

## Analgesic abuse and renal failure in Australasia

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Analgesic-induced renal papillary necrosis first became a significant factor in mortality tables for two Australian states, Queensland and New South Wales, about the year 1960 [1, 2], and the earliest descriptions of the clinical syndrome and renal pathology in Australasia (i.e., Australia and New Zealand) appeared during the following two years [3-5]. Nearly two decades earlier there had been a sharp increase in the prevalence of chronic gastric ulcer in young women living in the same two states [6-9], but the etiological role of analgesic abuse in that disease was not recognized until the 1960's [10-15]. Analgesic-induced nephropathy and gastric ulcer are still common in our community, representing the most serious elements of what has been termed in Australia "the analgesic syndrome." Their combined morbidity and mortality place minor analgesics fourth only to alcohol, tobacco, and sedatives in the table of our most harmful addictive drugs [16, 17].

It is the purpose of this review to describe the extent and pattern of non-narcotic analgesic abuse in Australasia and the prevalence of end-stage renal disease due to papillary necrosis. Preventive measures which have been introduced or proposed in this region are also discussed.

### Demography of analgesic abuse

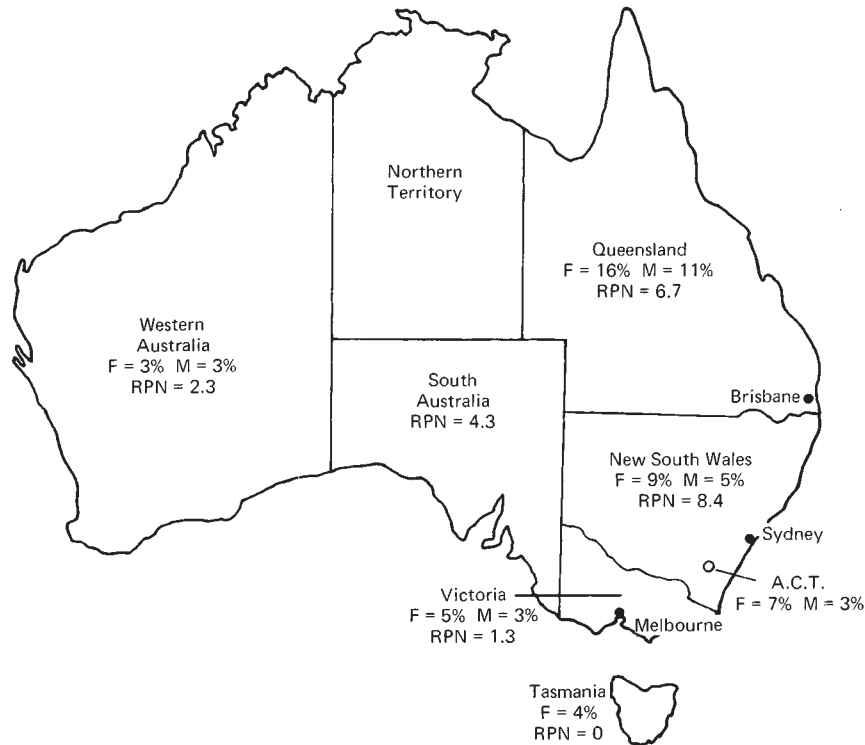
Analgesic abuse implies regular consumption, without the approval of a doctor, of powders or tablets for the sake of their psychotropic effects or else for complaints which either are caused by the analgesics themselves, or are trivial, so that the amount and type of drug taken are inappropriate [18-24]. When analgesics have been taken in the knowledge that they are potentially harmful [19, 20, 22, 23] and when there has been deception about the amount of drug consumed [19, 23, 25] or difficulty in ceasing the habit [20, 24, 25], it is clear that dependency has occurred.

Most Australian surveys of non-narcotic analgesic consumption have used information obtained by means of questionnaires which also dealt with other forms of drug intake and various health indices. As a result, their findings have related more often to the current rate of analgesic consumption than to the type of powder or tablet taken or the duration of, or reasons for, taking them. This has made it difficult to distinguish between legitimate heavy usage and drug dependence. The pattern of analgesic consumption, however, indicates that more often than not, instances of regular, daily ingestion over a period of a year or more have represented abuse.

