, he is reported for the first time to be suffering from a cough.

A cough would be a natural reaction to a drug, of which there are many, that is harmful to the lungs. On average, antibiotics were prescribed approximately *every 3.2 months* during the first 5 years of Alex's life. As may be seen from the examination of health records of non-diabetic children, good health does not necessarily follow treatment with drugs. It is a child with this sort of drug exposure that I would consider to be at a higher risk of asthma and diabetes.

Case B3: Geoffrey born 1988. Forceps delivery.

Date	Prescription	Condition treated
1988		Oral thrush
1989	**Pen-V**	Chest creps
1989	**Pen-V**	Rt. lung still few creps
1989		?conjunctivitis
1989		Loose smelly nappy
1989		Cough
1989		URTI
1989	**Amoxil**	Cough, vomiting, loose stools
1989		Croaky
1989		URTI
1989	**Amoxil**	Cervical glands swollen. Febrile, vomiting, throat red.
1989	**Pen-V**	Throat inflamed
1989		Lots of antibiotics recently. Mum says still wheezy.
1990	**Amoxil**	Febrile. Throat inflamed
1990		Miserable, tired, unwell. Pulling up legs. On Amoxil since yesterday. Few spots on tongue and white spots on palate. Wet and dirty nappies as usual.
1990		Coughing
1990		Vomiting
	Pen-V	URTI. Persistent cough ?asthma
1990	Ventolin	

1990		Cough looser
1990		URTI
1990		Sticky eye. Conjunctivitis
1990		Not improving
1991		?viral illness
1991		Off-colour.
1991		Cough
1991		URTI
1992	**Amoxil**	

Table 8.3 Case B3. Health records of a non-diabetic child.

Discussion

By thirteen months of age Geoffrey had been prescribed 5 courses of antibiotics, approximately one course *every 2.5 months.* After the first couple of courses of antibiotics, Geoffrey presented with possible conjunctivitis, diarrhoea and vomiting. As his total exposure to antibiotics increases, fever, inflamed throat and a persistent cough are reported with possible asthmatic symptoms developing.

It is also interesting to note Geoffrey received 3 courses of antibiotics during his *first* year of life. Yet despite frequent visits to the doctors during April 1990 - April 1992, he received only one course of antibiotics. Such variations in prescribing are often a reflection of variation in prescribing trends between doctors.

Case B4: Wayne born 1978.

Date	**Prescription**	**Condition treated**
1978		Four post-natal visits
1978		Nappy rash
1979		Vaccination
1979		Vaccination
1980		Vaccination
1981	**Amoxil**	Otitis media
1982	**Amoxil**	Otitis media
1982	**Amoxil**	URTI
1983	**Amoxil**	Tonsillitis. Impetigo
1983	**Amoxil**	Tonsillitis
1983	**Amoxil**	Bilateral otitis media
1984	**Amoxil**	URTI. Viral. 104^0F
1984	**Amoxil**	
1985	**Amoxil**	Cough
1985		Tonsillitis

1985	**Erythroped**	
1987	**Amoxil**	Bilateral otitis media
1988	**Amoxil**	Tonsillitis
1988	Chloramphenicol eye drops	Conjunctivitis
1988		Conjunctivitis
1990		Conjunctivitis
1991	**Amoxil**	Cough. Green sputum. Says not getting any better.
1991	**Amoxil**	Improving
1991		Bilateral ingrown toenails
1991	**Amoxil**	Infected toe nail again

Table 8.4 Case B4. Health records of a non-diabetic child.

Discussion

Upper respiratory tract infections were first reported following exposure to Amoxil, after which tonsillitis, cough and conjunctivitis were reported. In January 1984 Wayne is diagnosed as having a viral upper respiratory tract infection. This is interesting on several accounts: it occurs within two months of a prescription of Amoxil as has been seen to occur in other children; the doctor has diagnosed it as being of viral origin without any tests having been performed. If it was indeed a viral infection, an antibiotic should *not* have been prescribed.

The Amoxil that Wayne receives in May 1983 for tonsillitis does not appear to be of any use, as he complains of tonsillitis again the following month. In May 1985, he is inappropriately prescribed Amoxil for a cough and returns later the same month complaining of tonsillitis. It is this sort of profile of multiple exposures to Amoxil and recurring infected toe-nails that would lead me to place this child at higher risk of diabetes later in life.

Case B5: Claire born 1981. *Caesarean* for foetal distress.

Date	**Prescription**	**Condition treated**
1981	Eczema	
1982	Eczema	
1982	**Pen-V**	Glass in sole of foot
1982	**Septrin**	Throat?

1983	**Bactrim**	Cut finger
1983	**Septrin**	Otitis media
1983	**Septrin**	Now typical measles rash. Sore eyes
1983	**Septrin**	Otitis media
1983	Hydrocortisone cream	Eczema
1983		Vomited. Fever
1983	**Erythromycin**	Coryza. Cough
1983	**Septrin**	Catarrh++. Green sputum
1983	Piriton	*Rash*
1983	**Erythromycin**	
1983	**Amoxil**	Cold. *Rash*
1983	Phenergan	Cyst
1984	Dioralyte	Diarrhoea and vomiting. Cough, cold, wheezy
1984	**Erythromycin** Ventolin	Cough. Wheezy
1984	**Erythromycin**	Phlegm 3 days
1985		Seems to be having dysuria, red and sore down below
1985		Chicken-pox
1985	Sudafed	Catarrh
1985		Unwell. Vomiting. Earache
1985		Eczema right ear
1985		URTI
1986		URTI continuing
1986	Sudafed Chloramphenicol	Catarrh. Vomits. Conjunctivitis
1986		Rash on forearm
1986	Piriton	Catarrh. Eczema
1986	Sudafed, Phenergan	Still catarrhal
1986		*Mother wants antibiotic*
1986		Off-colour. Aches in both loins.
1986		Conjunctivitis
1987		Pea-sized gland in neck
1987		Pyrexial. Neck stiffness
1987		Diarrhoea and vomiting
1987		Pain in groin
1987	Sudafed	Cough
1987		Hernia
1987		Lump in groin

Table 8.5 Case B5. Health records of a non-diabetic child.

Discussion

After Claire's first exposure to penicillin-V to prevent possible infection following a wound in the sole of her foot in June 1982, Claire

developed a throat problem. After exposure to Septrin in May 1983, Claire returns to the doctors in June with eczema which is treated with a steroid cream. It is highly likely that her eczema and rashes in June and December 1983 were due to antibiotics she had been prescribed. After two more courses of antibiotics, otitis media was reported; after further courses of antibiotics and other drugs, *vomiting, fever, diarrhoea* and *wheezing* were reported.

During 1983, seven courses of antibiotics were prescribed. During 1985 to mid-1987, despite varied health problems and Claire's mothers request for antibiotics, no antibiotics were recorded as having been prescribed. Catarrh, conjunctivitis, fever, vomiting, earaches and pains of unknown origin were reported from time to time following Claire's multiple exposure to various drugs.

Case B6: Russell born 1978.

Date	Prescription	Condition treated
1979		Cough
1979		Cough
1981	**Amoxil**	Otitis media. Earache
1981	Sudafed	Swollen mucosa. Nasal obstruction
1981	**Erythromycin**	Ear infection
1981	**Amoxil**	Wheeze
	Sudafed	
1981	Sudafed	
1981		Wheeze
1981	**Amoxil**	Wheezy bronchitis
	Alupent	
1981	**Amoxil**	Cough, wheeze
1981	**Amoxil**	Cough, cold
1982	**Penidural**	Tonsillitis
1982	**Septrin**	
1982	**Amoxil**	Tight foreskin
1982		Fell
1982	**Amoxil**	Wheezy bronchitis
1982	Ventolin	URTI. Blocked nose
1982	**Penbritin**	Bad chest
1982	Actified	Chesty
1982	Actified	Chicken-pox
1983	Ventolin	
1983	Ventolin	

1983		Ringworm
1983	Canestan	
1983		Wheezy again after URTI
1983	**Ampicillin**	
1983	Ventolin	
1983	Ventolin	Painful ear
1984	**Ampicillin**	Swollen right side face
	Actified	Mumps
	Ventolin	
1984	**Ampicillin**	Wheezy, coughing
	Ventolin	
1984		Nasal obstruction
1984	**Erythromycin**	Cough, wheeze
	Salbutamol	
1984	Salbutamol	
1984	Ventolin	
1984	**Amoxil**	
1984	Ventolin	
1984	Ventolin	
1984	Ventolin	
1984	Ventolin	Wheezy
1985	**Ampicillin**	Measles
	Ventolin	
1985	**Ampicillin**	Occasional ear ache. Infected drums
1985	Ventolin	
1985	**Ampicillin**	URTI. Acute bronchitis
1985	Ventolin/Intal	
1985	**Ampicillin**	Febrile. Tonsils
1985	Ventolin/Intal	
1985	Ventolin/Intal	
1985	Intal	
1985	**Ampicillin**	Pyrexia. Glands
1985	Ventolin/Intal	
1985	Intal	
1985	**Ampicillin**	
1986	Intal	
1986	**Erythroped**	Mild asthmatic
1986	Intal	
1986	**Ampicillin**	Otitis media
1986	Intal	
1986	Ventolin	
1986	Intal, Ventolin	
1986	Intal, Ventolin	
1986	Intal, Ventolin	
1986	**Penicillin**	Otitis media
1986	Sudafed	
1986	Intal	
1986	Intal, Ventolin	

1987	Intal	
1987	**Amoxil**	Earache
1987	Intal	
1987	**Ceporex**, Ventolin	
1987	Intal	
1988	Intal, Ventolin	
1988	Intal, **Ceporex**	Fever, earache
1988	Intal	
1988	**Pen-V**	Otitis media
1989	Canestan	Nasty looking itchy spot on L foot
1989	Intal	
1989	Intal	
1989	Intal	
1990	Intal, Atrovent	Asthma
1990	**Fluocloxacillin**	Swollen R hand
1990		Blocked nose. Refer ENT if no improvement
1990	Intal	
1990	Ventolin inhaler	
1990	Ventolin	
1991	**Amoxycillin**	Chesty, pyrexia
1991	**Amoxycillin**	URTI. Advised to reduce Ventolin use.
1991	Volmax (Salbutamol)	
1991	Merbentyl	Bowel spasm and pain
1991	**Amoxycillin** Ventolin	Wheeze, cough
1991	**Amoxil**	Sore throat
1991	**Amoxil** Ventolin	?dash bronchitis

Table 8.6 Case B6. Health records of a non-diabetic child.

