

Side Effects of Drugs Annual 35

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Special reviews in SEDA-35

Galantamine (Chapter 1)	14
Adulteration of drugs of abuse and the problem of levamisole (Chapter 4)	55
Deaths associated with drugs of abuse (Chapter 4)	60
Uses of midazolam (Chapter 5)	77
Thromboembolism associated with antipsychotic drugs (Chapter 6)	86
Clozapine-induced myocarditis and pericarditis (Chapter 6)	100
Teratogenicity of antiepileptic drugs (Chapter 7)	133
Perampanel (Chapter 7)	142
The interaction of carbapenems with valproate (Chapter 7)	153
Takotsubo cardiomyopathy after opioid withdrawal (Chapter 8)	171
Genetic polymorphisms associated with adverse reactions to salicylates (Chapter 9)	202
The usefulness of combining ketamine and propofol (Chapter 10)	222
Management of rocuronium-induced anaphylaxis with sugammadex (Chapter 12)	245
Piribedil (Chapter 13)	263
Rotigotine (Chapter 13)	264
Iodopropynyl butylcarbamate—immunological reactions (Chapter 14)	279
Isotretinoin and suicide (Chapter 14)	283
New antihistamines (alcaftadine, bepotastine, bilastine, rupatadine) (Chapter 15)	295
Inhaled glucocorticoids and pulmonary infections (Chapter 16)	311
Adverse reactions during long-term use of long-acting beta ₂ -adrenoceptor agonists (Chapter 16)	315
Angiotensin converting enzyme (ACE) inhibitors and angioedema (Chapter 20)	364
Triapine (Chapter 23)	425
The interaction of carbapenems with valproate (Chapter 25)	447
Drug-drug interactions with antifungal azoles (Chapter 27)	484
Voriconazole-associated periostitis (Chapter 27)	488
Retinopathy due to chloroquine and hydroxychloroquine (Chapter 28)	496
Amantadine and visual impairment (Chapter 29)	530
Concomitant treatment of multidrug-resistant tuberculosis and human immunodeficiency virus (HIV) infection (Chapter 30)	551
Ecabet (Chapter 36)	642
Racecadotril (Chapter 36)	649
The risk of infections in patients taking TNF-alfa antagonists (Chapter 37)	666
The treatment of transthyretin amyloidosis (Chapter 41)	747
Pancreatitis and pancreatic cancer associated with incretin mimetics (Chapter 42)	771
Paradoxical hyperglycemia due to pasireotide (Chapter 43)	796
Leptin and analogues (Chapter 43)	799
Combinations of lipid-modifying drugs (Chapter 44)	807
Colesevelam (Chapter 44)	809
Statins and cataract (Chapter 44)	812
Methotrexate (Chapter 45)	821
Iodinated radiocontrast-induced nephropathy (Chapter 46)	864
Corn starch (Chapter 49)	901
Hyaluronidase (Chapter 49)	907

Cumulative indexes of special reviews, Annuals 4–34

Special reviews were introduced into the *Side Effects of Drugs* volumes in Annual 4. The following two indexes refer to the medications covered in these reviews and the systems involved. The format 34.322 refers to SEDA-34, p. 322.

1. Index of medications in special reviews

- abetimus, drug development, 29.460
- ACE inhibitors, *see* angiotensin converting enzyme inhibitors
- acetaminophen, *see* paracetamol
- acetylsalicylic acid, 21.100
 - angiotensin converting enzyme (ACE) inhibitors, drug-drug interaction, 28.124
- antithrombotic effectiveness, 12.74
- asthma, 17.94
- benefit to harm balance in preventing strokes and heart attacks, 27.109
- co-medication, 26.423
- gastrointestinal effects, 17.95, 18.90
- Reye's syndrome, 7.94, 8.93, 11.79, 15.85
- rhinosinusitis, 17.94
- respiratory disease, 31.193
- sensitivity, 12.75
- acupuncture, 5.430
 - incidence of adverse effects, 29.589
 - traumatic effects, 29.590
- adenosine, dyspnea and bronchospasm, 32.337
- adrenaline
 - myocardial infarction and vasospasm, 31.259
 - propranolol drug-drug interaction, 9.6
- aerosols, delivery, 27.172
- albumin, human, anaphylaxis, 14.296
- alcohol, 31.757
 - chlorpropamide, drug-drug interaction, 7.407
 - diabetes mellitus, 5.386
 - nitrous oxide, drug-drug interaction, 10.163
 - vitamin a, beta-carotene, drug-drug interaction, 24.442
- aldosterone antagonists, in heart failure, 24.246
- alkylating drugs, 31.721
- allopurinol, hypersensitivity, 10.89
- aluminium
 - in albumin solutions, 23.359
 - and renal failure, 10.202
 - toxicity in children, 10.202, 12.185
 - tumorigenicity, 31.383
- amantadine, corneal edema, 33.602
- amidopyrine, 4.63
- aminoglycoside antibiotics, 17.304
 - bacterial resistance, 7.282
 - comparative toxicity, 4.192
 - contact dermatitis, 13.225
 - dosage regimens, 20.234, 21.265, 23.264
 - nephrotoxicity, 15.268, 17.305
 - ototoxicity, 10.243, 14.222, 18.268
 - and ribostamycin, 15.270
- aminopenicillins, 5.261
- aminophenazone, 4.63
- aminophylline, allergic reactions, 7.5
- amiodarone, dysrhythmias, 25.211
 - eryptosis, 32.339
 - respiratory toxicity, 15.168
 - thyroid disease, 27.192, 31.327, 33.382
- amphetamines, 29.3
- amphotericin, 5.275, 9.247
 - liposomal, 17.319
 - nephrotoxicity, 10.248, 13. 231, 14.229, 27.276
- anabolic steroids
 - abuse, 29.508, 32.751, 33.869
- analgesics
 - agranulocytosis and aplastic anemia, 11.87
 - choice of drug and dose, 12.63
 - headache, 21.95
 - headaches in children, 23.114
 - nephropathy, 6.80, 21.98
 - occupational exposure, 34.181
 - urinary tumors, 6.80
- androgens, in women, 24.477
- anesthesia
 - dental, safety of, 16.122
 - general, and driving, 4.74
 - tumescent, 34. 213

- anesthetics
 halogenated, renal damage, 20.106
 local, and lipid emulsion, 32.261
 local, cartilage toxicity, 33.281
 local, combinations, 20.121
 local, hypersensitivity, 6.123
 local, drug-drug interactions, 4.85
 local, lipid rescue, 31.231
 local, neurotoxicity, 21.129, 25.152
 ocular, 17.542
 local, placental transfer, 8.127
- angiotensin converting enzyme (ACE) inhibitors
 acetylsalicylic acid, drug-drug interaction, 28.124
 angioedema, 22.225, 29.207, 31.352, 32.380, 34.322
 cough, 19.211
 indications, 24.233
- angiotensin II receptor antagonists
 angioedema 30.238
 tumorigenicity, 34.325
- anisoylated plasminogen-streptokinase activator complex (APSAC), 12.313
- anorectic drugs
 cardiac valvulopathy 22.3, 23.2, 24.4, 25.5
 primary pulmonary hypertension, 18.7, 21.2, 23.2, 25.5
- anthracyclines, 25.533
 cardiomyopathy, 7.428
- antiallergic drugs, ocular treatment, 11.420
- anti-anginal drugs, 9.183
- antibacterial drugs/antibiotics, *see also* individual names
 colitis, 4.197
 hormonal contraceptives, drug-drug interactions, 8.256
 intrapartum, 32.446
 neuromuscular blockers, drug-drug interactions, 5.131
 neutrophil function, 7.279
 resistance, 31.413, 32.445
- anticancer antimetabolites, 29.531
- anticholinergic drugs, 22.507, 31.273
 cardiovascular risks, 32.318, 33.364
 cognitive impairment, 34.246
- anticoagulants, oral
 pregnancy, 5.323
 skin necrosis, 29.358
- anticonvulsants, *see* antiepileptic drugs
- antidepressants, *see also* individual agents
 blood disorders, 6.22
 cardiac toxicity, 6.16
 during and after pregnancy, 21.17
 and emergent suicidality, 32.29
 mania, 29.18
 overdose, 28.14
 pregnancy, 32.31, 33.27
 relative risks, 11.16
- antidiarrheal agents, 5.335
- antidysrhythmic drugs
 in atrial fibrillation, 24.197
 prodyrhythmic effects, 17.218, 23.196
- antiepileptic drugs
 bone loss, 27.74
 cardiac repolarization, 34.86
 comparison, 25.78
 death, 23.83
 endocrine function, 9.55
 overdose, 22.84
 pregnancy, 4.42
 psychiatric effects, 22.82, 27.72
 suicidality, 33.127, 34.89
- antiestrogens, genotoxicity and tumorigenicity, 27.429
- antifungal drugs
 drug interactions (azoles), 24.318, 28.299, 29.282, 30.320, 31.459, 32.497, 33.545, 34.428
Pneumocystis jirovecii (carinii) pneumonia, 18.289
- antihelminthic drugs
 in hydatid disease, 9.274
 Mazzotti reaction, 31.507
 pharmacovigilance in developing countries, 32.571
- antihistamines
 cardiovascular adverse effects, 17.196, 22.176, 25.183, 26.180
 drowsiness/sedation, 8.163, 9.149, 21.170, 23.171, 26.182
- antihypertensive drugs, 4.144, 19.209
 combination therapy, 34.317
 in diabetes mellitus, 28.226
 fixed-dose combinations, 22.224
 individualizing therapy, 17.246
 perioperative period, 33. 413
 pregnancy, 6.206
 quality of life, 32.375
- anti-inflammatory drugs, *see* NSAIDs
- antimalarial drugs, 14.237, 17.325, 20.257
 adjunctive treatments, 24.330
 prophylaxis, 13.239, 23.304
- antimicrobial drugs, *see also* individual agents
 allergic reactions, 23.251
 coagulation disorders, 18.258
 colitis, 12.216, 17.303
 intestinal motility, 13.220
 male fertility, 16.262
 new, 13.210
 new, with adjuvants, 17.296
 the pill and pregnancy, 24, 274
 policies and politics, 16.273
 pregnancy, 11.231
 prescribing, 15.254
 preterm infants, 21.258

- prudent use, 25.279, 27.242, 28, 265
- resistance, 12.206, 13.210, 19.237, 20.228, 21.257, 22.265, 23.250, 24.273, 29.244, 31.413
- seizures, 18.261
- side chains, 16.264
- antioxidant vitamins, 20.363
- antiprotozoal drugs
 - african trypanosomiasis, 18.293
 - toxoplasmosis, 20.262
- antipsychotic drugs, 10.49
 - cardiac dysrhythmias, 5.42
 - comparisons of different types 25.53, 27.50
 - death, sudden, 7.63
 - deaths, 32.89
 - diabetes mellitus, 28.60, 33.94, 34.54
 - prescribing, 34.51
 - sexual dysfunction, 8.57
 - susceptibility factors, 9.49
 - teratogenicity, 10.50
 - and thermoregulation, 5.46
 - typical versus atypical, 33.89
 - use in conditions other than schizophrenia, 27.49
 - use in elderly patients, 30.59
 - weight gain, 26.56, 33.94, 34.54
- antiretroviral drugs, metabolic complications, 28.329, 33.582
- antischistosomal drugs, 12.261
- antiseptics, contamination, 9.228
- antithyroid drugs, pregnancy, 4.294, 13.377
- antituberculosis drugs, 16.341, 31.500
 - children, 32.557
 - drug-drug interactions, 5.294
 - genetic susceptibility, 28.342
 - hepatotoxicity, 25.363, 26.339, 31.495, 32.555, 34.479
 - multidrug resistance, 33.623
 - Mycobacterium avium*-complex infection, 20.278
 - pregnancy, 6.276
 - transplant recipients, 32.559, 33.627
- antitussive drugs, 4.121
 - over-the-counter, 5.170
- appetite suppressants
 - cardiac valvulopathies, 22.3, 23.2, 24.4, 25.5
 - primary pulmonary hypertension, 18.7, 21.2, 23.2, 25.5
- aprotinin
 - market withdrawal, 32.642
 - renal function, 33.724
- aripiprazole, 31.70
- arsenic, in drinking water, 34.351
- arylpropionic acids, stereoisomers 32.229
- ascorbic acid, deferoxamine and iron, drug-drug interaction, 8.239
- aspirin, *see* acetylsalicylic acid
- asthma medications, exacerbation of asthma, 20.165
- atovaquone, 19.266
- atracurium, 10.108
- auranofin, 8.224, 9.217, 10.207
- avoparcin
 - lessons from, 27.242
 - resistance, 29.244
- ayurvedic medicine, 7.462
- azathioprine, *see* thiopurines
- azoles, *see* antifungal drugs
- baclofen, withdrawal syndrome, 26.152
- bambuterol, cardiac failure, 23.181
- Bendectin® (dicyclomine + doxylamine + pyridoxine), in pregnancy, 6.316
- benfluorex, 34.3
- benoxaprofen, 7.109
- benzodiazepines
 - brain damage, 14.36
 - dependence, 6.37, 12.41
 - depression, 17.43
 - and driving, 7.46
 - mechanisms of action, 10.41
 - medicolegal aspects, 13.33
- benzoyl peroxide, sensitization, 8.151
- beta₂-adrenoceptor agonists, 18.159
 - asthma, 19.178, 21.179
 - asthma deaths, 17.164
 - long-acting, genetic susceptibility factors, 30.199, 31.310
 - long-acting, long-term safety, 33.357, 34.280
 - long-acting, respiratory adverse effects, 30.198, 31.309
 - pregnancy, 4.92
 - with theophylline, 9.10
- beta-adrenoceptor antagonists, *see also* individual names
 - anaphylactic reactions, 7.216
 - arthralgia, 11.164
 - asthma, 8.185
 - driving, 5.186
 - flying, 5.186
 - immunological function, 8.188
 - in myocardial infarction, 6.186, 7.212, 9.172
 - lactation, 5.194
 - in pregnancy, 5.194
 - in renal disease, 4.132
 - sexual function, 15.188
 - smoking, drug-drug interaction, 5.188
- beta-carotene, *see also* vitamin A
 - alcohol, vitamin A, drug-drug interaction, 24.442
 - tumorigenicity, 25.454
- beta-lactam antibiotics, *see also* individual names
 - effects on eukaryotic cells, 13.212
 - immediate hypersensitivity reactions, 14.211