Some 16% of the adult female, and rather more than 10% of the adult male population of Queensland take analgesics every day [19, 20, 22, 23, 26-28]. The rate of abuse falls, and the female preponderance disappears as one moves around Australia in a clockwise direction through New South Wales [21, 22, 24, 27, 29-33], the Australian Capital Territory [34], Victoria [22, 35, 36], and Tasmania [37] to Western Australia, where no more than 3% of the adult population of a provincial town were found to take analgesics regularly [38] (Fig. 1). No information is available from South Australia or the Northern Territory. In the three most populous states, where surveys have been conducted both in the capital cities (Sydney, Melbourne, and Brisbane) and in country towns, no difference was apparent between metropolitan and rural populations. Analgesic dependence is clearly less common in Christchurch [2], and probably elsewhere in New Zealand [39], than in the eastern Australian states.

The highest prevalence of analgesic abuse in any survey was that found in the aboriginal population of an "outback" country town in New South Wales [32]. On the other hand, the habit of taking analgesic powders appears to be uncommon amongst non-British immigrant communities [24, 40, 41].

Age-specific rates for regular analgesic consumption have shown a peak prevalence at about 50 years of age in Queensland and New South Wales [18-21, 30, 31, 39]. In communities where there is less habi-



**Fig. 1.** The distribution of (a) regular analgesic consumption and (b) end-stage renal failure due to renal papillary necrosis throughout the six Australian states. Beneath the name of each state is shown separately the percentage of adult females (F) and males (M) who take one or more analgesic powders or tablets every day, and beneath that, the yearly rate (per million of total population) of entrance of patients with renal papillary necrosis (RPN) into the maintenance dialysis/transplantation program in each state (data abstracted from the twice-yearly reports of the Australian Kidney Foundation Maintenance Dialysis Survey covering the period 1971–1976).

tuation to analgesics, however, the prevalence of daily ingestion has been highest in old age [34, 38] when chronic painful complaints are most common. The Queensland and New South Wales data could be explained either by considerable excess mortality among analgesic addicts during early middle age, or else by adoption of the analgesic habit in the first place by young adults, especially women, during or shortly after the second world war [19]. The evidence for this latter possibility now seems conclusive, particularly in respect of aspirin-induced gastric ulcer [6–15].

*Composition of analgesics taken by habitues.* Two brands, Bex<sup>®</sup> and Vincent's<sup>®</sup>, have been taken by more than two-thirds of analgesic habitues in this country [19, 21, 24, 27]. These are the only two Australian proprietary brands which contain caffeine, are available as powders, and are retailed chiefly through outlets other than pharmacies [19]. Both comprised aspirin, phenacetin, and caffeine (A.P.C.) prior to 1967 when Vincent's replaced phenacetin with salicylamide. Bex substituted para-

cetamol in 1975. Bex powders each contained twice as much phenacetin (350 mg), but rather less caffeine (68 to 75 mg) than Vincent's (85 to 91 mg per powder). Bex has been the more popular in Queensland [2, 19], whereas Vincent's appears now to have the greater share of the Sydney (N.S.W.) market [21, 24].

Tablets of aspirin, phenacetin (replaced by paracetamol during the last decade), and codeine are the preparations of choice for about one in ten Australian [21, 27] and nearly all New Zealand habitues [42, 43]. Single-drug tablets of aspirin or paracetamol alone are preferred to the compound preparations by about one quarter of Australians who take analgesics every day [2, 27, 28], and by a majority of those who take them less frequently [24, 27] or who live in communities where heavy analgesic consumption is relatively uncommon [36].

#### Causes of analgesic dependence in Australia

Headache has been the reason most often advanced for regular, daily ingestion of analgesics,

its frequency being 65% [27] and 42% [21] in two surveys. In the first, only 6% of habitues admitted to taking drugs for their psychotropic effect, whereas in the latter, 31% did so, a discrepancy due probably to different wording of the relevant questions. The findings illustrate what is familiar to clinical nephrologists in this part of the world, namely that the first Bex or Vincent's powder generally is taken on arising to "clear the head," while further doses are taken to relieve the dull headache or "let-down" feeling which follows elimination of the drugs. Caffeine-withdrawal headache is documented [44, 45], and phenacetin may also cause withdrawal symptoms [46], or headache [47]. That recurrent headache is often a result, rather than a cause of dependence on analgesics is born out by the observation that habitues may no longer suffer headaches so frequently once they overcome their addiction [42].