Discussion

After Russell's first course of erythromycin in June 1981 at the age of two, he is reported during the next month to be wheezing for the first time. Following subsequent exposure to Amoxil and Sudafed, Russell's wheeze continues and develops into wheezy bronchitis. In my opinion, both amoxycillin and Sudafed (which contains guaiphenesin and pseudoephedrine hydrochloride) are toxic to the lungs.

After the first course of antibiotics, ear 'infections' become a recurring problem. As the total exposure to antibiotics increases,

Russell begins to *wheeze,* suffer from *bronchitis* and eventually becomes asthmatic.

Case B7: Bruce born May 1983.

Date	Prescription	Condition treated
1984	**Amoxil**	URTI
1984		URTI, *rash*
1984	Actifed	Blocked nose
1984	**Amoxil**	?R otitis media
1985		Coughs, colds
1985		Diarrhoea
1985	**Penbritin**	Otitis media
1985	?	
1986		Cough
1987		Vomiting, pyrexial
1988	**Keflex**	Penile infection
1988	Linctus	Still coughing, pyrexial
1988	**Pen-V**	Throat infection
1988		Headaches this pm
1989		Knocked head
1989	Linctus	URTI
1989	Linctus	
1989	Sudafed	URTI
1989	**Amoxil**	L ear infection
1990	**Amoxil**	Bilateral otitis media

Table 8.7 Case B7. Health records of a non-diabetic child.

Discussion

The rash that Bruce presented with in May 1984, 15 days after a prescription for Amoxil, could have been related to his exposure to Amoxil. In addition, Amoxil does not appear to have cured what was diagnosed as an upper respiratory tract infection. Within 6 months of his first exposure to Amoxil, bronchitis, chest 'infections' and otitis media were reported. Note how after the course of Keflex (a cephalosporin) in March 1988 Bruce returns to the doctor during the same month with a cough and again the next month with a throat infection. Since cephalosporins share structural similarity with penicillins, if penicillins are harmful to lung tissue, cephalosporins are

also very likely to be so. If this is the case, this might explain episodes of coughing following exposure to such antibiotics.

Case B8: Paul born 1986.

Date	Prescription	Condition treated
1986	Xylometazoline	Stuffy nose, catarrh
1986	**Hydrocortisone**	Nappy rash
1986	Calpol	
1986	Xylometazoline	Cold, oral thrush
1986		Diarrhoea
1986	Fungilin oral suspension	Recurrence of thrush
1986	Fucidin cream	Cradle cap
1986	Sudafed	Snuffly, cough
1986	Fungilin oral suspension	
1987	Daktarin oral gel	Oral thrush
1987		Advice
1987		Chicken-pox
1987	Sudafed	URTI, diarrhoea
1987		Still pyrexial
1987		Fine now
1987	**Erythroped** Sudafed	URTI
1987	Alupent	Cough at night, nodes, throat red
1987		Cough++
1988	**Amoxil**, Alupent	Wheezy, bronchitis

Table 8.8 Case B8. Health records of a non-diabetic child.

Discussion

These records show that within approximately two weeks of a prescription for Erythroped (erythromycin) in October 1987, Paul returned to his doctor complaining of a *cough* and *swollen lymph nodes.* Within three weeks of his first exposure to erythromycin, Paul is reported to be coughing, with wheezy bronchitis first being reported within four months of exposure to erythromycin.

If erythromycin is harmful to lung tissue and is asthmogenic, Paul's wheezy bronchitis need not necessarily have been the result of an infection, but could have been the result of recent damage to the

lungs caused by exposure to erythromycin. If this was the case, the antibiotic Amoxil, which may also be asthmogenic, has been prescribed unnecessarily and is likely to cause further damage. Unfortunately the unsuspecting doctor and parents may continue to administer drugs to Paul if he returns later with further health problems following drug exposure.

Case B9: Sheila born 1979.

Date	Prescription	Condition treated
1979	Nystatin	Thrush
1979	**Penidural** (Benzathine penicillin)	*Viral* infection, chest clear
1979	Linctus **Penidural**	Cough
1980	Timodine	Nappy rash
1980	Timodine	
1980	Linctus	
1980	Linctus	
1980		Teething
1980		Teething
1980	**Penidural**	Throat infection, croup
1981	**Penidural**	
1981	Chlomycetin eye drops	
1981	Tar vaporizer	Croupy cough
1982	Merbentyl	Colicky, abdominal pains
1982	Benylin (diphenydramine)	?mumps
1982	Benylin	Chesty, mouth ulcers
1983	**Distaclor** (Cefaclor)	?Tonsillitis
1983	**Erythroped**	
1983		Mild conjunctivitis
1984	**Erythroped**	Nasty tonsillitis, pyrexial
1984	**Distaclor**	Tonsillitis++, fever++
1984	**Penidural**	
1984	**Penidural**	Tonsillitis
1984	**Penidural**	L otitis media
1985	**Distaclor**	Tonsillitis
1985		Scaly spots on arm
1986	**Penidural**	Tonsillitis
1986	**Penidural**	Blocked nose
1986		German measles
1986	**Penidural**	Tonsillitis
1986		Sore throat
1987	**Erythroped**	Throat infection, pyrexial

1987	**Pen-V**	Sore throat, large tonsils
1987	**Erythroped**	Tonsillitis. Smallpox
1987	**Pen-V**	Tonsillitis viral. Febrile
1988	**Erythroped**	Continue Calpol for temperature
1988		Cough
1989		Temperature and headaches, tonsils red and exudative
1989	**Pen-V**	Acute throat
1989	Vermox	Worms
1989	Canestan	Still itchy
1990		Mid-stream test
1990	**Septrin**	Sore throat
1990	**Amoxil**	Chesty cough. Bronchitis
1991	Dimotapp	
1991	Canestan	Itchy, sore below
1991	**Ampicillin**, Canestan	Itchy
1991	Sudafed	Cough, cold
1991	Trimethoprim	Urinary tract infection
1991	**Amoxil**	Symptoms +++
1991	Timodine cream	Itchy discharge
1991	Sudafed	Sore throat. Mother concerned as asthma runs in the family

Table 8.9 Case B9. Health records of a non-diabetic child.

Discussion

The first question this data raises, is why do babies of one month suffer from oral thrush? Is it possible there is an association between drugs to which babies have been exposed to at birth and such symptoms? Cases B2 and B3 who were born prematurely and with the use of forceps respectively, where drugs are perhaps more likely to be used, both suffered from oral thrush.

Before she was three months old, Sheila received Penidural, an antibiotic for an undiagnosed viral infection. The 'infection' occurred shortly after her exposure to Nystatin; the antibiotic Penidural was inappropriately prescribed as it serves no purpose for a viral infection. Frequent prescriptions for antibiotics between 1984-1987 sometimes only weeks apart, often seemed to lead to worsening symptoms. At the very least, they certainly didn't lead to good health!

As her exposure to antibiotics and other drugs increases, Sheila begins to suffer from conjunctivitis, *fever, tonsillitis, otitis media, headaches* and *vaginal thrush,* a pattern sometimes seen in diabetic children pre-diagnosis of diabetes.

Case R10: Neil born 1983

Baby admitted to Special Care Baby Unit (SCBU) after birth due to possible meconium aspiration. Mother suffers from hayfever.

Date	Prescription	Condition treated
1983	**Ampicillin**	
1984		Teething
1984	**Ampicillin**	
1984	?suspension	
1984		Advice
1984		Continual loose bowels. Stool specimen to lab
1984	Kaopectate	Diarrhoea and vomiting
1984		Advice
1985	Actified	URTI, cough, sputum white
1985		Diarrhoea 2-4 months and vomiting for 5 days. Generally unwell
1985		Normal lymph node
1985	**Pen-V**	Follicular tonsillitis. Nodes+++
1986	**Amoxil**	Right otitis media
1986		Pyrexia ?Unwell
1986		Refer to hospital – slight hepatomegally
1986		Always had a large tummy
1987		Verruca on foot
1988		Vague tummy pains for months
1988		Unwell, vomiting, pyrexia
1988		Headaches, vomiting, pyrexial
1989		Viral
1989	**Pen-V**	Persistent cough. Sub-acute tonsillitis, cervical lymph nodes
1990	**Amoxil**	Left otitis media
1991	**Amoxil**	Earache R otitis media
1991	**Septrin**	R otitis media
1991	**Amoxil**	L otitis media

Table 8.10 Case B10. Health records of a non-diabetic child.

Discussion

As Neil was admitted to a SCBU from another hospital after birth, he may have been administered drugs at birth which do not appear on his medical records. Also, as his mother was known to suffer from hayfever, it is possible that she may have had over-the-counter or prescription medicines during pregnancy. Most over-the counter medicines for hayfever contain *antihistamines,* potent drugs which often do not carry any warning for pregnant women.

Some 3-4 months after a prescription for Actified in March 1985, Neil is reported to have been suffering from diarrhoea for 2-4 months. Actified contains pseudoephedrine hydrochloride which can cause mild epigastric distress. Neil is first reported as suffering from otitis media in Jan 1986, the month following an exposure to the antibiotic Penicillin-V. As Neil's total exposure to antibiotics increases, episodes of otitis media become more frequent and seem to occur within 6 months following exposure to an antibiotic.