- misuse, 10.234
- pregnancy, 25.280
- bismuth, 6.217
 - encephalopathy, 4.166
- bisphosphonates, musculoskeletal reactions, 34. 787
- blood products, acquired immune deficiency syndrome (AIDS), 8.309
- blood substitutes, 5.314
- bone morphogenetic proteins, 34.579
- Bordetella pertussis*, *see* pertussis vaccine
- botulinum toxin A, use in primary axillary hyperhidrosis, 27.161
- budesonide, children, susceptibility factors, 30.194
- bupropion, 8.28
- caffeine, pancreatic cancer, 7.8
- calcium channel blockers, 5.196
 - angina, 8.191
 - hepatitis, 6.193
 - long-term safety, 20.185, 21.208, 22.214
 - withdrawal, 8.191
- cancer chemotherapy, interstitial pneumonia, 4.324
- captopril, 4.153, 6.201
- carbamazepine, skin reactions, 32.129
- carbapenems, seizures, 33.491
- cardiac glycosides, long-term treatment, 4.121
- carnitine, 13.269
- carotenoids, tumorigenicity, 25.454
- catecholamines, stress cardiomyopathy, 33.313
- ceftriaxone, 15.258
 - nephrolithiasis, 29.246
- cephalosporins
 - bleeding complications, 8.249
 - immunological reactions, 28.267
 - hypersensitivity reactions, cross-reactivity with penicillins, 30.280
 - and vitamin K, 12.210
- cerebral vasodilators, 5.204
- charcoal, activated, in digitalis overdose, 24.201
- chenodeoxycholic acid, 7.359
 - diarrhea, 4.258
- chinese medicines, injectable formulations, 32.880
- chloramphenicol, children, 15.267
- chlorhexidine, 5.254
- chloroquine, 15.286
 - retinopathy, 9.251
- chlorpropamide, alcohol drug-drug interaction, 7.407
- chondroprotective agents, 14.439
- chymopapain, 4.223, 10.277, 11.279, 14.264
- ciclesonide, 30.196
- ciclosporin, urinary system, 19.348
- cimetidine
 - compared with ranitidine, 9.313
 - gastric cancer, 6.162
 - mental confusion, 5.159
 - nephrotoxicity, 5.163
- clenbuterol, adulteration of street drugs with, 33.53
- clioquinol, subacute myelo-optic neuropathy (SMON), 4.253
- clofibrate, WHO study, 5.401
- clonidine, in opiate withdrawal, 5.68
- clozapine, 15.50
 - agranulocytosis, 22.1359
- cocaine
 - cardiovascular reactions, 18.5
 - fetotoxicity, 29.41, 30.35
 - prenatal exposure and perinatal effects, 27.1
 - second-generation effects, 20.24
- cocamidopropylbetaine, allergy, 19.151
- codeine, breast feeding, 31.154
- collagenase, 10.277
- complementary and alternative therapies, indirect risks, 27.521
 - esophagus, adverse effects on, 14.442
- contact lens solutions, 6.412
- contrast media
 - adverse reactions, 13.431, 24.525
 - anaphylactoid and allergic reactions, 20.422
 - delayed reactions, 26.513
 - in magnetic resonance imaging, 20.419
 - nephrotoxicity, 27.500, 28.556, 29.575, 31.731, 31.735, 32. 846, 34.751
 - sialadenitis, 32.845
 - systemic fibrosis, 32.852
- corticosteroids, *see* glucocorticoids
- corticotrophin-releasing hormone, 9.357
- cosmetics
 - adverse reactions, 13.117
 - contact allergy, 11.142, 16.150, 19.151
 - ingredient labeling 22.159
- co-trimoxazole, hypersensitivity reactions, 20.264
- cough remedies, *see* antitussive drugs
- COX-2 inhibitors, 24.115, 25.126, 26.116
 - adverse events, 33.241
 - cardiovascular disease, 29.116, 32.225
 - gastrointestinal adverse reactions, 32.225
- Cupressaceae, 34.775
- cyclopentolate, 34.763
- cytotoxic drugs, *see* cancer chemotherapy
- dabigatran, 34.544
- danaparoid sodium, 32.631
- dantrolene, 5.137
- dapsone, hematological abnormalities, 33.630
- daptomycin, muscle damage, 30.309

- Debendox[®] (dicyclomine + doxylamine + pyridoxine), pregnancy, 6.316
 deferiprone
 cardiac siderosis, 29.235
 pro-oxidant effects, 33.468
 deferoxamine, 16.247
 bone dysplasia, 23.241
 cardiac siderosis, 29.235
 bone dysplasia, 23.241
 cardiac siderosis, 29.235
 vitamin C and iron, drug-drug interaction, 8.239
 yersiniosis, 11.215
 demeclocycline, 5.266
 dental amalgam, 9.219, 10.210
 desferrioxamine, *see* deferoxamine
 dextropropoxyphene, dysmorphogenesis, 8.78
 dialysis, encephalopathy, 4.161
 diamorphine, progressive spongiform leukoencephalopathy, 24.40
 diazepam, tumor promoter, 6.39
 diclofenac, liver damage, 20.91
 dicyclomine + doxylamine + pyridoxine (Bendectin[®], Debendox[®]), in pregnancy, 6.316
 diethylstilbestrol
 in pregnancy, 6.351
 transgenerational effects, 31.657
 difetarzone, 8.293
 digitalis
 in atrial fibrillation, 24.197
 quinidine, drug-drug interaction, 6.173
 toxicity and overdose, treatment, 5.172
 digoxin, compared with other drugs in heart failure in sinus rhythm, 14.141
 compared with other drugs in chronic uncomplicated atrial fibrillation, 14.144
 in atrial fibrillation, 23.333
 in heart failure in sinus rhythm, 18.196
 dimethylfumarate, 32.295
 dimethylsulfoxide, 6.429
 diosmin, 34.311
 dipeptidyl peptidase IV inhibitors, 30.498
 dipyrrone, 4.63
 disinfectants
 bacterial resistance, 33.479
 contamination, 9.228
 dithranol, mutagenicity and tumorigenicity, 8.161
 diuretics
 diabetes mellitus, electrolyte abnormalities, and the ALLHAT trial, 27.219
 drug-drug interactions with NSAIDs, 12.80
 hypokalemia, 9.203
 hyponatremia, 29.219
 renal cell carcinoma, 23.225
 renal insufficiency, 25.250
 thiamine deficiency, 32.401
 DNA alkylating drugs, 31.721
 dofetilide, 26.208
 dopamine receptor agonists
 pathological gambling, 30.174
 sleep disorders, 26.160, 27.149
 doxycycline, 8.251
 sophageal ulceration, 7.276
 doxylamine, *see also* dicyclomine
 overdose and rhabdomyolysis, 31.298
 dronedarone, 33.386
 drotrecogin alfa (activated), 32.591
 ecstasy, *see* MDMA
 EDTA, pseudothrombocytopenia, 21.250
 endoperoxides, in malaria, 34.443
 endothelin receptor antagonists, in hypertension, 26.233
 enzyme inhibitors, 15.337
 epinephrine, *see* adrenaline
 erythromycin, versus the new macrolides, 21.269
 erythropoietin, pure red cell aplasia, 27.348
 status and safety, 16.400
 ethambutol, optic neuropathy, 30.358
 ethanol, *see* alcohol
 ethylene oxide, dialyser hypersensitivity, 11.219
 etomidate, adrenal suppression, 32.249
 etoposide, 27.477
 etretinate, ossification, 12.127
 euxyl K 400, contact allergy, 16.150
 exenatide, dosage regimens, 34.692
 Fansidar[®], 10.256
 prevention of malaria, 32.523
 fat emulsions, priapism, 11.313
 felbamate
 aplastic anemia, 19.68, 22.86
 benefit harm balance, 23.86
 fenfluramine
 cardiac valvulopathies, 22.3, 23.2, 24.4, 25.5
 primary pulmonary hypertension, 18.7, 21.2, 23.2, 25.5
 fenoterol, safety in severe asthma, 23.182
 fentanyl, buccal and transdermal administration, 20.77
 ferrous salts, 5.238
 deferoxamine, vitamin C, drug-drug interaction, 8.239
 overload, 8.230
 rheumatism, 7.254
 fertility drugs
 malignant melanoma, 26.434
 ovarian cancer, 24.474
 finasteride, 30.480
 fingolimod, 34.616
 fish oils, 13.460
 cholestasis, 34.534

- flecainide, in supraventricular dysrhythmias, 21.200
- flumazenil, 33.79
- fluoropyrimidines, 34.731
- fluoroquinolones, 12.250, 18.271
- fluorouracil, adverse reactions, 23.476
- folic acid, dietary supplementation, 19.369
safety aspects, 27.407
- formoterol, tolerance, 24.187
- fragrances, contact allergy, 20.149
- gadolinium salts, nephrotoxicity, 28.561, 31.735, 32.852
- gammabenzene hexachloride, 5.154
- general anesthesia, *see* anesthesia
- germanium, 16.545
- glafenine, 4.69
- glucocorticoids
aerosols in asthma, 4.271
bone, 16.447, 22.182, 25.195
contact allergy, 15.139, 21.158
dementia, 9.326
depot injections, 5.351
effective dose and therapeutic ratio, 23.175
and eyes, 29.481
and growth, 14.335
inhaled, children, risks in, 27.174
inhaled, effects on mouth and throat, 29.168
inhaled, effects on skin, 29.169
inhaled, fracture risk, 31.307
inhaled, growth inhibition, 26.186
inhaled, hypothalamic–pituitary–adrenal gland function, 31.305
inhaled, pneumonia risk, 32.311, 33.353, 34.277
inhaled, skeletal adverse effects, 33.355
inhaled, systemic availability, 24.185, 26.187
musculoskeletal adverse reactions, 21.417, 32.312
osteoporosis and osteonecrosis, 16.447, 19.377, 20.374, 21.417, 22.182, 28.473
perioral dermatitis, 5.151
preterm infants, 17.445
psychiatric effects, 7.375, 9.326
withdrawal syndrome, 8.351
- glatiramer, 34.617
- glucose solutions, hypophosphatemia, 11.312
- gold salts, 8.224, 9.217, 10.207
microhematuria, 7.252
pulmonary reactions, 5.236
- gonadotropin-releasing hormones (LH-RF or GnRH) and their analogues, 8.385
- grapefruit juice, drug-drug interactions 23.519
- green-lipped mussel extract, 6.416
- growth hormone
adults, 16.501
creutzfeldt–jakob disease, 11.371
insulin resistance, 24.504
tumorigenicity, 23.468, 34.705
- gusperimus, 34.618
- heart valves, 9.431
- hemin (haematin), 4.231
- heparin
low-molecular-weight, 12.311
skin necrosis, 5.326
thrombocytopenia, 5.326, 30.404, 32.626
thrombohemorrhagic complications, 5.326
- hepatitis B vaccine, demyelinating diseases, 21.331, 22.346, 24.374
- herbal medicines, warfarin, drug-drug interactions, 30.400
- heroin, *see* diamorphine
- hexachlorophene poisoning, 7.268
- histamine (H₂) receptor antagonists, 8.335, 13.330, 15.393
- HIV-protease inhibitors
insulin resistance, 22.317
lipodystrophy, 22.317
- HMG coenzyme A reductase inhibitors, drug-drug interactions, 25.530, 30.517
- “mad honey”, cardiotoxicity, 33.996
- hormonal contraceptives, injectable, 7.390
- hormone replacement therapy, 5.364
attitudes to, 33.853
breast cancer, 33.856
cardiovascular reactions, 31.659
endometrial cancer, 4.275
ovarian cancer, 32.740
- hormones, sex
breast cancer 11.346
tumors, 22.465
- HRT, *see* Hormone replacement therapy
- 5-HT, *see* Serotonin
- hydrochlorothiazide, non-cardiogenic pulmonary edema, 31.373
- hydrosmin, 34.311
- 5-hydroxytryptamine, *see* serotonin
- hypnotics, 20.30
avoiding adverse reactions, 21.37
- hydrocortisone, 10.338
- hydroxychloroquine, retinopathy, 9.251
- hypoglycemic drugs, combinations of, 27.458, 28.521
- imexon, 34.636
- immunization
adverse reactions, 24.364
and autoimmune disease, 27.336
bioterrorism, 25.378, 26.354
multiple, 27.334
surveillance after, 15.340, 22.333, 23.335, 24.364, 25.376, 26.353, 27.334
- immunotherapy, in leishmaniasis, 15.299

- incretin mimetics, 29.528
 indacaterol, 32.317
 indometacin, *see also* Osmosin®
 fetal and neonatal complications, 18.102
 in patent ductus arteriosus, 10.80
 influenza vaccine, 29.332, 33.659
 narcolepsy, 34.501
 inhalations, 9.33, 11.151
 insulins
 and cancer, 33.890
 edema, 11.364
 human, and allergic reactions, 8.379
 human, and hypoglycemia, 15.452
 inhalation, 30.495
 modes of administration, 26.464
 resistance, and growth hormone, 24.504
 synthetic analogues, 24.489
 interferon + ribavirin, 30.344
 interferons, psychological and psychiatric
 reactions, 29.384
 interleukin-2, 14.325
 intravenous therapy, infectious complications,
 8.320
 iodine, radioactive, 11.358
 malignant thyroid tumors, 5.383
 ipecacuanha, myopathy, 11.422
 irinotecan, 27.477
 iron chelators, combinations, 31.399
 iron, *see* ferrous salts
 isoniazid
 genetic susceptibility factors, 12.257
 hepatotoxicity, 4.211
 prophylactic, toxicity, 24.352
 isothiazolinones, 11.134
 isotretinoin, creatine kinase raised, 10.124

 Kathon® CG (methylchloroisothiazolinone
 + methylisothiazolinone), 11.134
 kava kava
 liver damage, 27.518
 adverse reactions, 28.579
 ketamine, urinary tract dysfunction, 33.268
 ketanserin, 8.199
 ketoconazole
 in fungal infections of the central nervous
 system, 8.269
 hepatotoxicity, 7.289, 8.265, 12.229
 ketorolac, risk of adverse reactions, 17.110
 khat, 30.43

 labetalol, 5.212
 lacosamide, 33.139
 lamotrigine, skin rashes, 20.62, 24.88
 latex, allergy, 31.761
 laxatives
 abuse, 13.336
 formulations, 7.355

 leflunomide, 29.435
 leukocytes, 6.293
 leukotriene receptor antagonists, Churg–Strauss
 syndrome, 24.183, 27.177, 29.174
 levacetylmethadol, 32.193
 levamisole, immunostimulation, 4.220
 levodopa, and malignant melanoma, 4.97, 31.267
 levonorgestrel, intrauterine administration,
 33.865
 levothyroxine, dosage, 9.341
 lipid-lowering drugs, 13.402, 15.479
 lithium
 adverse reactions, prevention and treatment,
 13.17, 17.28
 beneficial uses other than in bipolar disorder,
 27.19
 drug-drug interactions, 7.26, 16.13, 18.30
 efficacy, comparisons with other agents, 30.23
 intoxication, prevention and treatment, 17.29
 leukopenia, 5.22
 monitoring therapy, 11.24, 18.25
 mortality, 19.14
 nervous system toxicity, 10.27
 neuroprotection, 32.41
 nephrotoxicity, 4.22, 14.18, 19.16
 thyroid, 12.26
 uses, 33.39
 local anesthetics, *see* anesthetics
 loop diuretics, *see* diuretics
 Lorenzo's oil, 27.475
 Lyme disease vaccine, autoimmune disease,
 24.366

 macrolides, drug-drug interactions, 9.239, 14.220
 intestinal motility, 18.269
 “mad honey”, cardiotoxicity, 33.996
 magnesium, metabolism, 10.187
 malaria vaccines, 22.306
 mannitol, 28.236
 MAO inhibitors, *see* monoamine oxidase
 inhibitors
 MDMA (ecstasy)
 cognitive reactions, 26.32, 32.63
 deaths, 24.32
 epidemiology of use, 30.37
 measles immunization, *see also* mmr
 autism, 23.350
 Crohn's disease, 23.350
 neurological adverse reactions, 23.348
 subacute sclerosing panencephalitis, 29.335
 mebendazole, hypersensitivity reactions,
 12.263
 melatonin, 25.523
 meow meow, 34.41
 mephedrone, 34.41
 mercury, *see* dental amalgam
 metals, hypersensitivity, 6.225