The third, and only legitimate reason commonly given for regular analgesic ingestion is arthritis or other chronic musculoskeletal pain. This accounts for no more than one fifth of cases in Australia [21, 27].

Like other forms of drug dependence, addiction to non-narcotic analgesics is more prevalent among those who give a history of domestic disharmony [48, 49], neurosis, or other psychiatric disease [20, 22, 32, 49, 50]. There is a positive association with tobacco smoking [20, 48], and possibly with alcoholism [20, 22, 27, 32, 33, 50], but not with the use of sedatives or tranquilizers [22, 27, 33].

On the other hand, it has been observed in New South Wales that groups of women who have taken analgesics, even to the point of endangering their health, did not appear to be maladjusted mentally or socially, nor were they less able to be rehabilitated after renal transplantation than patients with non-analgesic end-stage renal failure [24, 40]. Psychopathic traits, therefore, can account for but a minority of cases of analgesic dependency, particularly in populations where the habit is very common. Moreover, some other explanation must be found for the demographic pattern of analgesic abuse, particularly the female preponderance and the striking geographic distribution. In Queensland and New South Wales, those principally affected are housewives, unskilled workers, and the poorly educated [19, 27, 40]; in both sexes, usage increases with worsening socio-economic status [21, 41, 51], but there is no evidence either that women who work are more liable to addiction than those who do not [21, 27, 37, 41], or that marital status is a significant factor [27, 41]. Regular analgesic consumption may start during the teen-age years [23, 37, 51, 52], but becomes more

widespread during young adult life [19, 21, 34, 38].

*The advertising and sale of analgesics.* Fewer than 10% of Australians obtain their analgesics by prescription [27, 35, 53], and less than half of all purchases of these drugs are made from pharmacies [19, 21]. In this latter respect, there is a notable difference between tablets of aspirin, 60% of which are sold by pharmacies, and Bex and Vincent's powders, of which only 10% are retailed through professionally supervised outlets. The six Australian states have yet to place any restriction on the advertisement or sale of non-narcotic analgesics other than a requirement (not universal) to print on the packet of phenacetin-containing preparations a warning against excessive usage. Codeine-containing preparations may be sold only by pharmacies. In 1967, federal regulations removed all phenacetin-containing drugs from the list of analgesics which could be obtained by prescription through the Australian National Health Service; in New Zealand, the opposite measure was introduced in 1975, *viz.*, to permit the supply of phenacetin only on a doctor's prescription.

The expenditure on advertising of analgesics by television, radio, and the press throughout Australia was about \$2 million in 1972 (cf, \$5.7 million on other pharmaceuticals, \$7.3 million on liquor, and \$11.0 million on tobacco, in a total advertising budget of \$204 million [54]). Vincent's also advertise widely on hoardings, and Bex by means of placards inside and outside milk bars, general stores and supermarkets.

Widespread advertising and ready availability has created in many Australian circles a tradition of taking a powder for any minor complaint, a tradition which is handed down from mother to daughter [24, 27, 37], but may not yet have become established in new Australian families whose mother tongue is not English [24, 40, 41]. On leaving school, young women are encouraged by their workmates to take powders to relieve the tedium of the job or to improve performance [24], and the same remedy is adopted later to overcome the stress of running a household with children and the boredom of suburban life. In these roles, caffeine-containing analgesics are used by some of our womenfolk much as others might take strong tea or coffee, or smoke cigarettes.

#### **Analgesic-induced end-stage renal failure**

Despite a high level of awareness in the community of the dangers of excessive analgesic consumption, and in the face of a generally good response of established analgesic nephropathy to active medical and urological therapy [25, 55-57], papillary necrosis remains the second most common cause of end-

stage renal failure in Australia, accounting for some 15 to 20% of patients entering maintenance dialysis and transplant programs [58–60]. The incidence is highest in Queensland [61] and New South Wales [62–64], and lowest in Victoria [65], Tasmania, and New Zealand [66, 67], conforming to the pattern of analgesic abuse (Fig. 1).