Case B11: Joshua born 1974

Date	Prescription	Condition treated
1975		Catarrh
1975	**Septrin**	Bronchitis. Failed to respond to Ampicillin (no GP record showing ampicillin found)
1976		Worried about cough
		Vomited, lethargic, pyrexial. Diagnose gastroenteritis
1977	**Ceporex**	Pain L ear. Drum bulging
1977	**Erythromycin**	Ear red
1977	**Erythromycin**	Still red
1977		Drums dull. Diarrhoea
1977	**Amoxil**	
1977	**Septrin**	
1978		Cough
1978		*Poor hearing test*
1978		Ears ok
1978	**Amoxil**	L otitis media
1978	**Ampicillin**	Otitis media, conjunctivitis
1978	**Keflex**	Painful ear again. Drum inflamed
1978	**Keflex**	

	Piriton	
1978	**Ampicillin**	Otitis media last 2 days
1978		Cough
1978		Still whooping
1978	**Erythromycin**	
1978	**Amoxil**	L otitis media
1978	Phenergan	Drums red
1978		Ears clear
1978	**Pen-V**	Tonsillitis, otitis media
1979		Headache
1979	**Amoxil**	Discharge L ear
1979		Enuresis
1979		Rash on face
1979	**Amoxil**	Discharge L ear
1979	**Amoxil**	R otitis media
1979		SOS call. Doubled up with pain for 1.5hrs. Looks well
1979		Glands? Mouth ulcer
1979	**Amoxil**	Bilateral otalgia, catarrh
1980		Catarrh, ears seen
1980		URTI
1980	**Amoxil**	Discharge. Otitis media
1980		Dry skin patch on neck
1980		*Scarred ear drums*
1980		*Audiogram poor*
1980		Waiting for grommets
1981		Rectal pain
1981	**Pen-V**	Feverish, vomiting, glands
1981		Advice. ?threadworms
1981	**Pen-V**	Vomited x10. Headache, red throat, tonsils
1981		Vomiting, headache, pyrexial, viral tonsillitis
1981		Vomited x20. ?Viral
1981		Vague abdominal pains
1981		Mild otitis media
1982		Painful neck
1982		X-ray report
1982		Advised
1982		Pyrexia, vomiting
1982		Headache, glands
1982		Rubella
1982	**Amoxil**	Otitis media
1983		Ear drums ok
1983	**Amoxil**	Deaf 3 days. Catarrh
1983	**Amoxil**	Vomiting. Red drums
1983		Well
1983		Feverish, vomiting, cervical lymphadenopathy
1984		Tonsillitis

1985		URTI
1985	Sudafed	
1987	**Distaclor**	L otitis media
1987	**Amoxycillin**	Catarrh, cough
1987		Headaches, migraine, abdominal pain for months, nausea
1987	**Cephalosporin**	Otitis media
1988		Frequent headaches for months
1988		Migraine. Refer to paediatrician. Headaches began 1yr ago, followed by tunnel vision R eye
1988	**Amoxycillin**	Flu-like symptoms
1989		?Glandular fever
1989	**Amoxycillin**	Otitis media
1991	**Pen-V**	Headache, vomiting
1991		URTI, hot and sweaty, red throat, brown sputum
1991	Sudafed	Pink ears. Catarrh
1991	**Amoxil**	Bilateral otitis media

Table 8.11 Case B11. Health records of a non-diabetic child.

Discussion

By 17 years of age, Joshua has received *thirty-one* courses of antibiotics and his health seems to have deteriorated over the years as his total exposure to antibiotics increased. From an initial problem with bronchitis in July 1975, which did not respond to septrin, Joshua returned to the doctors with further and varied problems following increasing exposure to antibiotics.

In October 1977, Joshua was prescribed *three* courses of antibiotics for an ear problem which did not seem to improve with antibiotic therapy. His health records show that he frequently returns to the doctors with further problems soon after a course of antibiotics. This could be interpreted as the drug not only having *no* therapeutic effect, but as being responsible for *additional* health problems.

In April 1979, Joshua is reported to be suffering from enuresis (bed-wetting) following a course of Amoxil the previous month. I have seen this in several records and wonder whether it could possibly be the result of kidney damage caused by antibiotics (see chapter 4). In November 1979, three days after a prescription of Amoxil, Joshua

was seen by a doctor on an SOS call-out due to acute abdominal pain. Interestingly, Joshua has been obese for many years, which would reduce the dose of drug per kilogram of bodyweight. Consequently, his obesity could have a protective effect against any potential toxic effects of a drug.

Case B12: Melissa born 1982

Date	Prescription	Condition treated
1982		Cough
1982	Timodine	Dermatitis
1982		Dermatitis
1982		?otitis media
1982	**Amoxycillin**	Tugging at ears. L drum has tiny node
1982		?Pneumonia
1982	**Erythromycin**	Pertussis contact
1982	**Erythromycin**	
1983	Actified	Heavy cold
1983	**Amoxil**	Both ears infected
1983	Dimotapp	Further ear infection 2 wks ago
1983		Pulling at both ears
1983		URTI mild
1983		Cough
1983	Prosobee	
1983	**Amoxil**	Otitis media
1984	Prosobee	
1984	Prosobee	
1984	Prosobee	
1984	Prosobee	
1984	Prosobee	
1985	**Amoxil**	Measles. Otitis media
	Later at 2pm	Convulsion 10mins. ?Febrile. Drowsy++
1985		Out of hospital
1985	Piriton	Chickenpox
	Calamine lotion	
1985		Threadworms
1985	Vermox	Threadworms

Extracts from health records:

1985	**Amoxil**	Wheezing
	Ventolin	
1986	**Erythromycin**	
1986	**Erythromycin**	Eczema infected again. Also has rubella-like erythromatous

		macropapular *rash* on trunk with cervical nodes.
1987		Miserable. Itchy. Pyrexial
1989	**Erythromycin**	
1989	**Erythromycin**	
1989		Shingles

Table 8.12 Case B12. Health records of a non-diabetic child.

Discussion

Some points of interest in these records are, within eight days of a prescription for amoxycillin in November 1982, Melissa returned to the doctors with uncertain pneumonia and was possibly still chesty and coughing in November for which prescriptions of erythromycin were given. Within two weeks of a prescription for Amoxil in 1983 for an ear infection, she developed a further ear infection. This would seem to suggest that the antibiotic was ineffective. In February 1985 after a prescription for Amoxil, Melissa was admitted to hospital suffering from *convulsions.*

After 4 courses of Amoxil and 2 of erythromycin, Melissa was reported to be *wheezing.* Within approximately 3 weeks of a course of erythromycin in 1986, she returned to the doctors with *eczema* and a *rash* that was characteristic of an adverse drug reaction. The rash was very likely to have been caused by erythromycin and unfortunately a further prescription for this drug was given. Three weeks after a course of Erythromycin in October 1989, she was reported to be suffering from shingles. This was possibly due to further exposure to erythromycin.

Summary

The health records of non-diabetic children studied, some of which are listed in Tables 8.1-8.12, reveal the following:

Antibiotics are sometimes <u>inappropriately</u> prescribed (eg. for colds, measles, 'viral' infections), ie. they are prescribed for conditions that will not be improved by antibiotic therapy.

Antibiotics are sometimes grossly over-prescribed, even on two consecutive occasions within a three week period.

Parents sometimes pressurize a doctor to prescribe an antibiotic.

Children who have experienced several exposures to antibiotics commonly suffer from fever, vomiting, diarrhoea and abdominal pain of unknown origin.

Children who have been prescribed a course of antibiotics often return to the doctors within one month complaining of a rash, which is rarely recognized by the doctor as possibly being due to drug exposure.

Soon after a course of antibiotics, some children appear to suffer from other health problems, or the condition for which the antibiotic was prescribed worsens.

Children who have been exposed to antibiotics on several occasions in general appear to suffer from tonsillitis and otitis media, these conditions appearing to increase in frequency and intensity with increasing exposure to antibiotics.

Following several prescriptions for antibiotics, erythromycin in particular, some children appear to develop symptoms of wheezing, which after further prescriptions for antibiotics, may develop into asthma (see chapter 8).

After several courses of antibiotics, some children seem to develop hearing problems.

Occasionally children are reported to be bed-wetting (enuresis) very soon after a course of Amoxil.

Discussion

Examination of the side-effects of chemicals that once were commonly used in medicine (see chapter 2), reveals that many are identical to side-effects experienced by some of the non-diabetic children whose health records are listed in Tables 8.1-8.12.

It may be argued that the illnesses suffered by these children following drug exposure are not necessarily related to drug use, but are conditions that would have appeared even in the absence of antibiotic therapy. However, there are patterns which appear with remarkable frequency and would be consistent with drug exposure being to blame for the following reasons:

Medical literature has already documented many health problems arising from exposure to antibiotics.

Exposure to antibiotics is known to confer a risk of developing asthma (see chapter 8).

Intravenous administration of ampicillin, which is very similar in structure to amoxycillin and may be considered to be a less potent antibiotic, has been reported to be associated with the loss of hearing in children treated for meningitis (1).

High doses of erythromycin given to adults are known to cause deafness. This, as in the case of ampicillin, is considered by the author to be a symptom of a drug that is toxic to the auditory system.

Many drugs are known to be ototoxic (ie. toxic to the ear's delicate tissues). For example, prolonged use of aspirin can cause tinnitus and deafness (over 200 drugs are known to cause

tinnitus); chloroquine can cause nerve damage several weeks after high-dose therapy has ended. The antibiotics kanamycin and neomycin can cause severe auditory damage, whilst gentamycin and tobramycin can damage the vestibular canals, causing dizziness and loss of balance.

In a study of 185 children treated with Amoxil, 41% were reported to have had at least one further episode of acute otitis media which required medical care, during the year after the trial.

In 1993, an Australian magazine Nature & Health[2] cited a publication[3] by American doctors which states that:

Children treated with amoxicillin for earaches suffered 2-6 times more recurrent infections.

Children treated with antibiotics for streptococcal tonsillitis suffered 2-8 times more recurrence.

Some antibiotics are known to be nephrotoxic, causing a functional or structural change in the kidneys. Since kidneys have the highest blood supply per gram of any tissue in the body, they receive a disproportionate sample of absorbed agents present in the blood supply. Enuresis occurring soon after exposure to antibiotics may be indicative of kidney damage caused by antibiotics (see chapter 4).

Many children, whose medical records have not been listed, were noted to have suffered from urticaria or pruritis (itching) soon after a prescription for an antibiotic. However, only in extremely rare instances has this been identified by the doctor as a possible reaction to the drug, in which case the drug is stopped and should not be

prescribed again. Some children after several exposures to antibiotics begin to suffer from genital thrush, a condition which is sometimes reported after antibiotic use. This association is easier to appreciate when one is aware of the fact that many pharmaceutical drugs and creams are capable of disturbing the body's normal bacterial flora.