- methylchloroisoithiazolinone
+ methylisothiazolinone, 11.134
- mercaptapurine, *see* thiopurines
- metamfetamine, 29.3
- metformin
contraindications, 28.515
lactic acidosis, 23.459, 29.526
- methotrexate
intellectual functioning, 7.428
treatment of toxicity, 33.950
- methylcathinone, 34.41
- methyldibromoglutaronitrile, contact allergy,
16.150, 19.151
- methylparatyrosine, 4.98
- methylphenidate, effects at different ages, 31.6
- methylthiotetrazole, 11.226
- metronidazole
mutagenicity, 4.206
tumorigenicity, 4.206
- metyrosine (α -methyl-p-tyrosine), 4.98
- mianserin, 5.18
- mibefradil, drug-drug interactions, 23.210
- midazolam, 15.112
- midodrine, 26.159
- milrinone, intravenous, acute heart failure,
21.196
- minocycline, skin pigmentation, 6.244
- mitomycin, hemolytic-uremic syndrome,
10.397
- MMR immunization, *see also* measles
autism, 23.350, 25.387, 28.363
Crohn's disease, 23.350, 25.387
- mometasone furoate, 30.197
- monoamine oxidase inhibitors, 10.15, 12.8, 13.6,
17.361
- monofunctional alkylating agents, 32.827
- morphine, managing adverse reactions, 26.98
- muscle relaxants
emergency medicine, 20.133
eyes, 21.145
hypersensitivity reactions, 27.138
intensive care, 19.140
- narcotic analgesics, *see* opioids
- neuroleptic drugs, *see* antipsychotic drugs
- neuromuscular blocking agents
anaphylaxis, 29.145
antibiotics, drug-drug interactions, 5.131
non-depolarizing neuromuscular blockers,
15.127
recovery in intensive care, 12.114
residual paralysis, 27.139
- niacin, extended-release, 16.440
- nickel, hypersensitivity, 34.358
- niflumic acid, 6.99
- nitrofurantoin, 6.268
geographical differences, 7.299
- nitrous oxide
alcohol, drug-drug interaction, 10.163
chronic exposure, 5.120
N-lost derivatives, 31.721
nomifensine, 11.15
non-steroidal anti-inflammatory drugs, *see*
NSAIDs
- noramidopyrine methanesulphonate, 4.63
- NSAIDs, *see also* COX-2 inhibitors
acute renal insufficiency, 28.122
adverse events, 33.241
blood pressure, 19.92, 27.102
cardiovascular adverse reactions, 32.225
children, 19.96
current controversies, 17.102
COX-2 inhibitors, 24.115, 25.126, 26.116
drug-drug interactions with diuretics, 12.80
dyspepsia, 28.120
gastrointestinal adverse reactions, 6.91, 10.76,
14.79, 17.95, 18.90, 18.99, 20.86, 21.96,
22.108, 23.114, 32.225
gastrointestinal damage, role of *Helicobacter*
pylori, 27.105
gastrointestinal damage, reducing, 30.125
gastrointestinal toxicity, prevention, 19.93
inflammatory bowel disease, 10.76, 25.131
inhibiting cardioprotective effects of
acetylsalicylic acid, 28.118
intracerebral hemorrhage, 28.119
necrotizing fasciitis, 28.121
nephrotoxicity, 5.88, 11.82, 18.100, 20.89,
24.120, 26.111
occupational exposure, 34.181
osteoarthritis, 11.87
skin reactions, 13.72
topical, 18.163
- ocular drugs
allergic reactions, 21.486
geriatric patients, 16.542
risk factors for adverse reactions, 22.507
- omeprazole, tumors, 16.423
- opioids
abuse, 29.44
addiction, maternal and neonatal, 6.73
adverse reactions, frequency, 32.183
adverse reactions, prevention, 24.100
death, 25.37
epidural and intrathecal administration,
6.68
obstetric use, 24.102
optimal prescribing, 34.145
pregnancy, 5.67
public health implications, 34.146
routes of administration, 30.106
tolerance in neonates, 23.97
withdrawal and clonidine, 5.68

- oral contraceptives, *see also* hormonal contraceptives
 antibiotics, drug-drug interactions, 8.256
 antimicrobial drugs, and pregnancy, 24.274
 and breast cancer, 15.426
 formulations, 24.472
 third-generation, 25.484, 26.442
 venous thromboembolism, 23.442
- oral hypoglycemic drugs, UDGp study, 4.301
- oral photochemotherapy, *see* PUVA
- orlistat, 30.429
- orthopedic implants, 6.225
- Osmosin[®] (indometacin), 8.103
- oxymorphone, 32.203
- oxyphenbutazone, 9.85
- paclitaxel, adverse reactions, 21.463
- pancreatic enzyme supplements, fibrosing colonopathy, 20.322
- paracetamol, 5.82
 asthma, 30.129
 hepatotoxicity in alcoholism, 12.76
 liver damage, 17.98, 18.94
 overdose, 13.68, 23.117
- parenteral nutrition
 bone reactions, 22.378
 cholestasis, 8.315, 22.376, 34.534
 infections 22.379
 liver, 5.318
- penicillamine, 10.218
 leukemia, 7.259
 respiratory adverse reactions, 4.179
 yellow nail syndrome, 9.223
- penicillins
 desensitization, acute, 23.252
 drug formulations, 9.232
 elastolysis, 9.231
 hypersensitivity reactions, cross-reactivity with cephalosporins, 30.280
 immunological reactions, 28.267
 nephritis, acute interstitial, 6.241
- peritoneal dialysis fluids, effects on peritoneum, 22.381
- Perna canaliculus* extract, 6.416
- peroxisome proliferator-activated receptors, *see also* thiazolidinediones
 dual agonists, 32.782
- pertussis vaccine, 10.287, 11.284, 11.285
- phencyclidine, 10.35
- phentermine, cardiac valvulopathies, 24.4
- phenylbutazone, 9.85
- phenylephrine, in anesthesia-induced hypotension, 34. 236
- pholcodine, 32.206
- photochemotherapy, *see* PUVA
- photodynamic therapy, cancers 32.832
- phytoestrogens, in foodstuffs, 31.655
- pilsicainide, 32.348
- piroxicam, 6.100
 gastrointestinal reactions, 10.85, 11.97, 12.91
- pivalic acid, and carnitine, 12.209
- plasma expanders, hemostasis, 4.240
- platinum compounds, 26.490
- polio vaccine, AIDS, 23.352
- polyaspartic acid, protective against nephrotoxicity, 17.305
- polyethylene glycol, electrolyte, mineral, metal, and fluid balance, 29.376
- polystyrene sulfonates, 25.271
- polyvinylpyrrolidone, storage disease, 22.522
- PPAR, *see* peroxisome proliferator-activated receptors
- pregabalin, 30.86
- probucol, 8.393
- propofol
 infusion syndrome, 26.135
 prevention of pain, 30.143, 34.201
- propolis, allergy, 17.181
- propoxyphene, 4.48
- propranolol, adrenaline, drug-drug interaction, 9.6
- protease inhibitors, drug-drug interactions, 33.628
- proton pump inhibitors, tumors, 23.383
- psilocybin, 31.49
- PUVA
 cataracts, 9.144
 malignant melanoma, 22.166
 mutagenicity, 4.104
 skin cancer, 4.104, 6.145
- pyrazinamide, in latent pulmonary tuberculosis, 27.323
- pyridoxine, *see* dicyclomine
- pyrimethamine + sulfadoxine (Fansidar[®]), 10.256
 prevention of malaria, 32.523
- pyrimidine analogues, 34.731
- pyrrolizidine alkaloids, 8.442, 10.433
- quinidine
 digitalis, drug-drug interaction, 6.173
 versus quinine, 15.295
- quinine, versus quinidine, 15.295
- ranitidine, comparison with cimetidine, 9.313
- rasagiline, 31.270
- rasburicase, 31.203
- renin inhibitors, 30.242
- retinoids, *see* vitamin A and individual names
- rhesus anti-D, prophylaxis, 13.297
- ribavirin + interferon, 30.344
- ribostamycin, and aminoglycosides, 15.270
- rifampicin, 4.215
- rocuronium, allergic reactions, 26.150
 and pholcodine, 31.249
- Rotashield, intussusception, 23.354

- rotavirus vaccine
 - intussusception, 34.504
 - Kawasaki disease, 31.522
- rubella vaccine, joints, 11.295
- salbutamol, adrenoceptor genotypes, 29.173
- salicylates, *see also* acetylsalicylic acid
 - Reye's syndrome, 7.94, 8.93
- salmeterol, tolerance, 24.187
- sapropterin, 32.609
- Seatone[®] (green-lipped mussel extract), 6.416
- sedatives, 29.128
- semapimor, 34.624
- serotonin
 - receptor antagonists, 15.391
 - selective serotonin reuptake inhibitors, drug
 - drug-drug interactions, 22.13
 - selective serotonin reuptake inhibitors,
 - gastrointestinal bleeding, 32.33
 - selective serotonin reuptake inhibitors,
 - suicidal behavior, 29.19, 31.18, 33.26
- sex hormones
 - cardiovascular complications, 8.359
 - drug-drug interactions, 9.332
 - nervous system, 8.362
 - psychological function, 8.362
 - tumors, 22.465
- smallpox vaccination, 27.339
- somatostatin, 15.468
- soybean oil, cholestasis, 34.534
- spinal manipulation, adverse reactions,
 - 29.591
- SSRIs, *see* Serotonin
- statins, *see* HMG Co-A reductase inhibitors
- steroids, *see* glucocorticoids
- Stevia* species, 34.777
- stimulants, in ADHD, 31.4
- sugammadex, 32.275
- sulfadoxine, *see* pyrimethamine
- sulfonamide derivatives, hypersensitivity
 - reactions, 30.252
- sulphonylureas, fluid retention, 4.303
- sumatriptan, 17.171
- sun screens, 5.152
- suprofen, nephrotoxicity, 12.88
- suramin
 - and AIDS, 10.277
 - patients with prostate cancer, 20.283
- Surgam[®], *see* tiaprofenic acid
- suxamethonium, postoperative myalgia, 28.155
- sympathomimetics, *see also* individual names
 - and beta₂-adrenoceptor agonists
 - cardiovascular adverse reactions, 5.9
 - in premature labor, 6.139
- tamoxifen, versus aromatase inhibitors, 30.475
- tampons, toxic shock syndrome, 6.427
- tar, *see also* dithranol
 - ultraviolet radiation and cutaneous
 - malignancy, 6.149
- taxanes, 33.935
- teniposide, 27.477
- tetrabenazine, 33.305
- tetracyclines
 - adverse reactions, 12.212, 26.268
 - chemically modified, 31.419
 - comparative toxicity, 22.268
 - and environment, 33.497
 - and metalloproteinases, 26.266
 - non-antimicrobial properties, 30.288
 - in pregnancy, 25.280
 - in rheumatology, 23.255
 - therapeutic effects, 24.278
- tetrahydrobiopterin, 32.609
- TGN 1412, 32.642
- theophylline, 7.1
 - asthma, 17.2, 18.1, 18.2
 - with β₂-adrenoceptor agonists, 9.10
 - intoxication, 6.2
 - pancreatic cancer, 7.8
 - susceptibility factors, 5.1
- thiazides, *see* diuretics
- thiazolidinediones
 - cardiovascular reactions, 31.697
 - musculoskeletal reactions, 32.779
 - peripheral edema, 29.531
- thiomersal
 - infant neurodevelopment, 33.453
 - in vaccines, 28.357
- thiopurines
 - cross-reactivity, 33.824
 - genetic susceptibility, 31.634
- thrombolytic agents, 4.247
- thyroid hormones, 29.464
- thyroxine, drug-drug interactions, 24.484
- tiaprofenic acid
 - cystitis, 18.106
 - gastric reactions, 12.89
- ticrynafen, *see* tienilic acid
- tienilic acid, 4.161, 5.229
- timolol, eye drops, 5.425
- titanium, allergy, 33.456
- TNF, *see* tumor necrosis factor
- tolcapone, 32.289
- topiramate, cognitive reactions, 26.81
- topoisomerase inhibitors, 27.477
- topotecan, 27.477
- total parenteral nutrition (tpn), *see* parenteral
 - nutrition
- transfusions, *see also* blood products
 - infection risk, 33.669
 - leukocytes, 6.293
- triptans, nervous system adverse effects 33.408
- trocetrapib, 32.816

- transfusions
 AIDS, 12.298
 complications, 12.300
 transmission of infectious agents, 34. 521
- trazodone, 7.19
- tretinoin, topical, teratogenicity, 18.164
- triazolam, 16.33
- tricyclic antidepressants
 endocrine reactions, 11.12
 mania, 13.8
- trimethoprim, 4.210, 5.287
- triphenylmethane dyes, 33.481
- L-tryptophan, 4.18
 eosinophilia–myalgia syndrome, 15.514
- tumescent anesthesia, 34. 213
- tumor necrosis factor antagonists, infection risk,
 29.395, 31.594
- tyrosine kinase inhibitors, 30.520
- ultraviolet radiation, see also puva
 tar and cutaneous malignancy, 6.149
- vaccines, *see also* individual agents
 adjuvants, 32.577
 autism, 31.516, 33.661
 combinations, 29.327, 30.369
 Guillain–Barré syndrome, 31.515
 HIV-infected individuals, 12.269
 Kawasaki disease, 31.522
 national compensation systems, 12.271
 poliomyelitis, 22.352
 surveillance, 34.499
 thiomersal in, 28.357
- vaginal tampons, toxic shock syndrome, 6.427
- valproate, overdose, 32.157
 polycystic ovary syndrome, 26.81
- vancomycin, 5.271
 lessons from, 27.242
 resistance, 29.244
- vigabatrin
 psychosis and abnormal behavior, 18.71
 visual field defects, 21.78, 24.95, 25.98, 26.82,
 33.178
- vecuronium (ORG NC 45), 7.144
- vitamin C, deferoxamine, drug-drug interaction,
 8.239
- vitamin E, 6.328
- vinca alkaloids, 28.538
- vitamin A, 17.436
 alcohol, beta-carotene, drug-drug interaction,
 24.442
 hypervitaminosis, 15.411
 and immunization, 33.691
 in pregnancy, 21.405
 and prostate cancer, 13.346
 teratogenicity, 10.122
- vitamin B6, debate, 23.420
- vitamin E, co-medication, 26.423
- vitamin K
 cancer, 23.424
 skin reactions, 25.461
- vitamins, in old age, 22.431
- voriconazole
 photosensitivity, 34.431
 tumorigenicity, 34.431
- warfarin, herbal medicines, drug-drug
 interactions, 30.400
- white cells, 6.293
- ximelagatran, hepatotoxicity, 30.411
- zidovudine, 13.246
- zileuton, 32.322
- zimeldine, 8.25
- zomepirac, 7.114, 8.108

2. Index of adverse effects and adverse reactions in special reviews

Cardiovascular

- angina exacerbation, calcium channel
 blockers, 8.191
- atrial fibrillation, antidysrhythmic drugs,
 24.197
- atrial fibrillation, digitalis, 24.197
- cardiac failure
 aldosterone antagonists, 24.246
 bambuterol, 23.181
- cardiac repolarization, antiepileptic drugs,
 34.86
- cardiac siderosis, deferoxamine/deferiprone,
 29.235
- cardiomyopathy, catecholamines, 33.313
- dysrhythmias
 amiodarone, 25.211
 antihistamines, 22.176
- hormone replacement therapy, 31.659
- hypertension, NSAIDs, 19.92, 27.102
- hypotension, anesthesia-induced,
 phenylephrine, 34.236
- myocardial infarction
 acetylsalicylic acid, 27.109
 adrenaline, 31.259
- prodysrhythmic reactions, antidysrhythmic
 drugs, 17.218, 23.196
- QT interval prolongation, 24.54
- valvulopathies
 fenfluramine, 22.3, 23.2, 24.4, 25.5
 phentermine, 24.4, 25.5
- vasospasm, adrenaline, 31.259

