

ARE ASTHMA AND DIABETES IATROGENIC DISEASES?

Internationally there are epidemics of diabetes and asthma which in some countries like the United Kingdom have existed for decades. They are two of the most frequent chronic diseases in children. As a result of studying the health records of children in England, I am of the opinion that these epidemics are mainly the result of drug exposures to antibiotics. Increases in incidence of both diseases also mimic the increase in antibiotic prescribing in the UK and internationally.

Table 1 shows the drugs prescribed to a child born in 1980 and attending a medical practice in England.

Year	Prescription	Symptoms
1980	Keflex (Cephalexin)	
1981	Septrin	URTI
1981	Piriton syrup given by chemist for <i>hay fever</i>	<i>Mother wants antibiotic</i> . None given
1981	Pen-V	URTI Cough++
1981	Emergency call-out	Grizzly refusing to eat or drink
1981	Bactrim	
1982	Bactrim	
1982	Keflex	URTI Cough++ Catarrh+
1982	Amoxil	<i>Wheezy</i>
1982	Penbritin	URTI
1983	Keflex	<i>Chesty</i> cough. Vomiting
1983	Amoxil	URTI
1983	Erythroped	<i>Chesty</i>
1983	Amoxil	Emergency call out
1983	Hydrocortisone cream	
1983	Erythroped (erythromycin)	Emergency call out
	Maxolon	URTI Vomiting Off food
1983	Keflex	Emergency call out. Pharyngitis
1983	Hydrocortisone cream	
1983	Vallergan syrup	<i>Allergic rash</i> . Cause?
1984	Keflex	URTI Emergency call-out
1984	Keflex	URTI Coughing
1984	Cephalex Alupent	
1984	Keflex	
1984		Cough
1984	Erythroped	Bronchitis
1984	Diprosone cream	
1984	Vallergan	
1984	Ceporex	Bronchitis
1985	Ceporex	<i>Chesty</i> cough
	Diprosone cream	Eczema on back
1985	Amoxil	<i>Wheezy chest</i>
1985	Amoxil	<i>Wheezy bronchitis</i>
1985	Triludan syrup	<i>Hayfever</i>
1985	Keflex	<i>Asthmatic</i>
	Ventolin	
1985	Distaclor Ventolin	
1985	Amoxil Ventolin	URTI
1985	Amoxil	URTI
1985	Hydrocortisone cream	6mths facial itching
1985	Fucidin cream	Impetigo
1986	Ceporex	URTI
1986	Keflex Ventolin	<i>Asthmatic wheeze</i>
1986	Ventolin	<i>Asthmatic</i>
1986	Ventolin	
1986	Ventolin	
1986	Erythroped	Chickenpox

Table 1. Drugs prescribed to a child in England before being diagnosed with asthma. Antibiotics are in bold.

By the time the child whose prescription history is detailed in table 1 was six years of age, it had received a total of 30 courses of antibiotics. After just *one* course of Keflex in 1980 the child returns to the doctors with an upper respiratory infection (URTI). Cephalosporins are stated in the American Hospital Formulary Service Drug Information¹ pharmacopeia, which in 2017 consisted of 3823 pages, and was published by the American Society of Health-System Pharmacists, as causing adverse effects of '*pleural effusion, pulmonary infiltrate, respiratory distress, cough and rhinitis*' so cephalosporins should be considered as being toxic to the respiratory system.

Indeed many drugs are known to exhibit pulmonary toxicity. Drug-induced lung diseases can cause bronchial asthma and toxic and allergic reactions². Toxicity is likely to be dose-dependent so the effects may not become apparent until a few courses have been taken. The effects of taking repeat courses of a drug or taking various drugs are not usually studied in clinical trials. As the drug information officer of the British drug company Beechams said to me in 1991, 'drug companies are not going to go looking for trouble'. Besides, this would only increase costs and a lot of money is invested in a drug before it comes to market.

As you look down table 1, it should become apparent that a URTI often occurs after the child has taken an antibiotic, and within a few years symptoms progress to wheezing and asthma. The younger a child is when exposed to a drug, the more likely it is to suffer from side effects due to immature body systems involved in absorption, metabolism and elimination of drugs³.

After the first two courses of the antibiotics Keflex and Septrin in 1980/81, the child is suffering from hay fever for the first time, although it seems that a pharmacist must have diagnosed hay fever when the symptoms may have been due to exposure to Septrin. However hay fever has been linked to antibiotics in a meta-analysis by Ahmadizar et al. 2018⁴. The child continues to be prescribed antibiotics with the result that by 1982 *wheezing* is reported for the first time after a course of Pen-V and two courses of Bactrim.