On the subject of rashes and the use of drugs, The Merck Manual of Diagnosis and Therapy states that:

> *Acute urticaria can be due to drug allergy and its cause is usually obvious. If the cause is not obvious, it is recommended that all non- essential drugs should be stopped until the reaction has stopped and that pruritis may be a symptom of systemic disease and is sometimes the only symptom. Many drugs can cause pruritis. Unproved associations with generalized itching include diabetes mellitus. If no skin disease is readily apparent, an underlying systemic disorder or drug-related cause should be sought. If feasible, all drugs should be stopped or chemically unrelated drugs substituted. If antihistamines (eg. Piriton) are at all helpful, the main reason may be because of their sedative effect.*

Comparison of the conditions that some of the diabetic (see chapter 7) and non-diabetic children reported in this chapter have suffered from, may be seen to be identical to certain side-effects of some toxic chemicals which used to be commonly used in medicine (see chapter 2). These include diarrhoea, convulsions, sore throats, abdominal pain, conjunctivitis, respiratory problems, rashes, thirst and fever. Conditions that we have seen with great frequency in the children studied in this chapter who have been exposed to antibiotics. As yet, we do not have any evidence to show that some of the health problems these children have experienced are not related to their

drug exposure. Younger children have a greater risk of damage to health following drug exposure. Without regard to their immature organs, children 3 years of age sometimes receive the same dose of a drug as children aged 9 years.

"All prescribed and over-the counter drugs are high risk substances for an infant. The main reason is immaturity of the liver and kidney organs. A mature liver is essential to break down circulating chemicals into smaller, less toxic units for excretion. In the infant this may be slow or impaired, so that toxic by-products accumulate and affect physiological functioning and well-being.

The infant is also at risk from iatrogenic (doctor-induced) disease because of parental anxiety or pressure to prescribe - often for superficial trivial complaints - which would be far better treated by simpler preparations, or just observed."
Dr Trevor Smith, The Side Effects Book, 1989.

Hearing problems in children in the UK are thought to have increased dramatically over recent years. A survey conducted in 1986 in the UK produced the startling result that an estimated 6:1,000 children had a hearing disability. The reason for the increase remains unknown. In the 1996-97 census in New Zealand, 7.7% of children under the age of 5 years were found to have chronic hearing loss. The reason for this high figure is also unknown. But at present, there are some 200 drugs that are toxic to the ears, including ampicillin, amoxycillin and erythromycin. It is my opinion that these antibiotics and other drugs are likely to be the major cause of these hearing problems.

Examination of events which ultimately lead to the introduction of a drug for widespread use does little to create confidence in the drug or the systems which exist even today, to ensure the safety of patients. Studies to look at the possible toxicity of penicillin began with a few experiments in mice. These were followed by tests on a human volunteer, as a result of which it was discovered that the preparation contained impurities which caused the patient to suffer from 'rigor', flu-like symptoms which caused shivering and a high temperature. A later purified version of the drug was then tested on rabbits and found to be free from the fever producing impurities.

This was followed by administering penicillin by a variety of routes to volunteers of the Oxford team and others on the staff of the Sir William Dunn School of Medicine. The results were considered to confirm the rabbit experiment and that the substance was non-toxic to humans. It was from this *handful* of observations that penicillin began to emerge for clinical use. Within a few months, penicillin had been tested on 6 patients, four of them children. The children were suffering from serious infections which included an infected blood clot in the brain; an infection of the bone of the hip; and a lung infection.

Professor Gordon T. Stewart, a former professor of epidemiology and pathology at the University of North Carolina who had been working with the Beecham Research Laboratories in England, where the semi-synthetic penicillins were being developed, wrote these sobering words about penicillin in 1965:

The results were convincing, each in a different way, and the absence of toxicity was almost as impressive as the rapid therapeutic effect. In the present day, when a clinical trial is becoming an exercise in statistics and bureaucracy, there is irony in the reflection that the massive efforts which followed were based

upon a few toxicity tests in rodents and upon a clinical trial in six selected subjects, two of whom died. Had the toxicity tests been extended to guinea-pigs, penicillin might have been rejected; had current regulations been in force, it would have been ineligible for submission.

In fact:

Penicillin would almost certainly not be allowed to come onto the market if it was 'discovered' today. Bodies such as the F.D.A. in America or the Medicines Commission in Britain would advise against it on account of the frequency of allergic side-effects. Penicillin might never have been developed at all if guinea-pigs, which are badly affected by the drug, instead of mice had been the first experimental animals on which it was tested.

As soon as 'large-scale' clinical tests with penicillin began in 1941, it became apparent there were side-effects associated with the use of the drug with some individuals only showing a reaction if they had been sensitized to it by a previous exposure. Angioedema, which includes symptoms of tightness of the chest, difficulty in breathing and *asthma-like* symptoms, were apparent even in those days. In rare cases, anaphylactic shock resulted in death if immediate treatment was not available. As far as I am aware, no studies have been carried out to look at the drug exposure history of infants who died suddenly and without explanation from cot-death, in which the infant stops breathing for some unknown reason. The question as to whether side-effects of penicillin should be regarded as toxic or allergic symptoms has been raised in the past.

There is considerable evidence however, that ampicillin rash is not always an allergic reaction. The evidence is provided by skin tests

in which patients receive a small amount of the substance under test, just lightly pricked or injected into the skin. If the patient is truly sensitive to the substance in an allergic fashion, a weal immediately arises at the point of treatment. Nearly ***70%*** *of people who had suffered from reactions to ampicillin have been shown not to be truly allergic to it.*
David Wilson, Penicillin in Perspective, 1976

In 1991, the booklet produced by the drug company Smith Kline Beecham in the UK, to market Amoxil to doctors, listed publications in medical journals concerning the efficacy of Amoxil as shown by clinical trials. The number of children in these groups tested with Amoxil never exceeded 103 and averaged 50. According to the manufacturers of Amoxil, there have not been any clinical trials to look at the effects of multiple exposures to Amoxil over many years:

"Thank you for your (the author's) recent letter requesting information on any studies which have investigated possible adverse events of repeated exposure of babies/children to Amoxil, over a period of approximately 10 years from the time of first exposure. I have performed a literature search and unfortunately, have been unable to locate any such studies."
Bencard (SmithKline Beecham), UK, 1992.

Unfortunately, it is usually on the basis of short-term testing that the public is exposed to potent chemicals. If many children and adults have experienced drug-induced side-effects, which were not detected as such by their doctors, our confidence in the design and reporting of clinical trials (for which members of the medical profession are responsible, and which enable drugs to enter routine clinical use), is surely ill-founded.

9

Drugs and Chemicals that can cause Asthma

On the appearance of any new drug an interesting cycle of events may often be observed. A trickle of favourable reports develops into a stream, and the drug then becomes fashionable. Then the stream of favourable reports dries, and accidents claim attention. The drug falls into relative disrepute, and its use may even be abandoned...
British Medical Journal, 1956.

The Disease

Bronchial asthma, most frequently referred to simply as asthma, is a sudden attack of difficult or laboured breathing, characterized by wheezing and difficulty in expelling air from the lungs due to muscular spasm of the tubes of the lungs. Treatment most frequently consists of the inhalation of drugs using a nebulizer or inhaler, which may contain gases acting as a propellant to expel the drug. Asthma has reached epidemic proportions in many industrialized societies. In the UK, with an approximate incidence of 4%, there are about 2 million asthma sufferers, of which more than 700,000 are under 16 years of age. Australia, which has an extremely low population density and much higher average annual temperatures compared to the UK, has an incidence of approximately 10%. This amounts to approximately 1.5 million sufferers. In the USA, the number of asthma patients doubled from 1982 to 1998, with some 20 million Americans in 2001 being classed as asthmatic. The condition costs the United States $14 billion annually.

Asthma and Children

Asthma is the most common chronic disease of childhood, with one child in every ten in the UK being diagnosed as asthmatic. In Australia, 1 in 8 children under 12 years, and 1 in 4 under 6 years are estimated as being asthmatic. Asthma has a high mortality rate; in the early 1990s, it accounted for almost 2000 deaths a year in the UK with 40% occurring in those under 65 years of age.

The disproportionate number of sufferers in the under-sixteen age group suggests the involvement of an environmental agent(s) to which younger generations have been increasingly exposed. My interest in asthma, with which I had no prior association, arose as a result of observations made during studies which looked at the health of diabetic children from birth to the time when diabetes was diagnosed. From interviews with, and questionnaires completed by parents of diabetic children who took part in a pilot study, I noted that some diabetic children were also asthmatic. This intrigued me, since many non-asthmatic children had a history of eczema or tonsillitis, which suggested a possible link between eczema and asthma (both of which are atopic conditions in which the person shows hypersensitivity to certain antigens) and tonsillitis and diabetes (conditions that involve and are thought to involve the immune system, respectively). The possibility of an indirect link between these conditions, in that they may result from a common exposure to antibiotics is discussed in chapter 7.

My later studies involving the examination of medical records of both diabetic and non-diabetic children produced the following observations:

The age at which children were being reported as wheezing with the result that some form of drug therapy, either oral or nasal was prescribed, was declining;

Wheeziness was often reported following several exposures to antibiotics, amoxycillin and erythromycin in particular.

The younger the age at which antibiotics were 'regularly' prescribed the younger the age at which 'asthmatic' symptoms were reported.

These observations prompted me to ask the following question:

Could exposure to antibiotics be causing asthma in children?

Chemical Exposure and Asthma

In the pamphlet 'Is Asthma Preventable?' produced by the National Asthma Campaign (UK), it states, in relation to the eradication of asthma, that the present understanding of asthma suggests that "this is unlikely to happen". On the other hand, if one asks the question 'Are any environmental agents known to cause asthma, rather than simply trigger an asthmatic attack?' the answer is *'Yes'.* Many chemicals are recognized as being capable of causing asthma, they include:

Isocyanates*. Chemicals used in the manufacture of plastic foam, inks, paints and adhesives.*

Acid anhydride and amine hardening agents*. Used in a wide variety of industries, including adhesives, plastics and moulding resins.*

***Proteolytic enzymes**. These are used in 'biological' washing powders.*

***Dusts** arising from barley, oats, rye, wheat, or maize. Tea and green coffee bean dust.*

***Glutaraldehyde**. An antiseptic chemical used in hospitals, laboratories, cooling towers and for leather tanning.*

***Azodicarbonamide**. A chemical used in the manufacture of expanded foam plastics used in wall coverings, floor coverings, insulation and packaging materials.*

***Ipecacuanha and Ispaghula**. Substances derived from plants and used in the manufacture of cough preparations and laxatives respectively.*

***Antibiotics**. Workers involved in the manufacture of antibiotics may be at risk.*

In fact, there are numerous drugs that can have an adverse effect on the lungs, and chemicals capable of causing asthma are very likely to provoke an attack in an asthmatic. Thus, each one of the everyday items in the above list such as paints, soaps, carpets and the chemicals in the excreta of dust mites can easily *provoke* an asthmatic attack.