- venous thromboembolism, oral
 - contraceptives, 23.442
- unspecified reactions
 - anthracyclines, 7.428
 - anticholinergic drugs, 32.318, 33.364
 - antidepressants, 6.16
 - antihistamines, 17.196, 25.183, 26.180
 - antipsychotic drugs, 5.42
 - calcium channel blockers, 20.185
 - cocaine, 18.5
 - coxibs, 29.116
 - “mad honey”, 33.996
 - NSAIDs, 32.225
 - propofol, 26.135
 - thiazolidinediones, 31.697
- Respiratory**
 - asthma
 - acetylsalicylic acid, 17.94, 31.193
 - beta-adrenoceptor antagonists, 8.185
 - fenoterol, 23.182
 - paracetamol, 30.129
 - in pregnancy, 28.186
 - asthma death, beta₂-adrenoceptor agonists, 17.164
 - asthma exacerbation, asthma medications, 20.165
 - bronchoconstriction, paradoxical, nebulizer solutions, 13.134
 - bronchospasm, adenosine, 32.337
 - Churg–Strauss syndrome, leukotriene receptor antagonists, 24.183, 27.177, 29.174
 - cough, angiotensin converting enzyme (ACE) inhibitors, 19.211
 - dyspnea, adenosine, 32.337
 - interstitial pneumonia, cancer chemotherapy, 4.324
 - pneumonia, glucocorticoids, 32.311, 33.353, 34.277
 - primary pulmonary hypertension, appetite suppressants, 18.7, 21.2, 23.2, 25.5
 - pulmonary edema, non-cardiogenic, hydrochlorothiazide, 31.373
 - rhinosinusitis, acetylsalicylic acid, 17.94
 - unspecified reactions
 - amiodarone, 15.168
 - beta₂-adrenoceptor agonists, long-acting, 30.198, 31.309
 - gold salts, 5.236
 - penicillamine, 4.179
 - sex steroids, 8.359
 - sympathomimetics, 5.9
- Ear, nose, throat**
 - glucocorticoids, inhaled, 29.168
- Nervous system**
 - brain damage, benzodiazepines, 14.36
 - Creutzfeldt–Jakob disease, growth hormone, 11.371
 - demyelinating diseases, hepatitis B vaccine, 21.331, 22.346, 24.374
 - drowsiness/sedation, antihistamines, 8.163, 9.149, 21.170, 23.171, 26.182
 - dystonias, 8.62
 - encephalopathy
 - bismuth, 4.166
 - dialysis, 4.161
 - Guillain–Barré syndrome, vaccines, 31.515
 - headache, analgesics, 21.95, 23.114
 - intracerebral hemorrhage, NSAIDs, 28.119
 - narcolepsy, influenza vaccine, 34.501
 - neurodevelopment impaired, thimerosal, 33.453
 - neuroleptic malignant syndrome, 11.47, 20.41
 - pain, propofol, 30.143, 34.201
 - poliomyelitis, vaccines, 22.352
 - progressive spongiform leukoencephalopathy, diamorphine, 24.40
 - seizures
 - antimicrobial drugs, 18.261
 - carbapenems, 33.491
 - sleep disorders, dopamine receptor agonists, 26.160, 27.149
 - strokes
 - acetylsalicylic acid, 27.109
 - risperidone, 28.76
 - subacute myelo-optic neuropathy (SMON), clioquinol, 4.253
 - subacute sclerosing panencephalitis, measles vaccine, 29.335
 - tardive dyskinesia, 14.47, 20.38
 - tardive syndromes, 17.54
 - Wernicke’s encephalopathy, alcohol/nitrous oxide drug–drug interaction, 10.163
 - unspecified reactions
 - anesthetics, local, 21.129
 - anticholinergic effects, 31.273
 - antiepileptic drugs, 22.84
 - anesthetics, intrathecal, 25.152
 - lithium, 10.27
 - measles immunization, 23.348
 - sex hormones, 8.362
 - triptans, 33.408
- Neuromuscular**
 - residual paralysis, neuromuscular blocking drugs, 27.139
- Sensory systems (vision)**
 - cataracts, oral photochemotherapy, 9.144
 - corneal edema, amantadine, 33.602
 - optic neuropathy, ethambutol, 30.358
 - retinopathy
 - chloroquine, 9.251
 - hydroxychloroquine, 9.251
 - visual field defects, vigabatrin, 21.78, 24.95, 25.98, 26.82, 33.178

- unspecified reactions
 - drug abuse, 12.33
 - glucocorticoids, 29. 481
 - muscle relaxants, 21.145
 - timolol, eye drops, 5.425
- Sensory systems (hearing)**
 - aminoglycosides, 10.243, 14.222, 18.268
- Psychological**
 - cognitive impairment, anticholinergic drugs, 26.32, 32.63, 34.246
 - cognitive reactions
 - MDMA (ecstasy), 26.32, 32.63
 - metamfetamine, 29.3
 - topiramate, 26.78
 - driving impaired
 - anesthesia, general, 4.74
 - benzodiazepines, 7.46
 - emotional arousal, antipsychotic drugs, 8.62
 - gambling, dopamine receptor agonists, 30.174
 - intellectual impairment, methotrexate, 7.428
 - unspecified reactions
 - drug abuse, 5.29
 - interferons, 29.384
 - sex hormones, 8.362
- Psychiatric**
 - autism, measles/MMR immunization, 23.350, 25.387, 28.363, 31.516, 33.661
 - dementia, glucocorticoids, 9.326
 - depression, benzodiazepines, 17.43
 - mania, antidepressants, 13.8, 29.18
 - mental confusion, cimetidine, 5.159
 - psychosis and abnormal behavior, vigabatrin, 18.71
 - suicidal behavior
 - antidepressants, 32.29
 - antiepileptic drugs, 33.127, 34.89
 - selective serotonin reuptake inhibitors (SSRIs), 29.19, 31.18, 33.26
 - unspecified reactions
 - antiepileptic drugs, 22.82, 27.72
 - glucocorticoids, 7.375
 - interferons, 29.384
- Endocrine**
 - adrenal suppression, etomidate, 32.249
 - endocrine function, antiepileptic drugs, 9.55
 - hypothalamic–pituitary–adrenal gland
 - function, glucocorticoids, inhaled, 31.305
 - ovarian hyperstimulation syndrome, valproate, 26.477
 - polycystic ovary syndrome, valproate, 26.81
 - thyroid disease, amiodarone, 27.192, 31.310, 33.382
 - thyroid disease, lithium, 12.26
 - unspecified reactions
 - tricyclic antidepressants, 11.12
- Metabolism**
 - diabetes mellitus
 - alcohol, 5.386
 - antihypertensive drugs, 28.226
 - antipsychotic drugs, 28.60, 33.94, 34.54
 - diuretics, 27.219
 - hyperlactatemia, nucleoside analogue reverse transcriptase inhibitors, 29.302
 - hypoglycemia, insulins, 15.452
 - insulin resistance
 - growth hormone, 24.504
 - HIV-protease inhibitors, 22.317
 - lactic acidosis, metformin, 23.459, 29.526
 - lipoatrophy, nucleoside analogue reverse transcriptase inhibitors, 29.302
 - lipodystrophy, HIV-protease inhibitors, 22.317
 - metabolic acidosis, propofol, 26.135
 - mitochondrial toxicity, nucleoside analogue reverse transcriptase inhibitors, 29.302
 - storage disease, polyvinylpyrrolidone, 22.522
 - weight gain, antipsychotic drugs, 26.56, 33.94, 34.54
 - unspecified reactions
 - antiretroviral drugs, 28.329, 33.582
- Nutrition**
 - thiamine deficiency, diuretics, 32.401
- Electrolyte balance**
 - electrolyte abnormalities, diuretics, 27.219, 29.219
 - hypokalemia, diuretics, 5.227, 9.203
 - unspecified reactions
 - polyethylene glycol, 29.376
- Mineral balance**
 - hypophosphatemia, glucose solutions, 11.312
 - unspecified reactions
 - polyethylene glycol, 29.376
- Metal balance**
 - polyethylene glycol, 29.376
- Fluid balance**
 - edema, insulin, 11.364
 - edema, thiazolidinediones, 29.531
 - fluid retention, sulphonylureas, 4.303
 - unspecified reactions
 - polyethylene glycol, 29.376
- Hematologic**
 - Agranulocytosis
 - analgesics, 11.89
 - clozapine, 22.59
 - aplastic anemia
 - analgesics, 11.89
 - felbamate, 19.68, 22.86
 - coagulation disorders, beta-lactam antibiotics, 18.258
 - eosinophilia–myalgia syndrome, tryptophan, 15.514
 - hemolytic disease of the newborn, 12anti-D prophylaxis, 293

- hemostasis impaired
 - cephalosporins, 8.249, 12.210
 - plasma expanders, 4.240
- leukopenia, lithium, 5.22
- neutrophil function impaired, antibiotics, 7.279
- pseudothrombocytopenia, EDTA, 21.250
- pure red cell aplasia, erythropoietin, 27.348
- thrombocytopenia, heparin, 5.326, 30.404, 32.626
- thrombohemorrhagic complications, heparin, 5.326
- unspecified reactions
 - antidepressants, 6.22
 - dapsone, 33.630
- Mouth**
 - glucocorticoids, inhaled, 29.168
- Salivary glands**
 - sialadenitis, iodinated contrast media, 32.845
- Gastrointestinal**
 - colitis
 - antimicrobial drugs, 12.216, 17.303
 - NSAIDs, 10.76
 - Crohn's disease, measles/MMR immunization, 23.350, 25.387
 - diarrhea, chenodeoxycholic acid, 4.258
 - dyspepsia, NSAIDs, 28.120
 - esophageal ulceration, doxycycline, 7.276
 - fibrosing colonopathy, pancreatic enzyme supplements, 20.322
 - gastrointestinal bleeding, acetylsalicylic acid, 17.95, 18.90
 - gastrointestinal ulceration, bleeding and perforation
 - NSAIDs, 11.97, 14.79, 16.103, 17.95, 18.90, 18.99, 19.93, 20.86, 21.96, 22.108, 23.114, 27.105, 30.125
 - Osmosin[®] (indometacin), 8.103
 - piroxicam, 10.85
 - inflammatory bowel disease, NSAIDs, 10.76, 25.131
 - intestinal motility altered
 - antimicrobial drugs, 13.220
 - macrolides, 18.269
 - intussusception, rotavirus vaccine, 23.354, 34.504
 - large bowel perforation and hemorrhage, NSAIDs, 10.76
 - unspecified reactions
 - NSAIDs, 6.91, 32.225
 - piroxicam, 12.91
 - selective serotonin reuptake inhibitors (SSRIs), 32.33
 - Surgam[®] (pyrimethamine + sulfadoxine) 12.89
- Liver**
 - hepatitis, calcium channel blockers, 6.193
 - Reye's syndrome
 - acetylsalicylic acid, 11.79, 15.85
 - salicylates, 7.94, 8.93, 11.79, 15.85
 - alcohol/vitamin A/beta-carotene, 24.442
 - unspecified reactions
 - antituberculosis drugs, 25.363, 26.339, 31.495, 32.555, 34.479
 - diclofenac, 20.91
 - isoniazid, 4.211
 - kava kava, 27.518
 - ketoconazole, 7.289, 8.265, 12.229
 - paracetamol, 12.76, 17.98, 18.94
 - parenteral nutrition, 5.318
 - ximelagatran, 30.411
- Biliary tract**
 - cholestasis
 - fish oils, 13.460
 - parenteral nutrition, 8.315, 22.376, 34.534
 - soybean oil, 34.534
- Pancreas**
 - pancreatic cancer, caffeine, theophylline, 7.8
- Urinary tract**
 - cystitis, tiaprofenic acid, 18.106
 - hemolytic-uremic syndrome, mitomycin, 10.397
 - microhematuria, gold salts, 7.252
 - nephritis, acute interstitial, penicillins, 6.241
 - nephrolithiasis, ceftriaxone, 29.246
 - renal cell carcinoma, diuretics, 23.225
 - renal insufficiency, diuretics, , 25.250
 - renal insufficiency, acute, NSAIDs, 28.122
 - urinary tract tumors, analgesics, 6.80
 - unspecified reactions
 - aminoglycosides, 15.268, 17.305
 - amphotericin, 5.275, 10.248, 13.231, 14.229, 27.276
 - analgesics, 21.98
 - anesthetics, halogenated, 20.106
 - aprotinin, 33.724
 - beta-adrenoceptor antagonists, 4.132
 - ciclosporin, 19.348
 - cimetidine, 5.163
 - contrast media, 27.500, 28.556, 29.575, 31.731, 31.735, 32.846, 34.751
 - gadolinium salts, 28.561
 - ketamine, 33.268
 - lithium, 4.22, 14.18, 19.16
 - NSAIDs, 5.88, 11.82, 18.100, 20.89, 24.120, 26.111
 - suprofen, 12.88
- Skin**
 - cancers, PUVA, 4.104, 6.145
 - contact allergy, 23.160
 - contact allergy, glucocorticoids, 15.139
 - contact dermatitis, aminoglycosides, 13.225
 - contact urticaria, 7.159
 - elastolysis, penicillins, 9.231
 - mutagenicity, PUVA, 4.104
 - necrosis
 - heparin, 5.326
 - oral anticoagulants, 29.358

- perioral dermatitis, glucocorticoids, 5.151
- photosensitivity, voriconazole, 34.431
- pigmentary changes,
 - minocycline, 6.244
 - PUVA, 9.130
- rashes, lamotrigine, 20.62, 24.88
- systemic fibrosis, contrast media, 32.852
- unspecified reactions
 - carbamazepine, 32.129
 - glucocorticoids, inhaled, 29.169
 - NSAIDs, 13.72
 - vitamin K₁, 25.461
- Nails**
 - yellow nail syndrome, penicillamine, 9.223
- Serosae**
 - peritoneum, peritoneal dialysis, 22.381
 - pleurodesis, 25.189
 - retroperitoneal fibrosis, 9.175
- Musculoskeletal**
 - arthralgia
 - beta-adrenoceptor antagonists, 11.164
 - rubella vaccination, 11.295
 - bone altered, parenteral nutrition, 22.378
 - bone dysplasia, deferoxamine, 23.241
 - bone loss, antiepileptic drugs, 27.74
 - bone mineral density reduced, glucocorticoids, 25.195
 - cartilage damaged, anesthetics, local, 33.281
 - creatine kinase raised, isotretinoin, 10.124
 - eosinophilia–myalgia syndrome, tryptophan, 15.514
 - fractures
 - glucocorticoids, inhaled, 31.307, 32.312
 - thiazolidinediones, 32.779
 - growth in children impaired
 - glucocorticoids, inhaled, 26.186
 - glucocorticoids, oral, 14.335
 - stimulants, 31.4
 - muscle damage, daptomycin, 30.309
 - myalgia, postoperative, suxamethonium, 28.155
 - myopathy, ipecacuanha, 11.422
 - ossification, etretinate, 12.127
 - osteoarthritis, NSAIDs, 1187
 - osteoporosis and osteonecrosis,
 - glucocorticoids, 16.447, 19.377, 20.374, 21.417, 22.182, 28.473
 - rhabdomyolysis
 - doxylamine overdose, 31.298
 - propofol, 26.135
 - rheumatism, ferrous salts, 7.254
 - unspecified reactions
 - bisphosphonates, 34.787
 - glucocorticoids, 33.355
- Sexual function**
 - priapism, fat emulsions, 11.313
 - sexual dysfunction, antipsychotic drugs, 8.57
- unspecified reactions
 - beta-adrenoceptor antagonists, 15.188
- Breasts**
 - gigantism of the female breast, 5.248
- Immunologic**
 - allergic reactions
 - aminophylline, 7.5
 - antimicrobial drugs, 23.251
 - insulins human, 8.379
 - latex, 31.761
 - rocuronium, 26.150
 - titanium, 33.456
 - anaphylactic reactions
 - beta-adrenoceptor antagonists, 7.216
 - albumin, human, 14.296
 - neuromuscular blocking agents, 29.145
 - autoimmune disease
 - immunizations, 27.336
 - Lyme disease vaccine, 24.366
 - allergy testing, chymopapain, 11.279
 - contact allergy, 23.160
 - cosmetics, allergic reactions, 11.142
 - Kathon[®] CG (methylchloroisothiazolinone + methylisothiazolinone), allergic reactions, 11.134
 - contact urticaria, 7.159
 - desensitization, penicillin, 23.252
 - hypersensitivity reactions
 - allopurinol, 10.89
 - anesthetics, local, 6.123
 - beta-lactam antibiotics, 14.211, 30.280
 - ethylene oxide, 11.219
 - mebendazole, 12.263
 - muscle relaxants, 27.138
 - nickel, 34.358
 - rocuronium, 31.249
 - sulfonamide derivatives, 30.252
 - immediate-type allergic reactions, 7.271
 - immune reactions and histamine release, 8.132
 - immune reconstitution disease, 29.315
 - immune sensitization, benzoyl peroxide, 8.151
 - immunological mechanisms of adverse reactions, beta-blockade, 8.188
 - immunostimulation, levamisole, 4.220
 - Kawasaki disease, rotavirus vaccine, 31.522
 - Mazzotti reaction, antihelminthic drugs, 31.507
 - sensitivity, aspirin, 12.75
 - unspecified reactions
 - cocamidopropylbetaine, 19.151
 - contrast agents, 20.422
 - cosmetics, 16.150, 19.151
 - co-trimoxazole, 20.264
 - Euxyl K 400, 16.150
 - fragrances, 20.149
 - glucocorticoids, 21.158

methyl dibromoglutaronitrile, 16.150, 19.151
ocular drugs, 21.486
propolis, 17.181