Bactrim consists of two chemicals, sulphamethoxazole and trimethoprim and amongst the long list of side effects are '*pulmonary infiltrates, cough, shortness of breath*'⁵. The lengthy list of other toxic effects is impressive. Rare side effects include problems breathing and swelling of the throat⁶. Another article medically reviewed by a Doctor of Pharmacy states that a less common side effect is breathing problems⁷. The Mayo Clinic, the top ranked hospital in America, states that difficulty with breathing is a side effect⁸ and that 'you should call your doctor right away if you experience shortness of breath or trouble with breathing'. Its website has the longest list of side effects and drug interactions that I've ever seen for amoxicillin. Perhaps this is because in America there's always an attorney ready to sue on a pro-bono or no win no fee basis.

In 1983, the child was prescribed hydrocortisone cream possibly for an 'allergic' rash which wasn't recorded. The rash or itching must have persisted because vallergran to treat itching was then prescribed by the doctor who queried the cause of the rash. The side effects of penicillins would not have been as well known in the 1980s, and the 1981 BNF⁹ says that penicillins can cause a rash, but this isn't mentioned with the dosage information and there is nothing to say that the drug should be discontinued if a patient presents with a rash.

Even today, rashes that occur soon after the administration of a penicillin are considered to be due to hypersensitivity of the patient, instead of considering them to be due to exposure to a toxin. Interestingly, exposure to poison ivy can also cause a rash, but this too is considered to be an allergic reaction. After more antibiotics in 1984 and 1985, the child is reported to be wheezing and is treated for hay fever and is finally diagnosed as asthmatic in 1985.

Unfortunately, Ventolin^{10,11} and Advair¹² commonly used to treat asthma have side effects which include cough, upper respiratory inflammation and chest tightness or pain which are symptoms of asthma. The MHRA Patient Information Leaflet (PIL) for salbutamol nebuliser solution on the MHRA Products website¹³ under possible side effects, includes *wheeziness, difficulty in breathing, coughing and bronchospasm*.

Advair was linked to 80 percent of asthma-related deaths in the USA, a conclusion based on a meta-analysis of 19 published trials. The Mayo Clinic also says that taking an inhaler can '*cause paradoxical bronchospasm, which means your breathing or wheezing will get worse*'. The fact that the inhalation of many dusts and chemicals is known to cause occupational asthma, should in my opinion lead one to question the safety of inhaling chemicals. The Chemical Safety Data Sheet by ThermoFisher for salbutamol sulfate¹⁴ to be used in a laboratory, states that the chemical may cause trouble breathing and in the case of inhalation, move to fresh air and in the case of skin contact wash immediately with plenty of water for 15 minutes.

The second child (table 2) shows the drugs prescribed to a child born in 1983 and attending a medical practice in England. The child was induced and had received 18 courses of antibiotics before being diagnosed with insulin dependent diabetes (T1D) at 8yrs. Like the child whose drug exposures are detailed in table 1, this child's medical records show nothing exceptional apart from prolific antibiotic prescribing. Similarities with the child detailed in table 1 show that a URTI was diagnosed as viral after Amoxil in 1984 without any diagnostic tests, and a rash after Amoxil in 1984 and otitis media that isn't resolved with Erythroped or Amoxil. It has been reported that children treated with amoxycillin for earaches suffered 2-6 times more recurrent infections¹⁵.

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. <i>Rash?</i> 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	Tonsillitis. Bilateral sub-acute otitis media.
	Dimotane	
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 2. Drugs prescribed to a child in England prior to the diagnosis of T1D.

In 1986 there were slight concerns about hearing after a course of Erythroped. Over 200 drugs are ototoxic and there have been many cases of hearing loss from erythromycin¹⁶. Erythromycin was not tested for auditory toxicity prior to release for clinical use being tested instead for vestibular toxicity.



Fig. 2 Young child injecting insulin

Table 3 shows the list of prescriptions for a child in rural England born in 1961, who was diagnosed with T1D in 1970 at 8yrs of age. Thirty-three of the drugs out of a total of 134 were antibiotics, and like the child shown in table 1, after prescriptions for antibiotics and a variety of other drugs, symptoms progressed from coughing to wheezing, green phlegm, barking cough, otitis media, asthma and finally diabetes.

The child only received Penicillin-V and Phenergan before 2 years of age followed by the drugs listed in table 3. Achromycin the antibiotic prescribed most frequently to the child, was commercialized in the late 1940s to early 1950s whereas amoxicillin came on to the market in 1972.

Prednisone	Achromycin	Mysteclin
Robitussin	Prednisone	Penbritin (ampicillin)
Phenergan	Prednisone	Prednisone
Euglate	Achromycin	Achromycin
Phenergan	Alupent	Achromycin
Alupent	Euglate	Ephedrine
Aminophyllin	Prednisone	Ledermycin
Dimotane	Intal spincaps	Aminophyllin
Alupent	Chloromycetin	Prednisone
Achromycin (tetracycline)	Achromycin	Prednisone
Codeine	Prednisone	Achromycin
Prednisone	Achromycin	Aminophyllin
Alupent	Achromycin	Alupent
Ephedrine	Penidural (a penicillin)	Achromycin
Achromycin	Strepto?	Prednisone
Alupent	Alupent	Alupent
Wel?	Alupent	Ledermycin
Sample of oxytetracycline	Avomine	Robitussin
Robitussin	Euglate	Prednisone
Penidural (a penicillin)	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

Table 3. Drugs prescribed to a child born in 1961 in England and diagnosed with T1D diabetes at 8 years.