*Post mortem* surveys have shown *advanced* papillary necrosis in 4 to 10% of necropsies in Brisbane (Queensland) [1, 2, 39], Sydney (New South Wales) [4, 68] and Melbourne (Victoria) [69] hospitals, but in less than 1% in Perth (Western Australia) [1] and Auckland (New Zealand) [1, 70], thus confirming that analgesic nephropathy is relatively more common in the eastern Australian states than elsewhere in Australasia. The higher figures quoted above must be interpreted with some care, since all came from hospitals with active renal units. In two hospitals which established renal failure programs in the late 1960's, Christchurch and the Royal Prince Alfred Hospital in Sydney, the autopsy incidence of *advanced* analgesic nephropathy rose from less than 1% in 1964 [1] to 3–5% in 1971 [2, 68].

The peak age incidence for patients with analgesic nephropathy starting maintenance dialysis is in the fifth decade [63]; in autopsy series, advanced papillary necrosis has been found chiefly in the 40 to 80-year-old age groups [1, 2, 4, 69].

Women comprise some 60 to 85% of end-stage or terminal renal failure due to analgesics [1, 2, 4, 39, 63, 68, 69], a distinctly higher proportion than might be expected from the sex ratio of analgesic abuse in Australia (Fig. 1). Possible explanations are that women analgesic habitues have, on average, a much heavier consumption of powders than do men, that the higher liquid (beer) intake by male habitues is protective, or that their kidneys are more vulnerable due to the greater susceptibility of the female urinary tract to ascending infection.

No estimate is available of the prevalence in this community of nonterminal renal papillary necrosis, but in the renal unit populations (in-patient and out-patient) of two large New South Wales hospitals (Sydney and Royal Newcastle), analgesic nephropathy is the most common diagnosis, accounting for 25 to 30% of all cases treated (Fig. 2).

#### Prevention

With an intensive educational program directed at the public and doctors by the Australian Kidney Foundation and individual urologists and nephrologists, official pronouncements on the dangers of non-narcotic analgesic abuse by the Royal Australasian College of Physicians [71] and the National Health

and Medical Research Council [72], improved standards of conservative therapy and replacement of phenacetin by salicylamide in Vincent's powders during 1967, one might have expected that the incidences of analgesic-induced end-stage renal failure would have fallen. There has, however, been no discernible change in the proportion of cases entering renal replacement programs between 1967 and 1975 [58, 59, 63], although the number coming to autopsy has diminished [2]. A factor to be taken into consideration is that criteria for acceptance on dialysis have been relaxed since the introduction of home dialysis programs in 1970–1971, so that patients in their 50's and early 60's, or those with extrarenal disease, two categories which include a high proportion of analgesic nephropathy, are now more likely to be considered for dialysis therapy. If phenacetin, not aspirin or paracetamol, were the major nephrotoxin [25, 73, 74], significant diminution in the amount of renal papillary necrosis in Australia would occur as a result of the recent substitution of paracetamol for phenacetin in Bex powders.

Nonetheless, it is clear that further preventive measures are necessary, at least in Queensland and New South Wales. Perhaps the simplest action would be to make proprietary analgesics less addictive by removing their psychotropic ingredients [52], in particular caffeine [64, 75]. Many medical commentators have proposed a restriction [71], or even a prohibition of advertising [20, 64] while confining all sales to pharmacies [25, 52, 71, 74, 76]. It is conceded, however, that single-drug analgesics would have to be excluded from these provisions. Few now advocate making a prescription necessary for the purchase of analgesics, except perhaps for phenacetin-, caffeine- or codeine-containing preparations [5, 35, 43, 56, 76].

So long as identification of individual cases of analgesic abuse depends upon specific questioning, the diagnosis will frequently be missed, because of oversight by the doctor or evasion by the patient. Screening programs [23, 24], renal clinics [63], and some gastroenterology clinics [49, 77] now regularly test their patients' urine for salicylate, using Phenistix (Ames) or a solution of ferric ions. Far more hitherto undetected cases would be identified were testing extended to hypertension and hematology clinics, and to general practitioners' surgeries. Tests for phenacetin derivatives are of less general application since they are laboratory rather than clinical procedures [78].