Autacoids

angioedema
angiotensin converting enzyme (ACE)
inhibitors, 22.225, 29.207, 31.352, 32. 380,
34.322
angiotensin II receptor antagonists, 30.238
red man syndrome, 17.312

Infection risk**AIDS**

blood products, 8.309
polio vaccine, 23.352
transfusions, 12.298
necrotizing fasciitis, NSAIDs, 28.121
toxic shock syndrome, vaginal tampons, 6.427
yersiniosis, deferroxamine, 11.215
unspecified reactions
blood donation, 34.521
intravenous therapy, 8.320
parenteral nutrition, 22.379
transfusions, 33.669
tumor necrosis factor antagonists, 29.395,
31.594

Body temperature

thermoregulation, antipsychotic drugs, 5.46
malignant hyperthermia, 18.112

Trauma

acupuncture, 29.590

Death

antiepileptic drugs, 23.83
antipsychotic drugs, 7.63, 32.89
calcium channel blockers, 22.214
digoxin, 32.333
ecstasy, 24.32
lithium, 19.14
opiates, 25.37, 29.44

Drug abuse

anabolic steroids, 29.508, 32.751, 33.869

Drug tolerance

opiods in neonates, 23.97

Drug resistance

drug resistance, antimicrobial drugs, 11.223,
12.208, 19.237, 20.228, 21.257, 22.265,
23.250, 24.273, 25.279, 29.244, 31.413,
32.445, 33.479
multidrug resistance, antituberculosis drugs,
33.623
staphylococcal resistance, aminoglycosides, 7.282

Drug dependence

benzodiazepines, 6.37, 12.41
opiates, 6.73

Drug withdrawal

baclofen, 26.152
calcium channel blockers, 8.191
glucocorticoids, 8.351

Genotoxicity

antiestrogens, 27.429

Mutagenicity

dithranol, 8.161
metronidazole, 4.206

Tumorigenicity

cutaneous malignancies, tar, ultraviolet
radiation, 6.149
endometrial cancer, hormonal replacement
therapy, 4.275
gastric cancer, cimetidine, 6.162
leukemia, penicillamine, 7.259
malignant melanoma, levodopa, 4.97
malignant melanoma, PUVA, 22.166
pancreatic cancer, caffeine, theophylline, 7.8
thyroid malignancies, ¹³¹I, 5.383
unspecified reactions
alcohol/vitamin A/beta-carotene, 24.442
aluminium, 31.383
angiotensin II receptor antagonists,
34.325
antiestrogens, 27.429
beta-carotene, 25.454
carotenoids, 25.454
diazepam, 6.39
dithranol, 8.161
fertility drugs, 24.474, 26.434
growth hormone, 23.468, 34.705
hormone replacement therapy, 32.740,
33.856
insulin, 33.890
levodopa, 31.267
metronidazole, 4.206
omeprazole, 16.423
oral contraceptives, 11.346, 15.426
proton pump inhibitors, 23.383
sex hormones, 22.465
vitamin K, 23.424
voriconazole, 34.431

Fertility

fertility, male, antimicrobial drugs, 16.262

Pregnancy

affective disorders in, 21.17
antibiotics, 11.231, 32.446
anticoagulants, 5.323
antidepressants, 32.31, 33.27
antiepileptic drugs, 4.42
antihypertensive drugs, 6.206
antimicrobial drugs, 24.274
antithyroid drugs, 4.294, 13.377
asthma, 28.186
Bendectin® (Debendox®; dicyclomine
+ doxylamine + pyridoxine), 6.316
beta₂-adrenoceptor agonists, 4.92, 6.139
beta-adrenoceptor antagonists, 5.194
beta-lactam antibiotics, 25.280
cocaine, 27.1

opiods, 5.67, 24.102
 placental transfer, local anesthetics,
 8.127
 tetracyclines, 25.280
 vitamin A, 21.405

Teratogenicity

antibiotics, 11.231
 antipsychotic drugs, 10.50
 dextropropoxyphene, 8.78
 diethylstilbestrol, 6.351
 retinoids, 10.122
 tretinoin, topical, 18.164

Fetotoxicity

cocaine, 20.24, 27.1, 29.41, 30.35
 diethylstilbestrol, transgenerational reactions,
 31.657
 indometacin, 18.102

Lactation

beta-adrenoceptor antagonists, 5.194
 cocaine, 31.154

Susceptibility factors

age, methylphenidate, 31.6
 age, theophylline intoxication, 6.2
 children, aluminium, 10.202, 12.185
 children, antituberculosis drugs, 32.557
 children, budesonide, 30.194
 children, inhaled glucocorticoids 27.174
 children, NSAIDs, 19.96
 elderly patients, antipsychotic drugs, 30.59
 genetic susceptibility, antituberculosis drugs,
 28.342
 genetic susceptibility, beta-adrenoceptor
 agonists, 29.173, 30.199, 31.310
 genetic susceptibility, isoniazid, 12.257
 genetic susceptibility, thiopurine toxicity,
 31.634
 HIV infection, immunization, 12.269
 intensive care, muscle relaxants, 19.140
 malignant hyperthermia, 6.113
 neonatal complications, indometacin, 18.102
 old age, vitamins, 22.431
 preterm infants, beta-lactam antibiotics,
 21.258
 renal failure, aluminium, 10.202
 transplant recipients, antituberculosis drugs,
 32.559
 unspecified reactions
 ocular drugs, 22.507
 theophylline, 5.1

Drug formulations

depot injections, glucocorticoids, 5.351
 enantiomers and racemates, 13.442
 oral contraceptives, 24.472
 penicillins, 9.232

Drug adulteration/contamination

of antiseptics and disinfectants, 9.228
 with clenbuterol, 33.53

Drug dosage regimens

aminoglycosides, 23.264
 errors, 28.587, 29.596
 labeling problems, cosmetics, 22.159
 levothyroxine, 9.341
 opiods, 30.106

Drug administration route

aerosols, delivery of, 27.172
 epidural and intrathecal opiates, 6.68
 infusion techniques, long-term, 5.388
 inhaled glucocorticoids, systemic availability,
 24.185
 inhaled insulin, 30.495
 injectable hormonal contraceptives, 7.390
 intraspinal narcotic analgesia, 7.134
 intrauterine levonorgestrel, 33.865
 intravitreal and parabalbar injection, 29.581

Drug overdose

antidepressants, 28.14
 digitalis, 5.172
 digitalis, charcoal, 24.201
 hexachlorophene, 7.268
 paracetamol, 23.117
 valproate, 32.157

Drug toxicity

digitalis, 5.172

Drug–drug interactions

acetylsalicylic acid *and* angiotensin converting
 enzyme (ACE) inhibitors, 28.124
 acetylsalicylic acid *and* NSAIDs, 28.118
 adrenaline *and* propranolol, 9.6
 alcohol *and* chlorpropamide, 7.407
 alcohol *and* vitamin A *and* beta-carotene,
 24.442
 anesthetics, local, 4.85
 angiotensin converting enzyme (ACE)
 inhibitors *and* acetylsalicylic acid, 28.124
 angiotensin converting enzyme (ACE)
 inhibitors *and* NSAIDs, 28.122
 antibiotics *and* neuromuscular blockers, 5.131
 antibiotics *and* oral contraceptives, 8.256
 antifungal azoles, 24.318, 28.299, 29.282,
 30.320, 31.459, 32.497, 33.545, 34.428
 antimicrobial drugs *and* oral contraceptives,
 24.274
 antituberculosis drugs, 5.294
 beta-carotene *and* alcohol *and* vitamin A,
 24.442
 chlorpropamide *and* alcohol, 7.407
 deferoxamine *and* vitamin C, 8.239
 digitalis *and* quinidine, 6.173
 diuretics *and* NSAIDs, 12.80
 foods *and* monoamine oxidase inhibitors, 13.6
 grapefruit juice, 23.519
 herbal medicines *and* warfarin, 30.400
 HMG Co-A reductase inhibitors, 25.530,
 30.517

lithium, 16.13
 lithium, 7.26
 lithium *and* selective serotonin reuptake inhibitors, 18.30
 macrolides, 14.220
 macrolides, 9.239
 mibefradil, 23.210
 monoamine oxidase inhibitors *and* foods, 13.6
 neuromuscular blockers *and* antibiotics, 5.131
 NSAIDs *and* angiotensin converting enzyme (ACE) inhibitors, 28.122
 NSAIDs *and* acetylsalicylic acid, 28.118
 NSAIDs *and* diuretics, 12.80
 oral contraceptives *and* antibiotics, 8.256, 24.274
 paracetamol, 13.68
 propranolol *and* adrenaline, 9.6
 protease inhibitors, 33.628
 quinidine *and* digitalis, 6.173
 selective serotonin reuptake inhibitors, 22.13

selective serotonin reuptake inhibitors *and* lithium, 18.30
 sex hormones, 9.332
 thyroxine, 24.484
 vitamin A *and* beta-carotene *and* alcohol, 24.442
 vitamin C *and* deferoxamine, 8.239
 vitamin C *and* deferoxamine, 8.239
 warfarin *and* herbal medicines, 30.400
Management of adverse drug reactions
 anesthetics, local, with lipid emulsion, 32.261
Methods
 ethnopharmacology, 14.429
 eukaryotic cells, effects of beta-lactams, 13.212
 hemolytic disease of the newborn, prophylaxis, 13.297
 lithium, monitoring, 11.24
 local anesthetic toxicity, lipid rescue, 31.231
 onchocerciasis, treatment, 14.261
 post-marketing surveillance, 14.210, 15.266, 24.274

Table of Essays, Annuals 1–34

SEDA	Author	Country	Title
1	M.N.G. Dukes	The Netherlands	The moments of truth
2	K.H. Kimbel	Germany	Drug monitoring: why care?
3	L. Lasagna	USA	Wanted and unwanted drug effects: the need for perspective
4	M.N.G. Dukes	The Netherlands	The van der Kroef syndrome
5	J.P. Griffin, P.F. D'Arcy	UK	Adverse reactions to drugs—the information lag
6	I. Bayer	Hungary	Science vs practice and/or practice vs science
7	E. Napke	Canada	Adverse reactions: some pitfalls and postulates
8	M.N.G. Dukes	Denmark	The seven pillars of foolishness
9	W.H.W. Inman	UK	Let's get our act together
10	S. Van Hauen	Denmark	Integrated medicine, safer medicine and “AIDS”
11	M.N.G. Dukes	Denmark	Hark, hark, the fictitious dogs do bark
12	M.C. Cone	Switzerland	Both sides of the fence
13	C. Medawar	UK	On our side of the fence
14	M.N.G. Dukes, E. Helsing	Denmark	The great cholesterol carousel
15	P. Tyrer	UK	The nocebo effect—poorly known but getting stronger
16	M.N.G. Dukes	Denmark	Good enough for Iganga?
17	M.N.G. Dukes	Denmark	The mists of tomorrow
18	R.D. Mann	UK	Databases, privacy, and confidentiality—the effect of proposed legislation on pharmacoepidemiology and drug safety monitoring
19	A. Herxheimer	UK	Side effects: freedom of information and the communication of doubt
20	E. Ernst	UK	Complementary/alternative medicine: what should we do about it?
21	H. Jick	USA	Thirty years of the Boston Collaborative Drug Surveillance Program in relation to principles and methods of drug safety research
22	J.K. Aronson, R.E. Ferner	UK	Errors in prescribing, preparing, and giving medicines: definition, classification, and prevention
23	K.Y. Hartigan- Go, J.Q. Wong	Philippines	Inclusion of therapeutic failures as adverse drug reactions
24	I. Palmlund	UK	Secrecy hiding harm: case histories from the past that inform the future
25	L. Marks	UK	The pill: untangling the adverse effects of a drug
26	D.J. Finney	UK	From thalidomide to pharmacovigilance: a personal account
26	L.L. Iversen	UK	How safe is cannabis?
27	J.K. Aronson	UK	Louis Lewin—Meyler's predecessor
27	H. Jick	USA	The General Practice Research Database
28	J.K. Aronson	UK	Classifying adverse drug reactions in the 21st century
29	M. Hauben, A. Bate	USA/Sweden	Data mining in drug safety
30	J.K. Aronson	UK	Drug withdrawals because of adverse effects
31	J. Harrison, P. Mozzicato	USA	MedDRA [®] : the Tale of a Terminology
32	K. Chan	Australia	Regulating complementary and alternative medicines
33	Graham Dukes	Norway	Third-generation oral contraceptives: time to look again?
34	Yoon K. Loke	UK	An agenda for research into adverse drug reactions

Mechanistic and clinical descriptions of adverse drug reactions

Adverse drug reactions are described in SEDA using two complementary systems, EIDOS and DoTS (1–3). These two systems are illustrated in [Figures 1 and 2](#) and general templates for describing reactions in this way are shown in [Figures 3–5](#). Examples of their use have been discussed elsewhere (4–8).

1. EIDOS

The EIDOS mechanistic description of adverse drug reactions (3) has five elements:

- the **Extrinsic** species that initiates the reaction ([Table 1](#));
- the **Intrinsic** species that it affects;
- the **Distribution** of these species in the body;
- the (physiological or pathological) **Outcome** ([Table 2](#)), which is the adverse effect;
- the **Sequela**, which is the adverse reaction.

Extrinsic species This can be the parent compound, an excipient, a contaminant or adulterant, a degradation product, or a derivative of any of these (e.g. a metabolite) (for examples see [Table 1](#)).

Intrinsic species This is usually the endogenous molecule with which the extrinsic species interacts; this can be a nucleic acid, an enzyme, a receptor, an ion channel or transporter, or some other protein.

Distribution A drug will not produce an adverse effect if it is not distributed to the same site as the target species that mediates the adverse effect. Thus, the pharmacokinetics of the extrinsic species can affect the occurrence of adverse reactions.

Outcome Interactions between extrinsic and intrinsic species in the production of an adverse effect can result in physiological or pathological changes (for examples see [Table 2](#)). Physiological changes can involve either increased actions (e.g. clotting due to tranexamic acid) or decreased actions (e.g. bradycardia due to beta-adrenoceptor antagonists). Pathological changes can involve cellular adaptations (atrophy, hypertrophy, hyperplasia, metaplasia, and neoplasia), altered cell function (e.g. mast cell degranulation in IgE-mediated anaphylactic reactions), or cell damage (e.g. cell lysis, necrosis, or apoptosis).

Sequela The sequela of the changes induced by a drug describes the clinically recognizable adverse drug reaction, of which there may be more than one. Sequelae can be classified using the DoTS system.