Chemicals in processed food

Many processed foods contain chemicals that can either cause asthma or are suspected of doing so. Amongst these are *common* food colours, preservatives and flavour enhancers. A few of these are shown in Table 9.1 together with their ‘additive’ number. In Europe,

additive numbers are known as E numbers and are the same number only prefixed with an E.

102	Tartrazine	220	Sulphur dioxide
104	Quinoline yellow	223	Sodium metabisulphite
132	Indigotine	621	Monosodium L-glutamate
124	Ponceau 4R		

Table 9.1 Food additives known to or suspected of causing asthma.

These are common food chemicals that are ubiquitous in colouring used in sweets, lollies and candy; preservatives used in everyday foodstuffs such as soda pop, fizzy drinks, beer and wine; and flavour enhancers such as monosodium glutamate (msg) used in chicken salt, on crisps, chips, in soups, sauces, pre-cooked meats and meals, to name but a few items.

It should be easy therefore, to understand why some asthmatic individuals experience asthmatic attacks after eating food made with chemicals that are thought to cause asthma.

Antibiotics and 'Occupational Asthma'

It is already accepted that exposure to antibiotics and chemical intermediates involved in their production, can cause asthma. In the UK today, the Department of Social Security pamphlet NI 237, readily available to the public in 1994, states that individuals who have been exposed in their working environment to antibiotics and subsequently develop asthma, may be entitled to compensation. This disease is given the name 'Occupational Asthma'. Since pamphlet NI 237 simply mentions antibiotics, without listing any particular drug, one can conclude that all antibiotics are considered to be potentially capable of causing asthma.

On the subject of occupational asthma, The National Asthma Campaign in the UK states in its pamphlet 'Is Asthma Preventable?'

> **"Asthma which only occurs at work or in certain environments, is special... industrial processes can cause dust and fumes that we rarely, if ever, encounter in everyday life, to leak into the air of the work place."**
> National Asthma Campaign, UK

However, any agent that presents an occupational risk can obviously also affect those who come into contact with it but do not necessarily work with it. It could also be considered equally, if not more harmful, to ingest a substance such as a drug than to breathe air which is contaminated with its dust. The question of whether an individual will be affected by a toxin is always dependent on many factors, such as the degree of exposure, the genetic constitution of the individual, and the individual's general health and diet.

One need only consider asbestos, and the legislation introduced by many Governments to ban its use as a building material and to have it removed from schools and underground-train tunnels, to realize that a substance posing an occupational risk, may equally constitute a risk to *anyone* who should come into contact with the material. Exposure to asbestos can cause asbestosis and mesothelioma, a cancer starting in the covering of the lungs or the lining of the abdomen; it is an accepted industrial disease. Those working in confined spaces such as the cargo hold of ships or with power tools, have been known to be particularly affected due to the density of the fibres in the air and the mechanical propulsion of the fibres towards the user, respectively. Thus with asbestos, we have one example of an occupational hazard which is now *also* accepted as posing a risk to the general public.

An association between *antibiotic* exposure and *asthma* is accepted by the medical profession and the Department of Social Security in the UK and the Health Department of Australia. However, doctors and the public are either apparently unaware of this association, or have not drawn from it what I consider to be a logical conclusion; i.e. exposure to certain or all antibiotics for medicinal purposes may actually *cause* asthma.

Antibiotics are known to have side-effects; 'allergic' reactions to antibiotics such as penicillin have been documented in medical literature for over fifty years. The severity of these side-effects may range from a simple rash to anaphylaxis, a life-threatening reaction which includes difficult or laboured breathing, which are also symptoms of an asthmatic attack. It is now time to reconsider whether the side-effects of antibiotics should any longer be described as 'allergies', implying that the problem lies with the patient rather than with the drug. It is time we acknowledged that drugs producing an 'allergic response' are *toxic* and are in fact producing side-effects which are often symptomatic of poisoning.

Some antibiotics reported in medical literature as causing asthma in certain individuals include penicillin[1,2,3], ampicillin[4], cephalosporins[7,8], spiramycin [10,11,12] amoxicillin[5,6], tetracycline[9] , and erythromycin[13]. Other drugs and antibiotics have also been reported to cause asthma. These references which represent but a few of those published, have been selected to illustrate that a correlation between antibiotics and asthma has been reported from several countries, and can result from exposure in a *variety* of forms. They include:

A hospital attendant suffering from conjunctivitis, nasal occlusion, watery rhinorrhoea, generalized pruritis, cough and

expiratory wheezing, which were attributed to repeated inhalation of small amounts of penicillin.
A farmer who developed generalized pruritis and moderately severe asthma on three occasions shortly after giving his cows injections of penicillin.

Some employees of a factory producing penicillin and a number of semi-synthetic penicillin antibiotics first developed asthma two years after starting work in the factory. These symptoms were found to be related to exposure to the dusts of ampicillin and other penicillin antibiotics, and also occurred following the administration of these antibiotics by mouth in clinical doses.

Employees of a pharmaceutical company producing amoxycillin suffering from rhinitis and asthma.
Workers in the pharmaceutical industry developing asthma after exposure to 7-aminocephalosporanic acid, an intermediate used in the production of cephalosporine.

An asthmatic adolescent who developed urticaria (a skin condition characterized by the appearance of an eruption of weals causing irritation) and anaphylaxis following ingestion of a drug containing three different tetracyclines.

A woman who worked as a chick breeder developed asthma and dermatitis after handling poultry feed containing antibiotic or chemotherapeutic drugs. Drugs contained in the feed included spiramycin and chlortetracycline. (Any substance which contacts skin has the potential to be absorbed into the body. Processed animal feed pellets often contain several drugs. Battery hens, due to the appalling conditions under which they are reared, are fed antibiotics and chemotherapeutic

drugs for unnatural growth promotion and to combat diseases which spread rapidly in large commercial hen houses with thousands of hens).

Up to some 72% of workers exposed to spiramycin showed symptoms of asthma, rhinitis or urticaria.

Individuals suffering anaphylactic attacks after oral or intramuscular exposure to penicillin. Laboratory studies using blood samples from these individuals showed the release of histamine (an enzyme that causes local dilation of the blood vessels and increased permeability of the blood vessel walls) by leucocytes (white blood cells which are primarily responsible for fighting infection and foreign substances).

These examples illustrate that pharmaceutical processes are not alone in the induction of asthmatic symptoms. There have been suggestions that very low-level exposure to antibiotics resulting from the ingestion of foodstuffs (eg. milk containing antibiotics) may result in sensitization to these chemicals such that a severe reaction may result from later exposure. There is the possibility therefore, some children who died after exposure to dairy products to which they were known to be allergic, actually suffered a reaction to antibiotics in milk. Regulations usually require a dairy cow receiving antibiotics to be taken out of production, but in practice, this does not always happen.

Since exposure to antibiotics in some individuals can cause *anaphylaxis*, involving difficult or laboured breathing, it seems plausible to conclude, especially in light of data shown in this book, that exposure to antibiotics in the form of medicines can also cause asthma. Until there are studies which vindicate antibiotics in the aetiology of asthma, it must be regarded as highly probable that

antibiotics such as penicillins (eg. amoxycillin), erythromycin and cephalosporins are a major cause of asthma in children and adults today, in countries where they are commonly prescribed.

10

Drug Abuse – The Toll

> **We have become obsessed with the curative approach, believing that we should strive to produce a pill for every ill, whereas the best hope for a healthier world must lie in identifying and attempting to abolish the causes of disease.**
> Dr. Donald Gould, 1985, The Black and White Medicine Show, How Doctors Serve and Fail their Customers.

Diabetes is a disorder in which the pancreas, a gland located beneath the left lower ribs, no longer produces sufficient insulin. Insulin, a hormone, is essential to survival since it is required for the breakdown and storage of fat and carbohydrates and regulates glucose levels. Without insulin, toxic levels of certain chemicals would build up within the body and eventually result in coma and death.

Treatment for diabetics today involves regular injections, usually self-administered, of exogenous insulin to replace that which would normally be produced by the pancreas. The insulin should not be administered too far in advance of eating, nor should it be given after eating. The type and dose of insulin injected varies mainly according to the type and quantity of food to be eaten, and amount of exercise to be undertaken by the individual. Failure to meet these constraints can result in the presence of too much or too little glucose in the body. In the first instance, a gross excess of glucose can cause hyperglycaemia and result in coma. In the second instance, too little glucose in the body, due to too much insulin having been given, or failure to consume sufficient carbohydrates to match the amount of

insulin injected, can result in a hypoglycaemic coma. Basically, the brain is starved of glucose, a condition which can prove fatal if not treated sufficiently quickly. These potential complications of diabetes are faced by diabetics on a daily basis.

For the adult diabetic, taught to recognize the symptoms associated with having too high or too low a blood glucose level, the management regime is strict and the difficulties are often compounded by high temperatures and infections which alter insulin requirements. But how much more difficult it is in the case of babies who have been diagnosed as diabetic and the burdens placed on their parents, who are faced with the task of caring for a young infant before it has even reached the stage of being able to communicate how it feels. As a baby grows up, how does it perceive its caretakers when it is pricked with a hypodermic syringe at regular intervals during each and every day? Toddlers can be sufficiently demanding when in good health, but how much more difficult it is for their parents having to cope with complaints that they are not able to eat what other children are eating.