It is coming to be realised that legislative controls and medical surveillance alone will not cure this or any form of drug abuse unless the underlying emo-

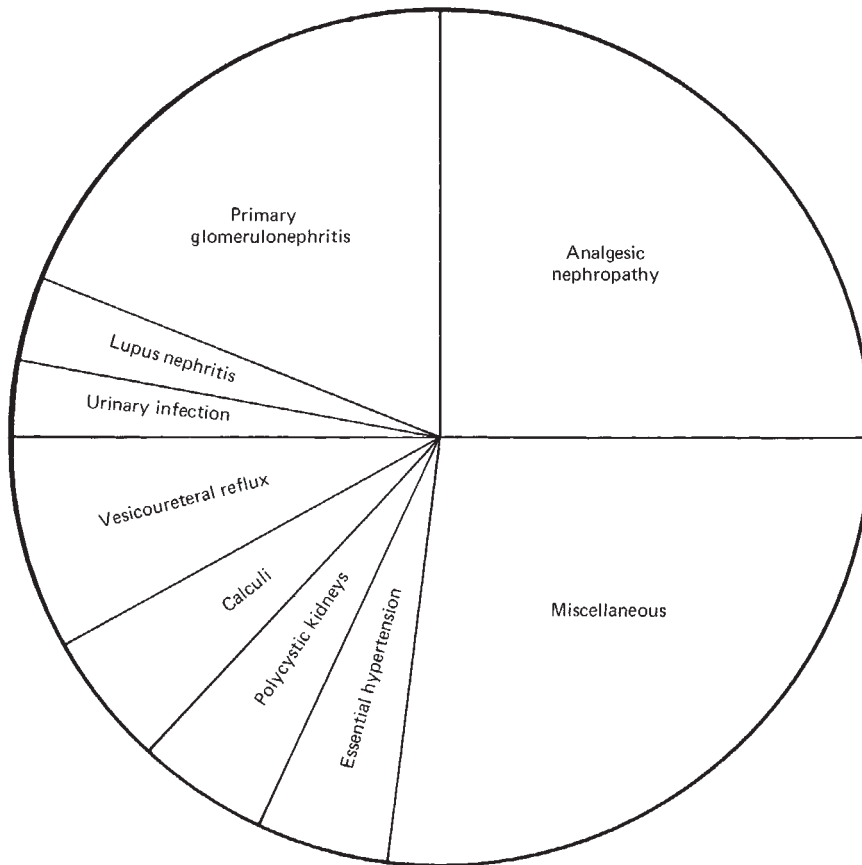


Fig. 2. The distribution of renal diseases found in 637 patients with nonterminal renal failure treated by the Sydney Hospital Renal Unit during the year 1976.

tional, social, domestic or economic causes are identified and eliminated. Analysis of these problems is beyond the competence of doctors in clinical practice, and we must look to the social engineer to devise a preventive program which combines education with correction of the predisposing factors and a minimum of controls necessary to prevent exploitation of the less intelligent and weaker-willed members of the community [32, 51, 52, 74].

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#### References

- BURRY AF: A profile of renal disease in Queensland: Results of an autopsy survey. *Med J Aust* 1:826-834, 1966
- BURRY AF, AXELSEN RA, TROLOVE P: Analgesic nephropathy: Its present contribution to the renal mortality and morbidity profile. *Med J Aust* 2:31-36, 1974
- BUCHANAN JG: Phenacetin induced chronic interstitial nephritis. *NZ Med J* 60:207-208, 1961
- JACOBS LA, MORRIS JG: Renal papillary necrosis and the abuse of phenacetin. *Med J Aust* 2:531-538, 1962
- MCCUTCHEON AD: Renal damage and phenacetin. *Med J Aust* 2:543-546, 1962
- BILLINGTON BP: Gastric ulcer: age, sex, and a curious retrogression. *Aust Ann Med* 9:111-121, 1960
- BILLINGTON BP: The Australian gastric ulcer change: Further observations. *Med J Aust* 2:19-20, 1960
- BILLINGTON BP: The Australian gastric ulcer change: Interstate variations. *Aust Ann Med* 12:153-159, 1963
- BILLINGTON BP: Observations from New South Wales on the changing incidence of gastric ulcer in Australia. *Gut* 6:121-133, 1965
- DOUGLAS RA, JOHNSTON ED: Aspirin and chronic gastric ulcer. *Med J Aust* 2:893-897, 1961
- DUGGAN JM: The relationship between perforated peptic ulcer and aspirin ingestion. *Med J Aust* 2:659-662, 1965
- GILLIES M, SKYRING A: Gastric ulcer, duodenal ulcer and gastric carcinoma: A case-control study of certain social and environmental factors. *Med J Aust* 2:1132-1136, 1968