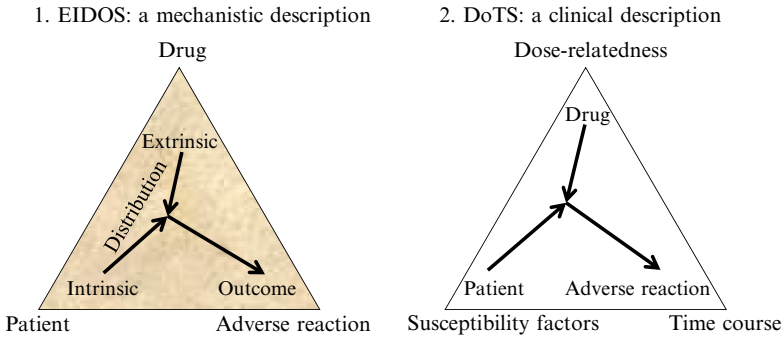


Figure 1 Describing adverse drug reactions—two complementary systems. Note that the triad of drug–patient–adverse reaction appears outside the triangle in EIDOS and inside the triangle in DoTS, leading to Figure 2.

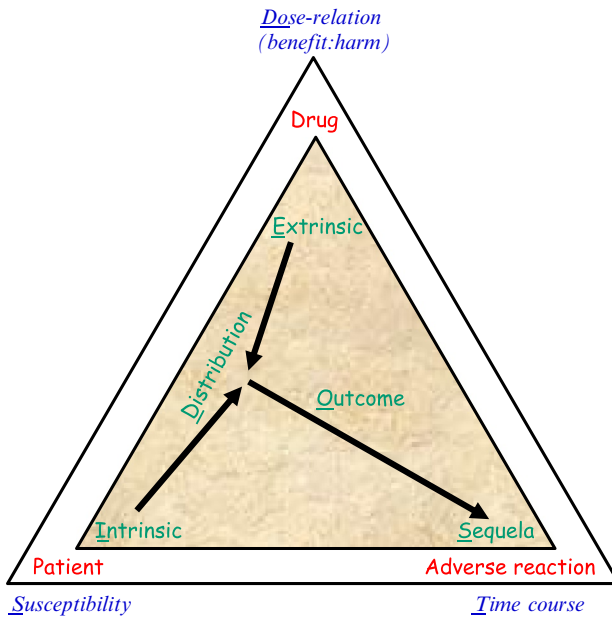


Figure 2 How the EIDOS and DoTS systems relate to each other. Here the two triangles in Figure 1 are superimposed, to show the relation between the two systems. An adverse reaction occurs when a drug is given to a patient (Gothic letters). Adverse reactions can be classified mechanistically (EIDOS; sans-serif letters) by noting that when the Extrinsic (drug) species and an Intrinsic (patient) species, are co-Distributed, a pharmacological or other effect (the Outcome) results in the adverse reaction (the Sequela). The adverse reaction can be further classified (DoTS; serif italics) by considering its three main features—its Dose-relatedness, its Time-course, and individual Susceptibility.

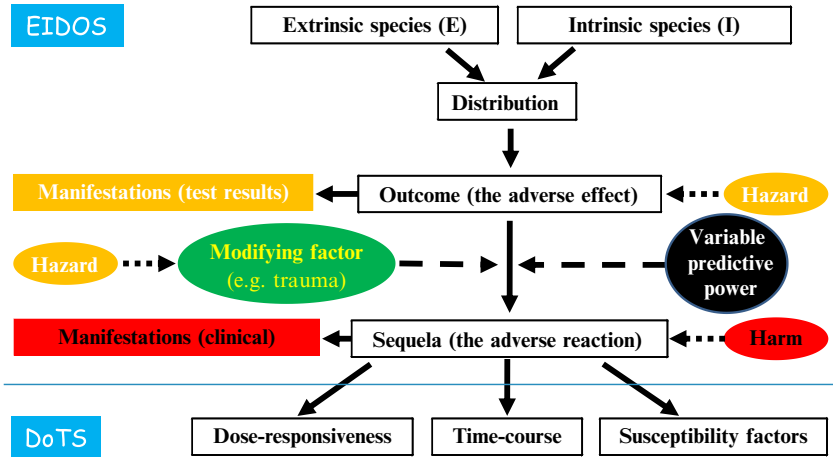


Figure 3 A general form of the EIDOS and DoTS template for describing an adverse effect or an adverse reaction.

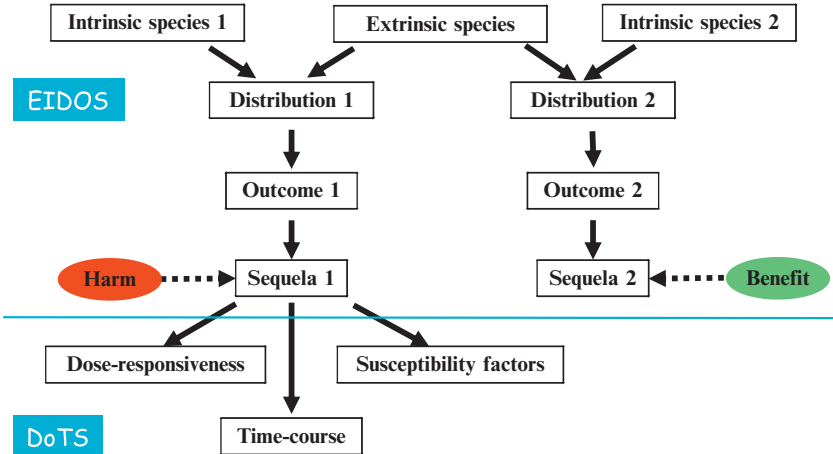


Figure 4 A general form of the EIDOS and DoTS template for describing two mechanisms of an adverse reaction or (illustrated here) the balance of benefit to harm, each mediated by a different mechanism.

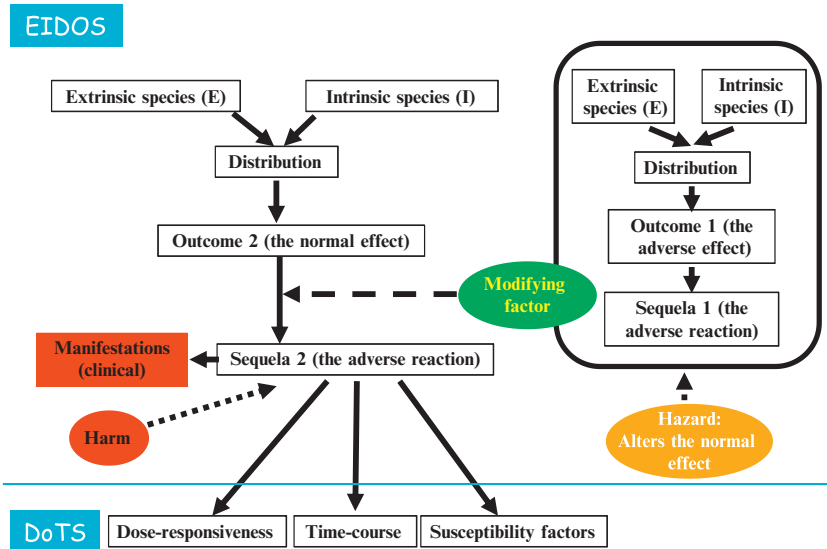


Figure 5 A general form of the EIDOS and DoTS template for describing an adverse drug interaction.

Table 1 The EIDOS mechanistic description of adverse drug effects and reactions

Feature	Varieties	Examples
E. Extrinsic species	<ol style="list-style-type: none"> 1. The parent compound 2. An excipient 3. A contaminant 4. An adulterant 5. A degradation product formed before the drug enters the body 6. A derivative of any of these (e.g. a metabolite) 	Insulin Polyoxyl 35 castor oil 1,1-ethylidenebis [L-tryptophan] Lead in herbal medicines Outdated tetracycline Acrolein (from cyclophosphamide)
I. The intrinsic species and the nature of its interaction with the extrinsic species: (a) molecular	<ol style="list-style-type: none"> 1. Nucleic acids <ul style="list-style-type: none"> o DNA o RNA 2. Enzymes <ul style="list-style-type: none"> o reversible effect o irreversible effect 3. Receptors <ul style="list-style-type: none"> o reversible effect o irreversible effect 4. Ion channels/transporters 	Melphalan Mitoxantrone Edrophonium Malathion Prazosin Phenoxybenzamine Calcium channel blockers; digoxin and Na ⁺ -K ⁺ -ATPase

Table 1 *The EIDOS mechanistic description of adverse drug effects and reactions—cont'd*

Feature	Varieties	Examples
	5. Other proteins <ul style="list-style-type: none"> ○ immunological proteins ○ tissue proteins 	Penicilloyl residue hapten N-acetyl-p-benzoquinone- imine (paracetamol [acetaminophen])
(b) extracellular	1. Water 2. Hydrogen ions (pH) 3. Other ions	Dextrose 5% Sodium bicarbonate Sodium ticarcillin
(c) physical or physicochemical	1. Direct tissue damage 2. Altered physicochemical nature of the extrinsic species	Intrathecal vincristine Sulindac precipitation
D. Distribution	Where in the body the extrinsic and intrinsic species occur (affected by pharmacokinetics)	Antihistamines cause drowsiness only if they affect histamine H ₁ receptors in the brain
O. Outcome (physiological or pathological change)	The adverse effect (see Table 2)	–
S. Sequela	The adverse reaction (use the Dose, Time, Susceptibility [DoTS] descriptive system)	–

Table 2 *Examples of physiological and pathological changes in adverse drug effects
(some categories can be broken down further)*

Type of change	Examples
1. Physiological changes	
(a) Increased actions	Hypertension (monoamine oxidase inhibitors); clotting (tranexamic acid)
(b) Decreased actions	Bradycardia (beta-adrenoceptor antagonists); QT interval prolongation (antiarrhythmic drugs)
2. Cellular adaptations	
(a) Atrophy	Lipoatrophy (subcutaneous insulin); glucocorticosteroid-induced myopathy
(b) Hypertrophy	Gynecomastia (spironolactone)
(c) Hyperplasia	Pulmonary fibrosis (busulfan); retroperitoneal fibrosis (methysergide)
(d) Metaplasia	Lacrimal canalicular squamous metaplasia (fluorouracil)
(e) Neoplasia	
○ benign	Hepatoma (anabolic steroids)
○ malignant	
■ hormonal	Vaginal adenocarcinoma (diethylstilbestrol)
■ genotoxic	Transitional cell carcinoma of bladder (cyclophosphamide)
■ immune suppression	Lymphoproliferative tumors (ciclosporin)
3. Altered cell function	IgE-mediated mast cell degranulation (class I immunological reactions)
4. Cell damage	
(a) Acute reversible damage	
○ chemical damage	Periodontitis (local application of methylenedioxymetamphetamine [MDMA, 'ecstasy'])
○ immunological reactions	Class III immunological reactions

Continued

Table 2 *Examples of physiological and pathological changes in adverse drug effects (some categories can be broken down further)—cont'd*

Type of change	Examples
(b) Irreversible injury	
○ cell lysis	Class II immunological reactions
○ necrosis	Class IV immunological reactions; hepatotoxicity (paracetamol, after apoptosis)
○ apoptosis	Liver damage (troglitazone)
5. Intracellular accumulations	
(a) Calcification	Milk-alkali syndrome
(b) Drug deposition	Crystal-storing histiocytosis (clofazimine) Skin pigmentation (amiodarone)

2. DOTS

In the DoTS system (SEDA-28, xxvii-xxxiii; 1,2) adverse drug reactions are described according to the **Dose** at which they usually occur, the **Time-course** over which they occur, and the **Susceptibility factors** that make them more likely, as follows:

- **Relation to dose**
 - Toxic reactions (reactions that occur at suprathreshold doses)
 - Collateral reactions (reactions that occur at standard therapeutic doses)
 - Hypersusceptibility reactions (reactions that occur at subtherapeutic doses in susceptible individuals)
- **Time course**
 - Time-independent reactions (reactions that occur at any time during a course of therapy)
 - Time-dependent reactions
 - Immediate or rapid reactions (reactions that occur only when drug administration is too rapid)
 - First-dose reactions (reactions that occur after the first dose of a course of treatment and not necessarily thereafter)
 - Early tolerant and early persistent reactions (reactions that occur early in treatment then either abate with continuing treatment, owing to tolerance, or persist)
 - Intermediate reactions (reactions that occur after some delay but with less risk during longer term therapy, owing to the “healthy survivor” effect)
 - Late reactions (reactions the risk of which increases with continued or repeated exposure)
 - Withdrawal reactions (reactions that occur when, after prolonged treatment, a drug is withdrawn or its effective dose is reduced)
 - Delayed reactions (reactions that occur at some time after exposure, even if the drug is withdrawn before the reaction appears)
- **Susceptibility factors**
 - Genetic
 - Age
 - Sex
 - Physiological variation (e.g. weight, pregnancy)
 - Exogenous factors (for example the effects of other drugs, devices, surgical procedures, food, smoking)
 - Diseases

The following reactions are described in figures in SEDA-34 and SEDA-35 using the EIDOS and DoTS systems. These descriptions supersede those in previous volumes.

Adrenaline: cardiac ischemia (Chapter 13)	35.257
Aldosterone receptor antagonists: hyperkalemia (Chapter 21)	35.392
Anesthetics, local: methemoglobinemia (Chapter 11)	35.237
Angiotensin converting enzyme inhibitors: angioedema (Chapter 20)	35.365
Angiotensin II receptor antagonists: angioedema (Chapter 20)	35.369
Antipsychotic drugs: hyperprolactinemia (Chapter 6)	35.92
Antipsychotic drugs: thromboembolism (Chapter 6)	35.91
Antipsychotic drugs: metabolic adverse effects (Chapter 6)	35.94
Bisphosphonates: osteonecrosis of the jaw (Chapter 49)	35.901
Catecholamines: takotsubo cardiomyopathy (Chapter 13)	35.256
Clozapine: myocarditis and pericarditis (Chapter 6)	35.103
Clozapine: neutropenia (Chapter 6)	35.105
Cocaine: ischemic cardiac events (Chapter 4)	35.66
Contrast media: nephrotoxicity (Chapter 46)	35.865
Dapsone: hemolytic anemia and methemoglobinemia (Chapter 30)	35.556
Diuretics, loop, thiazide, and thiazide-like: electrolyte disturbances (Chapter 21)	35.389
Dopamine receptor agonists: compulsive behaviors (Chapter 13)	35.262
Dopamine receptor agonists: fibrosis (Chapter 13)	35.261
Dopamine receptor agonists: sleep attacks (Chapter 13)	35.264
Ephedrine: cardiac ischemia (Chapter 13)	35.257
Ethambutol: optic neuropathy (Chapter 30)	35.557
Gadolinium salts: systemic fibrosis (Chapter 46)	35.868
Glucocorticoids: osteoporosis (Chapter 39)	35.724
Glucocorticoids: pneumonia (Chapter 16)	35.314
Heparin: type II thrombocytopenia (Chapter 35)	35.619
HMG co-enzyme A reductase inhibitors (statins): muscle damage (Chapter 44)	35.813
Incretin mimetics: nausea and vomiting (Chapter 42)	35.770
Iodides: sialadenitis (Chapter 46)	34.751
Methadone: torsade de pointes (Chapter 8)	35.179
Nitrofurantoin: lung damage (Chapter 26)	35.472
Noradrenaline: cardiac ischemia (Chapter 13)	35.257
Propofol infusion syndrome (Chapter 10)	35.226
Thiazolidinediones: reduced bone density and increased risk of fractures (Chapter 42)	34.697
Thionamides: neutropenia and agranulocytosis (Chapter 41)	35.754
Vigabatrin: visual impairment (Chapter 7)	35.155
Voriconazole: periostitis (Chapter 27)	35.488
Voriconazole: photosensitivity (Chapter 27)	35.487

The following reactions have also been described in previous editions of SEDA using the DoTS system:

Adrenaline: hypertension	30.170
Anticoagulants, oral: skin necrosis	29.358
Antituberculosis drugs: hepatotoxicity	31.495
Pseudoephedrine: toxic epidermal necrolysis	30.172
SSRIs: suicidal behavior	29.19
HMG co-enzyme A reductase inhibitors (statins): acute pancreatitis	31.715
Ximelagatran: liver damage	30.411

References

- [1] Aronson JK, Ferner RE. Joining the DoTS. New approach to classifying adverse drug reactions *BMJ* 2003; 327: 1222–5.
- [2] Aronson JK, Ferner RE. Clarification of terminology in drug safety. *Drug Saf* 2005; 28(10): 851–70.
- [3] Ferner RE, Aronson JK. EIDOS: A mechanistic classification of adverse drug effects. *Drug Saf* 2010; 33(1): 13–23.
- [4] Callréus T. Use of the dose, time, susceptibility (DoTS) classification scheme for adverse drug reactions in pharmacovigilance planning. *Drug Saf* 2006; 29(7): 557–66.
- [5] Aronson JK, Price D, Ferner RE. A strategy for regulatory action when new adverse effects of a licensed product emerge. *Drug Saf* 2009; 32(2): 91–8.
- [6] Calderón-Ospina C, Bustamante-Rojas C. The DoTS classification is a useful way to classify adverse drug reactions: a preliminary study in hospitalized patients. *Int J Pharm Pract* 2010; 18(4): 230–5.
- [7] Ferner RE, Aronson JK. Preventability of drug-related harms. Part 1: A systematic review. *Drug Saf* 2010; 33(11): 985–94.
- [8] Aronson JK, Ferner RE. Preventability of drug-related harms. Part 2: Proposed criteria, based on frameworks that classify adverse drug reactions. *Drug Saf* 2010; 33(11): 995–1002.