Many children diagnosed as diabetics show tremendous maturity in coming to terms with their condition, an obvious tribute to their parents and the medical staff responsible for looking after and educating them. But all their lives they will know that without proper attention to maintaining blood sugar levels within the normal range, health complications are likely to result. For diabetics, the complications can be very severe: coronary heart disease; renal failure; amputations of a major and minor nature; impotence; cataracts and blindness.

The diabetic child, through no fault of its own, invariably enters a *self-perpetuating* cycle of medical care after the diagnosis of diabetes.

Diabetics in general are more likely to suffer from infections for which they are likely to be prescribed drugs, are several times more likely to be admitted to hospital for treatment of infections, and to undergo surgery or to receive kidney dialysis or transplant. In their every-day lives diabetics also face problems. Even the diabetic who has no history of blackouts for example, may be discriminated against when it comes to obtaining: a driving licence or a job (employer's often have little understanding of the condition and simply look upon diabetics as a bad risk) or seeking mortgage insurance (most companies 'load' premiums for diabetics).

These problems simply add to the emotional cost of the disease, a cost that can never be quantified. The disease affects not only the diabetic but also their immediate family in particular, from parents to brothers and sisters who may feel neglected as a result of increased attention being received by the diabetic child. One sometimes hears of children who have wanted to be diabetic, like their brother or sister. Parents too, pay a heavy toll. How many mothers have had their post-pregnancy plans radically altered by the diagnosis of diabetes in their infant? Some parents, deeply concerned by the potential long-term pitfalls, visit their child's school each day to conduct a finger prick blood test to determine their child's blood sugar level.

It is unfair that diabetics and their families should, apart from the physical, mental and emotional costs, often also bear the brunt of job discrimination, higher car and mortgage insurance premiums, the cost of visits to hospital clinics, and the paraphernalia of treatment including drugs, hypodermic needles and meters to test blood glucose. If drugs are in any way responsible for their disease, diabetics are paying the price for the inadequacy of systems which have failed them, in every conceivable way.

The parents of diabetic children and the children themselves are the immediate sufferers, but there are also dangers to prospective diabetic mothers to be considered. With raised blood glucose levels, they may be prone to miscarriage and consequently undergo drug therapy in an attempt to prevent pre-term labour. These drugs as previously discussed, pose a hazard to the foetus.

Each visit to the hospital or doctor often results in further exposure to pharmaceutical products. These include the provision of insulin and syringes for the rest of the diabetic's life, drugs to control blood pressure and other symptoms more common in diabetics, dressings, solutions and equipment, and many other products which contribute to the considerable revenue of the drug companies. Any new symptoms following drug exposure will perpetuate the cycle with the patient probably being prescribed further drugs. As drug therapy diverts our attention and resources away from the discovery of the causes of disease and a methodology for disease prevention, the tragic irony is that it may well be responsible for causing further disease.

Asthma, the most common chronic disease of childhood in some industrialized countries, is another condition for which treatment is often administered on a daily basis. Breathing during an asthmatic attack involves having to fight against constricted air passages to pull air into the lungs, only to discover that the oxygen intake is a fraction of what is needed. This leaves the patient rapidly repeating the frightening and exhaustive process of forced expiration and intake of air. Asthmatics, like diabetics, may also enter a self-perpetuating cycle of drug therapy, as they usually receive regular prescriptions for drugs, all of which have side-effects which may lead to further health problems.

If any of the drugs discussed in this book are implicated in the onset of diabetes or asthma, immediate action is needed to try to discover whether drugs are the unknown environmental factor responsible for the unprecedented increase in these diseases. Prompt research is needed to ensure that these questions do not become increasingly difficult to answer as more drugs enter the marketplace. Even if these questions were answered in the very near future and drugs were found to be implicated and withdrawn from use, only time will show whether children who have been exposed in the past to these drugs but who have no symptoms of disease at present, will develop a disease in later years. As drugs that can cause diabetes are very likely to have damaged the pancreata of many people who are at present non-diabetic, and who will not show any signs of disease until further demands on the pancreas such as weight gain; pregnancy; chemical exposure perhaps from tobacco smoke or from other drugs or chemicals are experienced.

It is frightening to contemplate that at a time when the dangers of drug therapy are not fully appreciated we are rocketing into an era of drug use, ostensibly for disease prevention. For example, clinical drug trials with women thought to be at risk of breast cancer dose participants *before* any disease has been detected; *healthy* children with asthmatic parents are administered antihistamines to determine whether this will prevent asthma. Thus, it is not unlikely that some initially disease-free individuals will develop disease through experimentation with drugs.

Then there is talk of prophylactic drug therapy for pregnant women, whose foetuses are thought to be at risk from asthma. What a terrible irony, if a healthy foetus should develop a disease later in life from the side-effects of a drug its mother was given during pregnancy, due to her suffering from asthma that was caused by drugs!

11

What Now?

"…people must become full partners of health implementation…"
World Health Organisation Committee, 1983.

Any medical research requiring data on patients' health and lifestyles understandably runs into difficulties. To gain access to patient records, many requirements need to be fulfilled. Even when patients personally agree to an examination of their health records, resistance may be encountered from the medical profession. Hospital consultants may present the first barrier to a prospective study, simply by declining to allow their patients to be asked to participate in a study.

Some reasons for this opposition include a feeling by physicians that their patients have been over-studied, and in the case of children, that questions about lifestyle would add to the guilt that parents may already feel for their child's disease. On one occasion, I encountered a consultant in the UK, who wrote to me that he would:

> *"...rather avoid the hassle of an application to the hospital ethical committee, to ask for approval for the study."*

Fortunately, others were more willing to play a part in a study they must have considered worthwhile.

Reactions to applications to conduct a study can vary widely. Whilst one hospital approved of my study of 'environmental factors' in relation to diabetes, another hospital ethical authority in a neighbouring district considered the same study had *"no scientific merit".*

Since health-care is becoming increasingly financially oriented, it is perhaps not surprising that the medical profession or hospital administrators will not always support investigations of possible drug-related injury to health.

Once a consultant has given permission for patients to be studied, a lengthy application for study approval must usually be submitted to the hospital's ethical committee. If the study includes a questionnaire, objections may be raised by the ethical committee to some or all of the questions asked. Objections raised by some consultants to my study included:

"…women do not know what drugs have been administered to them during labour, and should therefore not be asked."

However, from my limited experience, I found that most mothers were aware both of the names of the drugs that they were given, and the reason for their use.

When approached for approval for a national study in the UK, to examine the health and background of children with diabetes pre-diagnosis, that was to be independently funded by myself, The Royal College of General Practitioners declined for the following reasons:

> "We noted that parents will be asked to give access to their child's medical records but they will not necessarily know what information these contain and therefore what they are agreeing to disclose to a third party. We noted that mothers will also be asked to grant you access to their medical records and we thought that again they would not know what information they had agreed to disclose...
>
> The Committee have considerable anxiety about the appropriateness of contacting parents directly and feel it would be preferable to contact the GP first so that the GP can advise you about the appropriateness of including any particular parent or patient in the study. Our anxieties about this stem from the knowledge that many parents of diabetic children feel that they are in some way responsible for their child's diabetes and we feel that your study could reinforce these feelings of guilt."

How ironic it will be if drugs, that the *medical* profession have been prescribing, are found to be responsible for causing diabetes in children.

Great power is wielded by doctors upon whom we are dependent for health-care. And any unjustified assumption of knowledge or the withholding of information from patients, can lead to an abuse of that power. However, it remains my belief that most members of the medical profession would support any investigation which examines the possible adverse effects of drugs they are prescribing. Although no-one really wants to begin to open a can of worms that may question the very heart of medicine and possibly show doctors to be

guilty of unwittingly causing harm to patients in unprecedented numbers, something has to be done and *now.*

Unfortunately, since legislation to hold individuals or organisations accountable in the event of drug related injury to health are few and far between, concern is unlikely to come freely from the manufacturers. If a drug has serious side-effects, manufacturers have much to gain from any delay in discovery. In the *unlikely* event that financial compensation will be paid to the victims of drug damage, it will very likely be only a fraction of the profit accruing to the manufacturers during the lifetime of the drug.

A drug information scientist of a major pharmaceutical company manufacturing antibiotics, discussing one of their drugs I consider needs investigating, agreed it was unlikely any company would involve themselves in studies to discover if one of their drugs had serious side-effects.

> ***"…to be realistic, pharmaceutical companies are basically there to make money they're not there to advance science... They're not going to go looking for trouble!"***

The profit motive of some pharmaceutical companies is not confined to drug manufacture. Some of these companies also have an interest in the extremely profitable agricultural pesticide and food industry, and will try to find other outlets for their chemicals. For example, *Lucozade* manufactured by the drug company Smith Kline Beecham and advertised as a 'pick-you-up', contains what could be considered to be a grossly overpriced solution of glucose containing an *unhealthy* concoction of chemicals. Lucozade contains sodium benzoate and sodium metabisulphite as preservatives; caffeine as a

cardiac stimulant; and sunset yellow (E110) to colour it. Although advertised as "Glucose energy in the most natural form the body can take", it is no wonder that the label states that it is "not suitable for babies or children under two years old". A *freshly* prepared drink of glucose made from glucose powder available from any pharmacy and free of any dye, preservatives and caffeine, would cost a fraction of the retail price of a bottle of Lucozade.

If some of the theories outlined in this book concerning the origin of asthma and diabetes alone are proved correct, and serve to explain why more and more people today are falling prey to health problems, then we are currently in the midst of what is probably the world's worst pharmacological disaster. For increasingly since the 1970s, children in industrialized countries have been exposed to potentially dangerous drugs and may as a result be walking time-bombs who will develop health problems once their bodies have reached the required level of exposure or enough time has elapsed for side-effects to become evident.

Apart from asthma and diabetes, there are numerous other diseases and health conditions of *unknown* origin. Some of these presently carry the label *'autoimmune disorder'.* They too could have arisen as a result of damage to cells of the body, following exposure to some medicinal drug. In my opinion, many conditions warrant investigation for their possible association with drug exposure. Some of them for no good reason are considered ‘congenital’ disorders; others have increased at a tremendous rate during the last fifty years; and with some, it is already known they can sometimes result from drug exposure. They include: asthma; blood disorders such as neutropenia, leucocytopenia; childhood cancers; Crohn's disease; coeliac disease; diabetes; ductus arteriosus; eczema; juvenile rheumatoid arthritis; childhood leukaemia; chronic fatigue syndrome;

multiple sclerosis; pyloric stenosis; strawberry coloured birth marks (capillary haemangioma) and systemic lupus erythromatosus.