13. GILLIES MA, SKYRING A: Gastric and duodenal ulcer: The association between aspirin ingestion, smoking and family history of ulcer. *Med J Aust* 2:280-285, 1969
14. CHAPMAN BL, DUGGAN JM: Aspirin and uncomplicated peptic ulcer. *Gut* 10:443-450, 1969
15. DUGGAN JM: Gastrointestinal haemorrhage, gastric ulcer and aspirin. *Aust Ann Med* 19:135-138, 1970
16. Australian Senate Select Committee: *Report on Drug Trafficking and Drug Abuse*. Canberra, Australian Government Publishing Service, 1971
17. Joint Committee of the Legislative Council and Legislative Assembly upon Drugs: *Progress Report*. Sydney, Government Printer of New South Wales, 1976
18. LAVAN JN, BENSON WJ, GATENBY AH, POSEN S: The consumption of analgesics by Australian hospital patients. *Med J Aust* 2:694-695, 1966
19. PURNELL J, BURRY AF: Analgesic consumption in a country town. *Med J Aust* 2:389-391, 1967
20. ABRAHAMS MJ, ARMSTRONG J, WHITLOCK FA: Drug dependence in Brisbane. *Med J Aust* 2:397-404, 1970
21. GILLIES MA, SKYRING AP, LIVINGSTONE E: The pattern and prevalence of aspirin ingestion as determined by interview of 2,921 inhabitants of Sydney. *Med J Aust* 1:974-979, 1972
22. FERGUSON D: Smoking, drinking and non-narcotic analgesic habits in an occupational group. *Med J Aust* 1:1271-1274, 1973
23. FINNIGAN D, BURRY AF, SMITH IDB: Analgesic consumption in an antenatal clinic survey. *Med J Aust* 1:761-762, 1974
24. COLLINS E, TURNER G: Maternal effects of regular salicylate ingestion in pregnancy. *Lancet* 2:335-338, 1975
25. KINCAID-SMITH P: Analgesic nephropathy: A common form of renal disease in Australia. *Med J Aust* 2:1131-1135, 1969
26. CVJETANOVIC DR, MENKENS MP: *A Study of Certain Aspects of (a) Immunization, (b) Consumption of Analgesics, (c) Knowledge of Vitamin C, (d) Breast Weaning in Mareeba, North Queensland, Australia*. Brisbane, Department of Social Medicine, University of Queensland, Project 390, 1965
27. DAVIES E, KELLEY G: *A Survey of Analgesic and Sedative Consumption in Sydney and Brisbane*. Kensington, Unisearch, 1968
28. SCHACHT P, BROWN J, BROWN R, SCHONFELD C: *The Redcliff Health Survey*. Brisbane, Queensland Department of Health, 1976
29. BAIN RG, UNWIN ML: *An Investigation into Immunization Procedures and Use of Analgesics in a Northern Rivers Township in New South Wales*. Brisbane, Department of Social Medicine, University of Queensland, Project 498, 1965
30. GEORGE A: Survey of drug use in a Sydney suburb. *Med J Aust* 2:233-237, 1972
31. GEORGE A: *1973 Survey of Drug Use in a Western Suburb of Sydney*. Sydney, Mental Health and Drug Education Programme, Health Commission of New South Wales, 1973
32. KAMIEN M: A survey of drug use in a part-aboriginal community. *Med J Aust* 1:261-264, 1975
33. REYNOLDS I, HARNAS J, GALLAGHER H, BRYDEN D: Drinking and drug taking patterns of 8,516 adults in Sydney. *Med J Aust* 2:782-785, 1976
34. HENNESSY BL, BRUEN WJ, CULLEN J: The Canberra mental health survey: Preliminary results. *Med J Aust* 1:721-728, 1973
35. KRUPINSKI J, STOLLER A, BAIKIE AG, GRAVES JE: *A Community Health Survey of the Rural Town of Heyfield, Victoria, Australia*. Melbourne, Mental Health Authority, Special Publication No. 1, 1970