Having been born in a rural area, I wonder if the prolific prescribing had anything to do with the fact that the child was visiting a dispensing doctor. Rural doctors are more likely to have their own pharmacies, so that patients living more than a mile from a pharmacy can leave with their prescribed drug. Dispensing doctors get paid a fee for each item dispensed and can also make a profit on the drug. They have been reported by Professor Goldacre in 2019¹⁷ as prescribing more costly branded drugs, as they can profit from the difference between the NHS payment and the wholesale price. Doctors in rural areas might also have fewer patients but still have overheads to meet so might be subconsciously motivated to prescribe.

In 1991, the incidence of T1D was lower in Northern Ireland which is serviced by the NHS, than in the Republic of Ireland in the south, where people used to have to pay £20 to visit a doctor, unlike Northern Ireland where

visits to the doctor are free. In Hokkaido Japan where medical services in 1991 were very expensive, the rate of T1D in children was one of the lowest in the world.

If one questions the efficacy of antibiotics one will discover that it has been shown by Professor Little in 2021¹⁸ in the *Lancet* that giving antibiotics is no better than giving no medicine.

Based on the examination of health records of diabetic and non-diabetic children in England in 1991 and examination of the drug structures of chemicals reported to cause diabetes, and publications linking antibiotics to asthma, I believe that both asthma and diabetes are iatrogenic diseases.

REFERENCES

1. AHFS 2017, published by the American Society of Health-System Pharmacists. Cephalosporins; Other Adverse Effects; page 56; 18:12.06.
2. Medici T, Fontana S. Medikamentöse Lungenerkrankungen (Medicinal lung diseases). Schweiz Med Wschr 1977; **107**: 162–171.
3. Elzagallaai A, Greff M, Rieder M. Adverse Drug Reactions in Children: The Double-Edged Sword of Therapeutics. Clin Pharmacol Ther 2017; **101**(6): 725–735.
4. Ahmadizar F, Vijverberg S, Arets H et al. Early-life antibiotic exposure increases the risk of developing allergic symptoms later in life: A meta-analysis. Allergy 2018; **73**(5); 967–1146.
5. AHFS 2017, published by the American Society of Health-System Pharmacists. Bactrim; Other Adverse Effects; page 403; 8:12.20.
6. Amoxicillin causes problems breathing. Medical News. Rare side-effects problems breathing and swelling in the throat. <https://www.medicalnewstoday.com/articles/amoxicillin-side-effects>.
7. Healthline.com. Side Effects of Amoxicillin (Amoxil, Trimox). Medically reviewed by Femi Aremu, PharmD.
8. MayoClinic.org. Drugs and supplements; Amoxicillin (Oral Route).
9. BNF 1981 Number 1. The British Medical Association and The Pharmaceutical Society of Great Britain. ISBN: 0 85369 140 1. ISSN: 0260–535X.
10. MayoClinic.org. Ventolin.

11. products.mhra.gov.uk. Patient Information Leaflet (PIL). Salbutamol.
12. Ramanujan K. Cornell Chronicle June 9, 2006. Common asthma inhalers cause up to 80 percent of asthma-related deaths, Cornell and Stanford researchers assert.
<https://news.cornell.edu/stories/2006/06/common-asthma-inhaler-causing-deaths-researchers-assert>.
13. products.mhra.gov.uk. Patient Information Leaflet (PIL). Salbutamol.
14. ThermoFisher Safety Data Sheet, Salbutamol sulfate.
15. Schmidt M, Smith L, Sehnert K. Beyond Antibiotics. North Atlantic Books, ISBN 1 55643 134X.
16. Rybak L, Ramkumar V, Mukherjea D. Ototoxicity of Non-aminoglycoside Antibiotics. Front Neurol 2021. Sec. Neuro-Otology Vol 12. <https://doi.org/10.3389/fneur.2021.652674>.
17. Goldacre B, Reynolds C, Powell-Smith A et al. Do doctors in dispensing practices with a financial conflict of interest prescribe more expensive drugs? A cross-sectional analysis of English primary care prescribing data. BMJ Open 2019; **9**: e026886.
18. Little P, Francis N, Stuart B. Antibiotics for lower respiratory tract infection in children presenting in primary care in England (ARTIC PC): a double-blind, randomised, placebo-controlled trial. Lancet 2021; **398**(10309): 1417–1426.