Definitive (between-the-eyes) adverse drug reactions

About 30% of the papers covered in the SEDA series are classified by our authors as anecdotal (reference numbers marked with the A tag). Although anecdotes have been regarded as being of little evidential value, and rank low in evidence hierarchies, in some cases they provide striking evidence of adverse drug reactions. For example, so-called designated medical events [1], when they occur, are so often caused by drugs that a drug-event association is highly likely to be real, indeed is almost pathognomonic. Such events include Stevens–Johnson syndrome, anaphylaxis, aplastic anemia, and the form of polymorphous ventricular tachycardia known as “torsade de pointes”.

An even more convincing category of anecdotal evidence consists of a small number of reports that are definitive on the basis of one or at most a few reports (so-called “between-the-eyes” reactions) [2,3]. There are four categories of such reactions, described at the foot of Table 3, which gives examples.

Table 3 *Examples of definitive anecdotal adverse drug reactions*

Event	Examples	Confirmatory tests/characteristics
<i>1a. Extracellular deposition of drug or metabolite</i>		
Baroliths	Barium [4]	X-ray, visual inspection; chemical analysis
Bezoars and gastrointestinal obstruction	Colestyramine [5], sucralfate, modified-release formulations, guar gum, ion exchange resins [6–8]; magnesium salts [9]; nifedipine [10,11]; psyllium [12]	Visual inspection; chemical analysis
Biliary lithiasis or pseudolithiasis	Atazanavir [13]; ceftriaxone [14]; sulindac [15,16]	Infrared spectroscopy
Nephrolithiasis, urinary crystals or debris	Aciclovir, amoxicillin, atazanavir [17], ciprofloxacin, ephedrine/guaifenesin, floctafenine [18], indinavir [19], magnesium trisilicate, methotrexate, primidone, sulfasalazine [20], sulfonamides, triamterene [21,22]; ceftriaxone [23,24]; felbamate [25]; ketamine [26]; Djenkol beans [27]	Microscopy, infrared spectroscopy, x-ray diffraction, mass spectroscopy
Respiratory damage	Minocycline [28]	Bronchial aspiration
<i>1b. Intracellular deposition of drug or metabolite</i>		
Calcinosis, subcutaneous	Calcium-containing heparins [29]	Histology
Conjunctival deposition	Tetracycline [30,31]	Wood’s lamp

Continued

Table 3 Examples of definitive anecdotal adverse drug reactions—cont'd

Event	Examples	Confirmatory tests/characteristics
Corneal deposition	Fluoroquinolones [32,33] Gold [34] Adrenochromes from adrenaline [35] or ibopamine [36,37]	Scanning electron microscopy, hplc, infrared spectrophotometry Confocal microscopy Histology
Eyelids, deposition	Gold [38]	Histology
Gut, crystal deposition	Sodium polystyrene sulfonate [39]	Microscopy
Histiocytes, crystal deposition	Aluminium-containing vaccines [40] Clofazimine [41]	Electron microprobe analysis Visual inspection, polarizing microscopy
Intraglomerular crystal deposition	Foscarnet [42]	Fourier transform infrared spectroscopy
Lipoid pneumonia	Mineral oil [43]	Gas chromatography/mass spectrometry
Lymphadenopathy	Gold [44]	Light microscopy, scanning EM
Nail deposition	Tetracycline [45] Clofazimine [46]	Wood's lamp Light microscopy
Pneumonitis	Sodium polystyrene sulfonate [47–49]	
Retina, crystal deposition	Methoxyflurane [50]; canthaxanthin [51]	hplc
Skin pigmentation	Amiodarone [52]	hplc, electron microscopy, energy dispersive x-ray microanalysis
2. Specific anatomical location or pattern of injury		
Esophageal ulcers	Bisphosphonates, potassium chloride, quinidine, tetracyclines [53]	Localization to areas of esophageal lesions
Extravasation reactions	Cancer chemotherapeutic agents [54]	Anatomical contiguity to drug administration
Fulminant encephalomyelitis	Inadvertent intrathecal ionic contrast medium [55]; inadvertent intrathecal vincristine [56]	Anatomical pattern of injury
Hemangiosarcoma	Thorotrast [57]	Anatomical localization in sites of drug accumulation or persistence
Inflammatory response in a tumor	Picibanil [58]	Direct observation of application site localization
Nicolau syndrome*	Bismuth [59]; cyanocobalamin [60]; penicillins [61–64], NSAIDs [65,66]; glatiramer acetate [67,68], glucocorticoids [69]; vitamin K ₁ [70,71]	
Nasopalatal damage	Topical cocaine [72]	Application site localization
Nodulosis	Apomorphine [73]	Anatomical contiguity to drug administration
Oral damage after topical application	Salicylates [74]; desloratadine [75]; ecstasy [76]; garlic [77]; metronidazole [78]	Application site localization
Small bowel obstruction	Gelatin hemostatic agent [79,80]	Application site localization

Table 3 Examples of definitive anecdotal adverse drug reactions—cont'd

Event	Examples	Confirmatory tests/characteristics
3. Physicochemical dysfunction or tissue damage		
Oligohidrosis	Topiramate [81] Zonisamide [82,83]	Iontophoresis Acetylcholine loading test, heat-loading test
Photosensitivity	Carbamazepine, dapsone, certain NSAIDs, triflusal [84]; fenofibrate [85]; flutamide [86]; terbinafine [87]; voriconazole [88]	Phototesting, photopatch testing
Taste disturbance	Certain NSAIDs [89]	Gustatometry, electrogustatometry
Dry mouth	Omeprazole [90]	Measurement of salivary flow
4. Infection-related		
Infection unrelated to product contamination	Bacille Calmette-Guerin [91–93]; <i>Escherichia coli</i> Nissle 1917 [94]; lactobacillus [95,96]; mumps vaccine [97]; varicella vaccine [98–100]	Polymerase chain reaction, DNA enzyme immunoassay electrophoresis, bacterial culture, strain typing, DNA fingerprinting; genomic sequencing
Infection due to product contamination	Intravenous gentamicin [101]; propofol [102]	Endotoxin assay, plasmid and restriction endonuclease analysis

*Attributable to the drug or an excipient or to the action of intramuscular injection

1. *Extracellular (1a) or intracellular (1b) tissue deposition of the drug or a metabolite* In such cases objective physicochemical testing shows that the pathological lesion is composed of the drug or a metabolite. The lesion has to be accessible for biopsy or some form of in situ examination, and the event must not have been possible in the absence of the drug.
2. *A specific anatomical location or pattern of injury* Here the location or pattern of damage is sufficiently specific to attribute the effect to the drug without the need for implicit judgment or formal investigation. The mechanism of injury can be related to either physicochemical or pharmacological properties of the drug.
3. *Physiological dysfunction or direct tissue damage that can be proved by physicochemical testing* This group includes adverse events that involve physiological dysfunction or tissue damage for which documentation by physicochemical testing is feasible.
4. *Infection as a result of administration of a potentially infective agent or because of demonstrable contamination* Adverse drug reactions related to infections can be due to contamination of the treatment or to a product that consists of live microbes. The infecting organism has to be proved to be the same as the organism contained in the product or contaminating the batch of product.

References

- [1] Hauben M, Madigan D, Gerrits CM, Walsh L, Van Puijenbroek EP. The role of data mining in pharmacovigilance. *Expert Opin Drug Saf* 2005; 4(5): 929–48.
- [2] Aronson JK, Hauben M. Anecdotes that provide definitive evidence. *BMJ* 2006; 332(7581): 1267–9.
- [3] Hauben M, Aronson JK. Gold standards in pharmacovigilance: the use of definitive anecdotal reports of adverse drug reactions as pure gold and high grade ore. *Drug Saf* 2007; 30(8): 645–55.
- [4] Champman AH, el-Hasani S. Colon ischaemia secondary to barolith obstruction. *Br J Radiol* 1998; 71(849): 983–4.
- [5] Cohen MI, Winslow PR, Boley SJ. Intestinal obstruction associated with cholestyramine therapy. *N Engl J Med* 1969; 280(23): 1285–6.

- [6] Taylor JR, Streetman DS, Castle SS. Medication bezoars: a literature review and report of a case. *Ann Pharmacother* 1998; 32(9): 940–6.
- [7] Guy C, Ollagnier M. Sucralfate et bezoard: bilan de l'enquête officielle de pharmacovigilance et revue de la littérature. [Sucralfate and bezoars: data from the system of pharmacologic vigilance and review of the literature.] *Thérapie* 1999; 54(1): 55-8.
- [8] Koneru P, Kaufman RA, Talati AJ, Jenkins MB, Korones SB. Successful treatment of sodium polystyrene sulfonate bezoars with serial water-soluble contrast enemas. *J Perinatol* 2003; 23(5): 431–3.
- [9] Shigekawa Y, Kobayashi Y, Higashiguchi T, Nasu T, Yamamoto M, Ochiai M, Tsuji T, Yamaue H. Rectal obstruction by a giant pharmacobezoar composed of magnesium oxide: report of a case. *Surg Today* 2010; 40: 972–4.
- [10] Niezabitowski LM, Nguyen BN, Gums JG. Extended-release nifedipine bezoar identified one year after discontinuation. *Ann Pharmacother* 2000; 34(7–8): 862–4.
- [11] Yeen WC, Willis IH. Retention of extended release nifedipine capsules in a patient with enteric stricture causing recurrent small bowel obstruction. *South Med J* 2005; 98(8): 839–42.
- [12] Shulman LM, Minagar A, Weiner WJ. Perdiem causing esophageal obstruction in Parkinson's disease. *Neurology* 1999; 52(3): 670–1.
- [13] Jacques AC, Giguère P, Zhang G, Touchie C, la Porte CJ. Atazanavir-associated choledocholithiasis leading to acute hepatitis in an HIV-infected adult. *Ann Pharmacother* 2010; 44(1): 202–6.
- [14] Bickford CL, Spencer AP. Biliary sludge and hyperbilirubinemia associated with ceftriaxone in an adult: case report and review of the literature. *Pharmacotherapy* 2005; 25(10): 1389–95.
- [15] Tokumine F, Sunagawa T, Shiohira Y, Nakamoto T, Miyazato F, Muto Y. Drug-associated cholelithiasis: a case of sulindac stone formation and the incorporation of sulindac metabolites into the gallstones. *Am J Gastroenterol* 1999; 94(8): 2285–8.
- [16] Eda A, Yanaka I, Tamada K, Wada S, Tomiyama T, Sugano K. Sulindac-associated choledocholithiasis. *Am J Gastroenterol* 2001; 96(7): 2283–5.
- [17] Viglietti D, Verine J, De Castro N, Scemla A, Daudon M, Glotz D, Pillebout E. Chronic interstitial nephritis in an HIV type-1-infected patient receiving ritonavir-boosted atazanavir. *Antivir Ther* 2011; 16(1): 119–21.
- [18] Moesch C, Rince M, Raby C, Leroux-Robert C. Identification d'un metabolite de la floctafénine dans un calcul urinaire. [Identification of metabolite of floctafenine in urinary calculi.] *Ann Biol Clin (Paris)* 1987; 45(5): 546–50.
- [19] Huynh J, Hever A, Tom T, Sim JJ. Indinavir-induced nephrolithiasis three and one-half years after cessation of indinavir therapy. *Int Urol Nephrol* 2011; 43(2): 571–3.
- [20] DeMichele J, Rezaizadeh H, Goldstein JI. Sulfasalazine crystalluria-induced anuric renal failure. *Clin Gastroenterol Hepatol* 2012; 10: A32.
- [21] Daudon M, Jungers P. Drug-induced renal calculi: epidemiology, prevention, and management. *Drugs* 2004; 64(3): 245–75.
- [22] Hauben M, Reich L, Gerrits C. Comparative performance or proportional reporting ratios (PRR) and multi-item gamma-Poisson shrinker (MGPS) for the identification of crystalluria and urinary tract calculi caused by drugs. *Pharmacoepidemiol Drug Saf* 2005; S014: 7.
- [23] Tasic V, Sofijanova A, Avramoski V. Nephrolithiasis in a child with acute pyelonephritis. Ceftriaxone-induced nephrolithiasis and biliary pseudolithiasis. *Pediatr Nephrol* 2005; 20(10): 1510–1, 1512–3.
- [24] Gargollo PC, Barnewolt CE, Diamond DA. Pediatric ceftriaxone nephrolithiasis. *J Urol* 2005; 173(2): 577–8.
- [25] Parent X, Schieffer F. Cristallurie de felbamate. [Felbamate crystalluria.] *Ann Biol Clin (Paris)* 2010; 68(5): 609–13.
- [26] Chu PS, Ma WK, Wong SC, Chu RW, Cheng CH, Wong S, Tse JM, Lau FL, Yiu MK, Man CW. The destruction of the lower urinary tract by ketamine abuse: a new syndrome? *BJU Int* 2008; 102(11): 1616–22.