36. CHRISTIE D, MCPHERSON L, KINCAID-SMITH P: Analgesics and the kidney: A community-based study. *Med J Aust* 2:527-529, 1976
37. CARINGTON-SMITH D: *Do Women Need Drugs to Cope with Life?* Hobart, Health Education Council, Health Services Department, 1974
38. CULLEN KJ, WOODINGS T: Alcohol, tobacco and analgesics: Busselton, 1972. *Med J Aust* 2:211-214, 1975
39. BURRY AF, DEJERSEY P, WEEDON D: Phenacetin and renal papillary necrosis: Results of a prospective autopsy investigation. *Med J Aust* 1:873-879, 1966
40. NIALL P: Analgesic nephropathy in end stage renal failure programmes in N.S.W. *Aust NZ J Med* 4:425-426, 1974
41. JARVIE W, MCCALDEN G: *The Incidence of Analgesic Nephropathy in the Hunter Region*. Newcastle, Datex, 1976
42. VAUGHAN JV, FLEISCHL P, NATHAN M, TAYLOR RC: Chronic renal disease and analgesic abuse. *NZ Med J* 66:794-797, 1967
43. BAILEY RR, NEALE TJ, LITTLE PJ: Analgesic nephropathy. *NZ Med J* 79:1053-1057, 1974
44. DREISBACH RH, PFEIFFER C: Caffeine-withdrawal headache. *J Lab Clin Med* 28:1212-1219, 1943
45. RITCHIE JM: Central nervous system stimulants (continued): The xanthines, Chapter 19, in *The Pharmacological Basis of Therapeutics* (5th ed), edited by GOODMAN LS, GILMAN A, New York, Macmillan, 1975, p. 367
46. WOODBURY DM, FINGL E: Analgesic-antipyretics, anti-inflammatory agents, and drugs employed in the therapy of gout, Chapter 17, in *The Pharmacological Basis of Therapeutics* (5th ed), edited by GOODMAN LS, GILMAN A, New York, Macmillan, 1975, p. 325
47. ZOLLINGER HU: Chronic abuse of phenacetin and kidney lesions, Chapter 26, in *The Kidney (International Academy of Pathology Monograph)*, edited by MOSTOFI FK, SMITH DE, Baltimore, Williams and Wilkins, 1966, p. 523
48. CLARKSON AR, LAWRENCE JR: The clinical features of analgesic nephropathy, in *Renal Infection and Renal Scarring* (2nd ed), edited by KINCAID-SMITH P, FAIRLEY KF, Melbourne, Mercedes, 1970, p. 375
49. DUGGAN JM: The analgesic syndrome. *Aust NZ J Med* 4:365-372, 1974
50. DAWBORN JK, FAIRLEY KF, KINCAID-SMITH P, KING WE: The association of peptic ulceration, chronic renal disease, and analgesic abuse. *Quart J Med N.S.* 35:69-83, 1966
51. GRAVES G: Epidemiology of drug use in Melbourne, in *Drug Use by the Young Population of Melbourne*, edited by KRUPINSKI J, STOLLER A, Melbourne, Mental Health Authority, Special Publication No. 4, 1973, p. 22
52. IRWIN RP: Minor analgesic use among high-school students: Indications for renal morbidity and mortality. *Med J Aust* 2:522-527, 1976
53. BRIDGES-WEBB C: Drug medication in the community. *Med J Aust* 1:675-679, 1972
54. Australian Broadcasting Control Board: *Broadcasting and Television Year Book*. Melbourne, 1974
55. PEARSON HH: Residual renal defects in non-fatal phenacetin nephritis. *Med J Aust* 2:308-313, 1967
56. KINCAID-SMITH P, NANRA RS, FAIRLEY KF: Analgesic nephropathy: A recoverable form of chronic renal failure, in *Renal Infection and Renal Scarring* (2nd ed), edited by KINCAID-SMITH P, FAIRLEY KF, Melbourne, Mercedes, 1970, p. 385
57. STEELE TW, EDWARDS KDG: Analgesic nephropathy: Changes in various parameters of renal function following cessation of analgesic abuse. *Med J Aust* 1:181-187, 1971