Until appropriate investigations have been conducted, there is no evidence at present to vindicate drugs as an important factor in the development of any of these diseases.

What about Government participation? It has been said that only economic arguments will persuade governments to be concerned with health issues. In this instance, economic arguments abound. If amoxycillin, erythromycin, or a single injection of ergometrine or oxytocin is capable of causing diabetes, it very likely involves expenditure of less than £10 and in the case of ergometrine less than £1 to render one child diabetic. Therefore, the expenditure on drugs to make some 1500 children diabetic, (in 1988, 1600 children in the UK became diabetic) might amount to less than £5,000. But if these children live to retirement age, the cost to the State for insulin *alone* during their lifetime at 1990 prices, will amount to over £30,000,000.

This does not include the cost of out-patient attendances; occupation of 'acute' hospital beds; treatment of sight-threatening retinopathy and of end-stage renal failure; and National Insurance and other payments made at times of sickness and disability. The economics are persuasive, but sadly, medical, political and legal systems often take time to activate and meanwhile families will feel the futility of help having come too late.

Medicine has a dreadful past, because it makes progress.
The myth grows up by default, as a result of silence, that these drugs (benzodiazepines) are safe.

It is probably the arrogance of power in the medical profession that has lead to problems. Doctors act as though they know. Because medicine means well, that doesn't mean that it does good.

What is needed is a Committee on the Safety of Patients and not a Committee on the Safety of Medicines.
Charles Medawar, London 1992

Epidemiological studies must commence now and if concentrated on children, who developed a disease at a very young age, could provide important and immediate data. Failure to initiate research right away, will make it increasingly hard to obtain answers, as prescribing trends change and more drugs come onto the market.

Today especially, many university and hospital research departments are heavily dependent on the financial support of pharmaceutical corporations, which can inevitably influence the type and direction or research undertaken. Obviously, with the complex inter-relationship that exists, between chemical and drug companies and some research trusts and foundations, research that may implicate pesticides or drugs in any disease will be unlikely to be pursued.

Pharmaceuticals are a major plague in society today and without the interest and co-operation of patients, parents, victims, physicians and politicians, society will never begin to discover the extent of damage caused by poisonous prescriptions in use today.

References & Bibliography

Chapter 4

1 Schmidt MA, Smith LH and Sehnert KW. Beyond Antibiotics, North Atlantic Books, ISBN 1 55643 134 X

Chapter 6

1 Rerup CC. Drugs producing diabetes through damage of the insulin secreting cells. Pharmacological reviews 1970; 2(4): 485-518.
2 Karam JH et al. Insulinopenic diabetes after rodenticide (Vacor) ingestion. Diabetes 1980; 29: 971-978.
3 Belehu A and Naafs B. Diabetes mellitus associated with pentamidine mesylate. Lancet 1982; 1:1463.
4 Sai P et al. Pentamidine, a new diabetogenic drug in laboratory rodents. Diabetologia 1983; 25: 418-423.
5 Collins RJ et al. Case Report: IDDM associated with pentamidine. J Med Sci 1989; 297 (3): 174-175.
6 Thomas DJB et al. Salbutamol-induced diabetic ketoacidosis. Br Med J 1977, August 13: 438.
7 Tibaldi JM. Diabetic ketoacidosis and insulin resistance with subcutaneous terbutaline infusion: A case report. Am J Obstet Gynecol 1990; August: 509-510.
8 Seifer DB et al. IDDM associated with danazol. Am J Obstet Gynecol 1990, February 474-475.
9 Thomas JW et al. Anti-insulin antibodies and clinical characteristics of patients with systemic lupus erythematous and other connective tissue diseases with steroid induced diabetes. The Journal of Rheumatology 1987; 14(4): 732-735.
10 Alavi IA et al. Steroid-induced diabetic ketoacidosis. Am J Med Sci 1971; 262(l): 15-23.
11 Bhatnagar SK et al. Diabetogenic effect of nifedipine. Br Med J 1984; 289:19.
12 Bending JJ et al. Diabetogenic effect of cyclosporin. Br Med J 1987, February 14: 401-402.
13 Poje M and Rocic B. Diabetogenic action of alloxan-like derivatives of uric acid. Experientia 1980; 36: 78-79.
14 Epand RM et al. Mechanism of action of diabetogenic zinc-chelating agents. Mol Pharmacol 1985; 27: 366-374.
15 Maske H et al. Beobachtungen uber den zinkstoffwechsel beim alloxan diabetes. Arch Exp Pathol Pharmakol 1952, 216; 457-472.
16 Lazarow A et al. Protection against alloxan diabetes with cobalt, zinc, and ferrous iron. Anat Record 1951; 109:377.
17 Tadros WM et al. Protective effects of trace elements (Zn, Mn, Cr, Co) on alloxan-induced diabetes. Indian J Exp Biol 1982; 20: 93-94.
18 Niebergall PJ et al. metal binding tendencies of various antibiotics. J Pharm Pharmac 1966, 18: 729-738.

Chapter 7

1 Jones FE and Hanson DR. Develop Med Child Neurology 1977; 19: 593.
2 Wadsworth M and Jarret R. Lancet (ii), 1977; 1172-1174.
3 Calnan H and Peckharn C. Lancet (i), 1977; 589-590.
4 Stewart-Brown S, Haslum M and Butler NR. Br Med J, 1983; 286: 1855-1856.
5 Diabetes Epidemiology Research International Group. Geographic Patterns of Childhood IDDM. Diabetes 1988; 37: 1113-1119.

6 Wilson D. Penicillin in Perspective, 1976. ISBN 0-571-10839 3
7 Baum M and Metcalfe A. Incidence of insulin dependent diabetes in children aged under 15 years in the British Isles during 1988. Br Med J 1991; 302: 443-447.
8 Bloom A, Hayes TM and Gamble DR, Register of newly diagnosed diabetic children. BMJ 1975; 3:580-3.
9 Francome C. Changing Childbirth: Interventions in Labour in England and Wales (1989) ISBN 0 946741115.
10 Harriet Sergeant. Not Such a Happy Event; The Bulletin, March 30, 1993.

Chapter 8

1 Jones FE and Hanson DR. Develop Med Child Neurology 1977; 19:593.
3 Beyond Antibiotics, Mr Michael A. Schmidt, Dr Lendon Smith & Dr Keith Sehnert, North Atlantic Books, ISBN 1 55643 134 X.

Chapter 9

1 Gervais, P. L'Asthme professionnel par allergie aux penicillines. Le Poumon et le Coeur, 1966, T. XXII, no. 5.
2 Reisman RE, and Arbesman CE. Systemic allergic reactions due to inhalation of penicillin. Journal of the American Medical Association, 1968, 203, No. 11:184-5.
3 Rudzki E. Polski Tydgonik Lekarski, 1983, 38, Part 24: 743-745.
4 Davies RJ et al. Asthma due to inhaled chemical agents: ampicillin, benzyl penicillin, 6-amino penicillanic acid and related substances. Clinical Allergy, 1974, 4:227-247.
5 Carlessi G et al. Aspetti di igiene ambientale e di patologia da inquinamento da amoxicillina in una industria farmaceutica. Nuovi-Annali D'Igiene Microbiol, 1979, 30, Part 2: 185-96.
6 Anfosso F et al. Etude comparee in vitro de l'allergenicite de la penicilline G et de l'amoxicilline chez des sujets allergiques a la penicilline. Nouv. Presse Med., 1975, 4: 2457-9.
7 Briatico-Vangosa G et al. Asma bronchiale da acidio 7-aminocefalosporanico (7-ACA) in lavatori addetti alla produzione di cefalosporine. Med. Lavoro, 1981, 488-493.
8 Coutts H et al. Asthma in workers manufacturing cephalosporins. British Medical Journal, 1981, 283:950.
9 Fawcett IW. Allergy to a tetracycline preparation - a case report. Clinical Allergy, 1976, 6: 301-3.
10 Paggiaro PL et al. Bronchial asthma and dermatitis due to spiramycin in a chick breeder. Clinical Allergy, 1979, 9: 571-4.
11 Malo J-L, and Cartier A. Occupational asthma in workers of a pharmaceutical company processing spiramycin. Thorax 1988, 43. 371-7.
12 Moscato G et al. Bronchial asthma due to spiramycin and adipic acid, Clinical Allergy, 1984, 14: 355-361.
13 Medici TC and Fontana, A. Theme principal: Reactions immunologiques au cours des affections pulmonaires. Schweiz. Med. Wschr. 1977, 107, 6:162-171.

American Hospital Formulary Service 91, American Society of Hospital Pharmacists, Inc. ISBN 1 87990700 3.

A Modern Herbal. The Medicinal, culinary, cosmetic and economic properties, cultivation and folklore of herbs, grasses, fungi, shrubs and trees with all their modern

scientific uses. Mrs M Grieve FRHS. Edited and introduced by Mrs CF Leyel. ISBN 0 224 00998.

Baillieres Nurses Dictionary, BF Weller and RJ Wells, Bailliere Tindall Ltd. ISBN 0 7020 1456 7.
British National Formulary, Number 22 (September 1991) A joint publication of the British Medical Association and the Royal Pharmaceutical Society of Great Britain. ISBN 0 85369 252 1.

Goodman and Gilman's The Pharmacological Basis of Therapeutics. 1985. Alfred Gilman, Louis Goodman, Theodore W Rall, Ferid Murad. Macmillan Publishing Company.