- [27] Areekul S, Muangman V, Bohkerd C, Saenghirun C. Djenkol bean as a cause of urolithiasis. *Southeast Asian J Trop Med Public Health* 1978; 9: 427–32.
- [28] Li C, Kuo S, Lee J. Life-threatening complications related to minocycline pleurodesis. *Ann Thorac Surg* 2011; 92: 1122–4.
- [29] Bonnacarrère L, Templier I, Carron PL, Maurizi J, Salameire D, Beani JC, Blaise S. Calcinosé cutanée et sous-cutanée après injection d'héparine calcique: à propos de deux cas. [Two cases of iatrogenic cutis and subcutis calcinosis after calcium-containing heparin injection.] *J Mal Vasc* 2009; 34(5): 366–71.
- [30] Messmer E, Font RL, Sheldon G, Murphy D. Pigmented conjunctival cysts following tetracycline/minocycline therapy. Histochemical and electron microscopic observations *Ophthalmology* 1983; 90(12): 1462–8.
- [31] Morrison VL, Kikkawa DO, Herndier BG. Tetracycline induced green conjunctival pigment deposits. *Br J Ophthalmol* 2005; 89(10): 1372–3.
- [32] Eiferman RA, Snyder JP, Nordquist RE. Ciprofloxacin microprecipitates and macroprecipitates in the human corneal epithelium. *J Cataract Refract Surg* 2001; 27(10): 1701–2.
- [33] Parent X, Marchal A, Patillon JC. Cristallisation cornéenne de fluoroquinolones en présence de magnésium. [Corneal precipitation of fluoroquinolones with magnesium.] *Ann Biol Clin (Paris)* 2005; 63(1): 89–92.
- [34] López JD, del Castillo JMB, López CD, Sánchez JG. Confocal microscopy in ocular chrysiasis. *Cornea* 2003; 22(6): 573–5.
- [35] Bhosai SJ, Lin CC, Greene J, Bloomer MM, Jeng BH. Rapid corneal adrenochrome deposition from topical ibopamine in the setting of infectious keratitis. *Eye (Lond)* 2013; 27(1): 105–6.
- [36] Kanoff JM, Colby K. Pigmented deposits on a Boston keratoprosthesis from topical ibopamine. *Cornea* 2010; 29(9): 1069–71.
- [37] Kaiser PK, Pineda R, Albert DM, Shore JW. 'Black cornea' after long-term epinephrine use. *Arch Ophthalmol* 1992; 110(9): 1273–5.
- [38] Lockington D, Chadha V, Russell H, Cauchi P, Tetley L, Roberts F, Kemp E. Histological evidence of tissue reaction to gold weights used for mechanical ptosis. *Arch Ophthalmol* 2010; 128(10): 1379–80.
- [39] Abraham SC, Bhagavan BS, Lee LA, Rashid A, Wu TT. Upper gastrointestinal tract injury in patients receiving Kayexalate (sodium polystyrene sulfonate) in sorbitol: clinical, endoscopic, and histopathologic findings. *Am J Surg Pathol* 2001; 25: 637–44.
- [40] Culora GA, Ramsay AD, Theaker JM. Aluminium and injection site reactions. *J Clin Pathol* 1996; 49(10): 844–7.
- [41] Sukpanichnant S, Hargrove NS, Kachintorn U, Manatsathit S, Chanchairujira T, Siritanaratkul N, Akaraviputh T, Thakerngpol K. Clofazimine-induced crystal-storing histiocytosis producing chronic abdominal pain in a leprosy patient. *Am J Surg Pathol* 2000; 24(1): 129–35.
- [42] Zanetta G, Maurice-Estépa L, Mousson C, Justrabo E, Daudon M, Rifle G, Tanter Y. Foscarinet-induced crystalline glomerulonephritis with nephrotic syndrome and acute renal failure after kidney transplantation. *Transplantation* 1999; 67(10): 1376–8.
- [43] Bandla HP, Davis SH, Hopkins NE. Lipoid pneumonia: a silent complication of mineral oil aspiration. *Pediatrics* 1999; 103(2): E19.
- [44] Rollins SD, Craig JP. Gold-associated lymphadenopathy in a patient with rheumatoid arthritis. Histologic and scanning electron microscopic features. *Arch Pathol Lab Med* 1991; 115(2): 175–7.
- [45] Hendricks AA. Yellow lunulae with fluorescence after tetracycline therapy. *Arch Dermatol* 1980; 116(4): 438–40.
- [46] Dixit VB, Chaudhary SD, Jain VK. Clofazimine induced nail changes. *Indian J Lepr* 1989; 61(4): 476–8.
- [47] Haupt HM, Hutchins GM. Sodium polystyrene sulfonate pneumonitis. *Arch Intern Med* 1982; 142(2): 379–81.

- [48] Fenton JJ, Johnson FB, Przygodzki RM, Kalasinsky VF, Al-Dayel F, Travis WD. Sodium polystyrene sulfonate (Kayexalate) aspiration: histologic appearance and infrared microspectrophotometric analysis of two cases. *Arch Pathol Lab Med* 1996; 120(10): 967–9.
- [49] Idowu MO, Mudge M, Ghatak NR. Kayexalate (sodium polystyrene sulfonate) aspiration. *Arch Pathol Lab Med* 2005; 129(1): 125.
- [50] Nadim F, Walid H, Adib J. The differential diagnosis of crystals in the retina. *Int Ophthalmol* 2001; 24(3): 113–21.
- [51] Goralczyk R, Barker FM, Buser S, Liechti H, Bausch J. Dose dependency of canthaxanthin crystals in monkey retina and spatial distribution of its metabolites. *Invest Ophthalmol Vis Sci* 2000; 41(6): 1513–22.
- [52] Adams PC, Holt DW, Storey GCA, Morley AR, Callaghan J, Campbell RW. Amiodarone and its desethyl metabolite: tissue distribution and morphologic changes during long-term therapy. *Circulation* 1985; 72(5): 1064–75.
- [53] O'Neill JL, Remington TL. Drug-induced esophageal injuries and dysphagia. *Ann Pharmacother* 2003; 37(11): 1675–84.
- [54] Adami NP, de Gutiérrez MG, da Fonseca SM, de Almeida EP. Risk management of extravasation of cytostatic drugs at the Adult Chemotherapy Outpatient Clinic of a university hospital. *J Clin Nurs* 2005; 14(7): 876–82.
- [55] van der Leede H, Jorens PG, Parizel P, Cras P. Inadvertent intrathecal use of ionic contrast agent. *Eur Radiol* 2002; 12(Suppl 3): S86–93.
- [56] Alcaraz A, Rey C, Concha A, Medina A. Intrathecal vincristine: fatal myeloencephalopathy despite cerebrospinal fluid perfusion. *J Toxicol Clin Toxicol* 2002; 40(5): 557–61.
- [57] Yamasaki K, Yamasaki A, Tosaki M, Isozumi Y, Hiai H. Tissue distribution of Thorotrast and role of internal irradiation in carcinogenesis. *Oncol Rep* 2004; 12(4): 733–8.
- [58] Lanuza García A, Bañón Navarro R, Llorca Cardenosa A, Delgado Navarro C. Resultado sin éxito en el tratamiento de un linfangioma orbitario con OK-432. Picibanil. [Unsuccessful treatment with OK-432 picibanil for orbital lymphangioma.] *Arch Soc Esp Oftalmol* 2012; 87(1): 17–9.
- [59] Corazza M, Capozzi O, Virgili A. Five cases of livedo-like dermatitis (Nicolau's syndrome) due to bismuth salts and various other nonsteroidal anti-inflammatory drugs. *J Eur Acad Dermatol Venereol* 2001; 15(6): 585–8.
- [60] Luton K, García C, Poletti E, Koester G. Nicolau syndrome: three cases and review. *Int J Dermatol* 2006; 45(11): 1326–8.
- [61] De Sousa R, Dang A, Rataboli PV. Nicolau syndrome following intramuscular benzathine penicillin. *J Postgrad Med* 2008; 54(4): 332–4.
- [62] García-Vilanova-Comas A, Fuster-Diana C, Cubells-Parrilla M, Pérez-Ferriols MD, Pérez-Valles A, Roig-Vila JV. Nicolau syndrome after lidocaine injection and cold application: a rare complication of breast core needle biopsy. *Int J Dermatol* 2011; 50(1): 78–80.
- [63] Karimi M, Owlia MB. Nicolau syndrome following intramuscular penicillin injection. *J Coll Physicians Surg Pak* 2012; 22(1): 41–2.
- [64] Köhler LD, Schwedler S, Worret WI. Embolia cutis medicamentosa. *Int J Dermatol* 1997; 36(3): 197.
- [65] McGee AM, Davison PM. Skin necrosis following injection of non-steroidal anti-inflammatory drug. *Br J Anaesth* 2002; 88(1): 139–40.
- [66] Kim KK. Nicolau syndrome in patient following diclofenac administration: a case report. *Ann Dermatol* 2011; 23(4): 501–3.
- [67] Koller S, Kränke B. Nicolau syndrome following subcutaneous glatiramer-acetate injection. *J Am Acad Dermatol* 2011; 64(2): e16–7.
- [68] Martínez-Morán C, Espinosa-Lara P, Nájera L, Romero-Maté A, Córdoba S, Hernández-Núñez A, Borbujo J. Embolia cutis medicamentosa (síndrome de Nicolau) tras inyección de acetato de glatiramer. [Embolia cutis medicamentosa (Nicolau syndrome) after glatiramer acetate injection.] *Actas Dermosifiliogr* 2011; 102(9): 742–4.

- [69] Cherasse A, Kahn MF, Mistrih R, Maillard H, Strauss J, Tavernier C. Nicolau's syndrome after local glucocorticoid injection. *Joint Bone Spine* 2003; 70(5): 390–2.
- [70] Puvabanditsin S, Garrow E, Weeraseshiri R, Joshi M, Brandsma E. Nicolau's syndrome induced by intramuscular vitamin K injection in two extremely low birth weight infants. *Int J Dermatol* 2010; 49(9): 1047–9.
- [71] Koklu E, Sarici SU, Altun D, Erdeve O. Nicolau syndrome induced by intramuscular vitamin K in a premature newborn. *Eur J Pediatr* 2009; 168(12): 1541–2.
- [72] Seyer BA, Grist W, Muller S. Aggressive destructive midfacial lesion from cocaine abuse. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002; 94(4): 465–70.
- [73] Manson AJ, Hanagasi H, Turner K, Patsalos PN, Carey P, Ratnaraj N, Lees AJ. Intravenous apomorphine therapy in Parkinson's disease: clinical and pharmacokinetic observations. *Brain* 2001; 124(Pt 2): 331–40.
- [74] Sapis S, Bimstein E. Cholinergic gel induced oral lesion: report of case. *J Clin Pediatr Dent* 2000; 24(2): 103–6.
- [75] Kluger N. Oral ulcerations caused by incorrect administration of desloratadine. *J Eur Acad Dermatol Venereol* 2009; 23(20): 234.
- [76] Brazier WJ, Dhariwal DK, Patton DW, Bishop K. Ecstasy related periodontitis and mucosal ulceration—a case report. *Br Dent J* 2003; 194(4): 197–9.
- [77] Bagga S, Thomas BS, Bhat M. Garlic burn as self-inflicted mucosal injury—a case report and review of the literature. *Quintessenz Int* 2008; 39(6): 491–4.
- [78] Szyszkowska A, Pulawska M, Kopper J, Malicka M. *Annales-Universitatis Mariae Curie-Skłodowska Sectio DDD Pharmacia* 2009; 22(2): 173–6.
- [79] Clapp B, Santillan A. Small bowel obstruction after FloSeal use. *JLS* 2011; 15(3): 361–4.
- [80] Kudesia R, Worley Jr MJ. Hemostatic agent related small-bowel obstruction following a caesarean delivery. *J Gynecol Surg* 2010; 26(3): 197–9.
- [81] Ben-Zeev B, Watemberg N, Augarten A, Brand N, Yahav Y, Efrati O, Topper L, Blatt I. Oligohydrosis and hyperthermia: pilot study of a novel topiramate adverse effect. *J Child Neurol* 2003; 18(4): 254–7.
- [82] Shimizu T, Yamashita Y, Sato M, Togo A, Wada N, Matsuishi T, Ohnishi A, Kato H. Heat stroke-like episode in a child caused by zonisamide. *Brain Dev* 1997; 19(5): 366–8.
- [83] Okumura A, Hayakawa F, Kuno K, Watanabe K. Oligohydrosis caused by zonisamide. *No To Hattatsu* 1996; 28(1): 44–7.
- [84] Lee AY, Joo HJ, Chey WY, Kim YG. Photopatch testing in seven cases of photosensitive drug eruptions. *Ann Pharmacother* 2001; 35(12): 1584–7.
- [85] Jeanmougin M, Manciet JR, De Prost Y, Reygagne P, Pinquier L, Dubertret L. Photo-allergie au fénofibrate. [Fenofibrate photoallergy.] *Ann Dermatol Venereol* 1993; 120(8): 549–54.
- [86] Martín-Lázaro J, Buján JG, Arrondo AP, Lozano JR, Galindo EC, Capdevila EF. Is photopatch testing useful in the investigation of photosensitivity due to flutamide? *Contact Dermatitis* 2004; 50(5): 325–6.
- [87] Spiewak R. Systemic photoallergy to terbinafine. *Allergy* 2010; 65(8): 1071–2.
- [88] Epaulard O, Leccia MT, Blanche S, Chosidow O, Mamzer-Bruneel MF, Ravaud P, Thiebaut A, Villier C, Lortholary O. Phototoxicity and photocarcinogenesis associated with voriconazole. *Med Mal Infect* 2011; 41(12): 639–45.
- [89] Schiffman SS, Zervakis J, Westall HL, Graham BG, Metz A, Bennett JL, Heald AE. Effect of antimicrobial and anti-inflammatory medications on the sense of taste. *Physiol Behav* 2000; 69(4–5): 413–24.
- [90] Teare JP, Spedding C, Whitehead MW, Greenfield SM, Challacombe SJ, Thompson RP. Omeprazole and dry mouth. *Scand J Gastroenterol* 1995; 30(3): 216–8.
- [91] Trevenzoli M, Cattelan AM, Marino F, Sasset L, Donà S, Meneghetti F. Sepsis and granulomatous hepatitis after bacillus Calmette-Guerin intravesical installation. *J Infect* 2004; 48(4): 363–4.

- [92] Ströck V, Dotevall L, Sandberg T, Gustafsson CK, Holmäng S. Late bacille Calmette-Guérin infection with a large focal urinary bladder ulceration as a complication of bladder cancer treatment. *BJU Int* 2011; 107(10): 1592–7.
- [93] Thamthitiwat S, Marin N, Baggett HC, Peruski LF, Kiatkulwiwat W, Panumatrasmee V, Varma JK, Nateniyom S, Akarasewi P, Maloney SA. *Mycobacterium bovis* (Bacille Calmette-Guérin) bacteremia in immunocompetent neonates following vaccination. *Vaccine* 2011; 29(9): 1727–30.
- [94] Guenther K, Straube E, Pfister W, Guenther A, Huebler A. Severe sepsis after probiotic treatment with *Escherichia coli* NISSLE 1917. *Pediatr Infect Dis J* 2010; 29(2): 188–9.
- [95] Kunz AN, Noel JM, Fairchok MP. Two cases of *Lactobacillus* bacteremia during probiotic treatment of short gut syndrome. *J Pediatr Gastroenterol Nutr* 2004; 38(4): 457–8.
- [96] Land MH, Rouster-Stevens K, Woods CR, Cannon ML, Cnota J, Shetty AK. *Lactobacillus* sepsis associated with probiotic therapy. *Pediatrics* 2005; 115(1): 178–81.
- [97] Kashiwagi Y, Kawashima H, Takekuma K, Hoshika A, Mori T, Nakayama T. Detection of mumps virus genome directly from clinical samples and a simple method for genetic differentiation of the Hoshino vaccine strain from wild strains of mumps virus. *J Med Virol* 1997; 52(2): 195–9.
- [98] Chouliaras G, Spoulou V, Quinlivan M, Breuer J, Theodoridou M. Vaccine-associated herpes zoster ophthalmicus and encephalitis in an immunocompetent child. *Pediatrics* 2010; 125(4): e969–72.
- [99] Theodoridou K, Papaevangelou V, Papadogeorgaki E, Quinlivan M, Theodoridou M, Kakourou T, Breuer J. Actinic varicella vaccine rash. *Pediatr Infect Dis J* 2011; 30(12): 1116–8.
- [100] Banovic T, Yanilla M, Simmons R, Robertson I, Schroder WA, Raffelt NC, Wilson YA, Hill GR, Hogan P, Nourse CB. Disseminated varicella infection caused by varicella vaccine strain in a child with low invariant natural killer T cells and diminished CD1d expression. *J Infect Dis* 2011; 204(12): 1893–901.
- [101] Hauben M, Reich L. Endotoxin-like reactions with intravenous gentamicin: results from pharmacovigilance tools under investigation. *Infect Control Hosp Epidemiol* 2005; 26(4): 391–4.
- [102] Bennett SN, McNeil MM, Bland LA, Arduino MJ, Villarino ME, Perrotta DM, Burwen DR, Welbel SF, Pegues DA, Stroud L, Zeitz PS, Jarvis WR. Postoperative infections traced to contamination of an intravenous anesthetic, propofol. *N Engl J Med* 1995; 333(3): 147–54.