58. DISNEY APS, ROW PG, and a Subcommittee of the Australian Kidney Foundation: Australian maintenance dialysis survey. *Med J Aust* 2:651-656, 1974
59. DISNEY APS: AKF maintenance dialysis survey report, 1975. *Aust NZ J Med* 6:98, 1976
60. Third Report by a Subcommittee: Australian national renal transplantation survey. *Med J Aust* 2:656-660, 1974
61. CLUNIE GJA, HARTLEY LCJ, RIBUSH NT, EMMERSON BT, MORGAN TO: An integrated service for the treatment of irreversible renal failure. *Med J Aust* 2:403-408, 1971
62. JEREMY D, MURNAGHAN GF, ROBERTSON MR, FARNSWORTH RH, TREW PA, TYNAN AP, ANNETTS DL, FRAWLEY JE: Long term results of cadaver kidney transplantation. *Aust NZ J Med* 3:436, 1973
63. STEWART JH, MCCARTHY SW, STOREY BG, ROBERTS BA, GALLERY E, MAHONY JF: Diseases causing end-stage renal failure in New South Wales. *Br Med J* 1:440-443, 1975
64. WOLK H: *The Role of Analgesics in Chronic Renal Failure*. Sydney, Division of Health Services Research, Health Commission of New South Wales, Discussion Paper D75/1, 1975
65. HEALE WF, LAVER MC, MATHEW TH, KINCAID-SMITH P: The pathogenesis of chronic renal failure. *Aust NZ J Med* 3:330, 1973
66. DOAK PB, BOWIE EA, DALTON NT, DOUGLAS R, DUKE AJ, MACLAURIN CH, MONTGOMERIE JZ, NORTH JDK, SMITH HL, SORRELL VF: Four years' experience with cadaveric renal transplantation. *NZ Med J* 73:117-123, 1971
67. URQUHART-HAY D, MORRISON RBI, MCLWAIN J, STEPHENSON CBS, CABLE JV, LENNANE RJ, FONG R: Two years' experience with cadaveric renal transplantation. *NZ Med J* 74:295-301, 1971
68. ARNOLD L, COLLINS C, STARMER GA: Renal papillary necrosis: The incidence at autopsy in a hospital population in Sydney. *Bull Postgrad Comm Med Univ Syd* 29:228-235, 1974
69. NANRA RS, HICKS JD, MCNAMARA JH, LIE JT, LESLIE DW, JACKSON B, KINCAID-SMITH P: Seasonal variation in the post-mortem incidence of renal papillary necrosis. *Med J Aust* 1:293-296, 1970
70. ROBINSON KB, HERDSON PB: The incidence of kidney disease in two hundred necropsies. *NZ Med J* 78:517-519, 1973
71. The Royal Australasian College of Physicians: Statement on analgesic nephropathy. *Med J Aust* 1:1388-1389, and *NZ Med J* 70:39-40, 1969
72. Editorial: Analgesics: A warning. *Med J Aust* 1:1364-1365, 1969
73. NANRA RS, KINCAID-SMITH P: Chronic effect of analgesics on the kidney. *Progr Biochem Pharmacol* 7:285-323, 1972
74. STEWART JH, GALLERY EDM: Analgesic abuse and kidney disease. *Aust NZ J Med* 6:498-508, 1976
75. COLLINS E, TURNER G: A suggestion for reducing the incidence of habitual analgesic consumption. *Med J Aust* 1:863, 1973
76. ROSS P: A.P.C. as a cause of renal disease. *Med J Aust* 2:539-543, 1962
77. DUGGAN JM: The Phenistix test in the detection of analgesic abuse. *Med J Aust* 1:659-660, 1972
78. WELCH RM, CONNEY AH: A simple method for the quantitative determination of *N*-acetyl-*p*-aminophenol (APAP) in urine. *Clin Chem* 11:1064-1067, 1965