Glossary and Acronyms

adenoid	resembling a gland. Generally applied to abnormal lymphoid growth in the nasopharynx
aetiology	the science of the cause of disease
albuminuria	the presence of albumin in the urine, usually symptomatic of kidney disease
alkaloid	nitrogen-containing naturally occurring organic chemical compounds (eg. morphine and quinine) obtained from plants
Alupent	orciprenaline sulphate; acts as a bronchodilator and is now regarded as less suitable and less safe than other bronchodilators, as it is more likely to cause arrhythmias and other side-effects.
anaemia	a condition in which the blood is deficient in red blood cells, haemoglobin or total volume
analeptic	stimulating the central nervous system; restorative
anaphylaxis	sometimes fatal hypersensitivity to foreign substances (eg. drugs or insect venom) due to sensitization resulting from earlier contact with the causative agent
antibacterial	directed or effective against bacteria
antibiotic	chemical substance produced by certain bacteria and fungi, which prevent the growth of, or destroy, other bacteria
antibody	a specific form of blood protein able to counteract the effects of bacterial antigens or toxins
anti-emetic	an agent which can prevent vomiting
antigen	any substance which in suitable conditions can stimulate the production of antibodies
aplastic anaemia	a condition in which the bone marrow is unable to produce red blood corpuscles; a rare condition of unknown cause in most cases, but may be caused by drugs
arrhythmias	unusually abnormal alteration in the rhythm of the heartbeat
asthmogenic	agent capable of causing asthma
Atrovent	a bronchodilating drug containing ipratropium bromide
autonomic	acting or occurring involuntarily
BNF	British National Formulary; drug reference book commonly used by doctors in the UK. Contains names of drugs and variety of forms in which they are available, the manufacturer, dosing regimes and *scant* information about cautions, contra-indications and side-effects.
bacteria	a large group of microorganisms many of which cause disease
benzene	a flammable poisonous liquid used as a solvent
bitters	an alcoholic solution of bitter and aromatic plant products
bradycardia	relatively slow heart action
candidiasis	infection by the *Candida* fungus, popularly known as thrush
Canestan	antifungal preparation containing clotrimazole
carcinoma	a cancerous tumour originating in the tissue covering an external surface or lining a body cavity
cephalosporin	any one of a group of wide-spectrum antibiotics derived from the mould cephalosporium
chelate	a compound containing a ligand (typically organic) bonded to a central metal atom at two or more points
chemotherapy	the use of drugs in the treatment or control of disease
cholestasis	arrest of the flow of bile due to obstruction of the bile ducts
chloasma	hyperpigmentation of the facial skin in women

chymotrypsin	an enzyme that breaks down proteins and is released from the pancreas into the intestines during digestion
conjunctivitis	inflammation of the mucus membrane that lines the inner surface of the eyelids and is continued over the front part of the eyeball
CSM	Committee on the Safety of Medicine
dermatitis	disease or inflammation of the skin
diabetogenic	agent capable of damaging the pancreas such that its ability to produce and secrete insulin is destroyed
Dimotane	systemic nasal decongestant containing the chemical brompheniramine maleate, phenylephrine hydrochloride and phenylpropanolamine hydrochloride . The BNF states that it is of doubtful value.
Dimotapp	a systemic nasal decongestant containing brompheniramine maleate, phenylephrinehydrochloride and phenylpropanolamine hydrochloride. The BNF states that it is of doubtful value
Dioralyte	oral rehydration salts to restore fluid and electrolyte loss in diarrhoea, contains sodium chloride, sodium bicarbonate, potassium chloride, citric acid and glucose
Diprosone	a topical corticosteroid containing betamethasone
Distaclor	a cephalosporin antibiotic containing the drug cefaclor
dyscrasias	an abnormal condition of the body or of one of its parts
dyspepsia	indigestion
dyspnoea	difficult or laboured breathing
dysphonia	impairment of voice quality and the ability to form proper speech sounds principally caused by malfunction of the vocal chords
dysuria	difficult or painful micturition
ECG	electroencephalogram
elixir	a sweetened liquid (eg a syrup) containing a drug
embryocidal	substance that is toxic to the embryo
encephalopathy	a disease in which the functioning of the brain is affected by some agent or condition (eg. virus, toxin)
endometrium	the mucous membrane lining the uterus
ENT	ear, nose and throat
enuresis	involuntary urination, especially by children at night
enzyme	a protein which will catalyze a biological reaction, making it take place at a faster rate
eosinophilia	abnormal increase in the number of eosinophils in the blood that is characteristic of allergic states and parasitic infections
epigastric	the part of the upper abdomen immediately over the stomach
exfoliative	to shed or cast off in scales, layers
gastrointestinal	of or involving both the stomach and intestine
haematuria	an abnormal presence of blood or blood cells in the urine
haemorrhage	a copious loss of blood from the blood vessels
heartburn	burning sensation behind the lower part of the breastbone, usually caused by the regurgitation of acid from the stomach into the gullet
hepatic	of or resembling the liver
hypersensitivity	abnormally sensitive to an allergen, a drug
hypertension	abnormally high blood pressure
hypokalaemia	abnormally low levels of potassium in the blood

hypotension	abnormally low blood pressure
iatrogenic	A disease inadvertently caused by a doctor or his/her practices, but today more commonly due to the drugs that are prescribed
immunoresponse	the reaction of a body to the introduction of a foreign substance (antigen) where antibodies are produced which bind onto and destroy the antigen
Intal	drug containing sodium cromoglycate and used in the prophylaxis of asthma. Its safety in pregnancy has not been established
Jaundice	yellowish coloration of the skin, tissues and body tissues caused by the deposition of bile (digestive juice produced by the liver) pigments
Keflex	cephalosporin drug containing cephalexin
lactulose	a semi-synthetic disaccharide used to counter constipation
leucopenia	condition, characteristic of some diseases, in which the number of white blood cells circulating in the blood is abnormally low
leukaemia	an acute or chronic disease characterized by extreme overproduction of white blood cells
Lymphadenopathy	disease condition of the lymph nodes
meconium	the dark green substance forming the first faeces of a newborn infant
micturition	the act of passing urine
monozygotic	derived from a single ovum, and so identical
Mucodyne	a drug containing carbocisteine which is used to reduce sputum viscosity
multiform	having many forms or appearances
myocarditis	inflammation of the myocardium, the middle muscular layer of the heart wall
nebulizer	an apparatus for reducing a liquid to fine spray. An atomizer
nephritis	acute or chronic inflammation of the kidney
neuritis	an inflammatory or degenerative condition of a nerve resulting especially in pain, disturbances, and impaired or lost reflexes
neuropathy	an abnormal, usually degenerative, state of nerves of the nervous system
Nystatin	an antifungal drug obtained from a fungus; side-effects include nausea, vomiting, diarrhoea
oedema	abnormal accumulation of fluid beneath the skin causing swelling (eg. in the ankle)
osmotic	a process of diffusion by which molecules of a solvent tend to pass through a semi-permeable membrane from a less concentrated solution into a more concentrated one
otitis	inflammation of the ear. (otitis media – refers to the middle ear)
palpitation	rapid and forceful contraction of the heart of which the person is conscious
panacea	a remedy for all diseases or problems
pancreas	large gland of vertebrate animals that is situated beneath the stomach in the first loop of the small intestines and secretes pancreatic juice and the hormone insulin
pancreatitis	inflammation of the pancreas
paresthesis	loss of sensation
parturition	the act of giving birth to a child

pertussis	whooping cough
Pen-V	penicillin-V; phenoxymethylpenicillin
pharmacopoeia	an authoritative book containing a list of medicinal drugs with their uses, preparation and dosages
pharyngitis	inflammation of the pharynx
phenobarbitone	tranquillizer from the barbiturate group of drugs
photosensitivity	an abnormal degree of sensitivity of the skin to sunlight
Piriton	an antihistamine containing chlorpheniramine maleate and used to relieve hay fever and urticaria
pituitary	small oval gland that secretes hormones directly into the bloodstream
plankton	the organisms inhabiting the surface layer of a sea or lake, consisting of small drifting plants and animals
platelet	minute particle in blood important in blood clotting
poison	any substance which, applied to the body or taken internally, can cause injury to any part or cause death
polydipsia	abnormal thirst. It may be a symptom of diabetes
polyuria	an abnormally large output of urine due to either an excessive intake of liquid or to disease, often diabetes
Prosobee	a food supplement
proteolysis	the breakdown of protein or peptides (chains of two or more linked amino acids) with the formation of simpler products
pruritis	any of a variety of conditions or skin disorders marked by an intense sensation of itching
pyloric	relating to or affecting the region where the stomach opens into the small intestine
pyloric stenosis	stricture of the pyloric orifice. It may be a thickening of the tissue, ulceration or a malignant growth
pyrexia	abnormal rise in body temperature; fever
rodenticide	something, eg. a poison, that kills, repels, or controls rodents
renal	relating to the kidney
rhinorrhoea	abnormal discharge of mucus from the nose
SLE	systemic lupus erythematosus, a severe potentially fatal form of erythema multiforme, associated with widespread lesions of the skin and mucous membranes
Sudafed	an expectorant containing guaiphenesin and pseudoephedrine hydrochloride
systemic	pertaining to or affecting the body as a whole
tachycardia	relatively rapid heart action
teratogen	something that causes developmental malformations in foetuses
tetracycline	any of several broad-spectrum antibiotics obtained especially from a soil bacterium
thrombocytopenia	a condition characteristic of some diseases in which the number of blood platelets circulating in the blood is abnormally low
thrombosis	the formation or presence of a blood clot within a blood vessel
Timodine	a topical preparation containing hydrocortisone and Nystatin, an antimicrobial drug
tinnitus	a sensation of noise (eg. ringing or roaring) with no external cause

tonsil	either of two small oval lumps of spongy tissue situated one on each side at the back of the mouth
tonsillitis	inflammation of the tonsils
toxin	any of various poisonous substances produced by microorganisms and causing certain diseases; any other poisonous substance of plant of animal origin
triludan	an antihistamine used to relieve hay fever and urticaria
trypsin	enzyme secreted in the stomach that is capable of digesting proteins
URTI	upper respiratory tract infection
urticaria	nettle rash or hives; an acute or chronic skin condition characterized by the recurrent appearance of an eruption of weals, causing great irritation. The cause may be certain foods, infection, drugs or stress
Vallergan	antihistamine/tranquillizer used in the treatment of urticaria and pruritis
Vermox	a drug containing mebendazole used to eradicate threadworms; the recommended dose for adults *and* children is a single 100mg dose.
vertigo	disordered state marked by loss of balance and the sensation that one's surroundings are whirling dizzily, that often results from the awareness of being at great height, giddiness
virus	any of a group of very simple organisms that are smaller than bacteria and can cause disease in animals and plants
xylometazoline	topical preparation used in the treatment of conjunctivitis