

## **CHAPTER 2**

### **2.0 THE PERVASIVENESS OF NON-COMPLIANCE IN MEDICAL FIELDS OTHER THAN ONCOLOGY**

Non-compliance is a problem in all fields of medicine to a greater or lesser degree. It runs across all age groups, though obviously peaking at some, such as adolescence. This section does not, in general, go into the reasons for non-compliance; it simply highlights the extent of the problem, its magnitude and distribution in all fields. Though this study focuses on non-compliance in the oncology patient with a good prognosis, it is obviously part of a broader problem and in studying these aspects it should have relevance for other fields. The interventions worked out should also have relevance for other medical fields. In this chapter a basis is laid for placing non-compliance in oncology into the wider context of general medicine.

#### **2.1 Hypertension**

A comprehensive work on non-compliance was put together in 1979 by Haynes, Taylor and Sackett. Sackett had observed that his hypertensive patients' unpredictable and often disappointing responses to therapy were the result of neither "resistant" disease nor inadequate drugs, but were due to low compliance. He began to work together with Haynes and Taylor on compliance research. For the next 30 years, researchers all over the world did studies on non-compliance in hypertension and other fields of health care, as medicine has become

increasingly aware of the extent of the problem.

The major precursor of death from cerebrovascular accident is elevated blood pressure, and although efficacious medication exists for the control of hypertension, non-compliance in patients with this condition is notoriously high (Allen, 1998). This has been confirmed by research in different parts of the world. (Williams, 1998; Balazovjech and Hnilica, 1993; Ben Hamida, Oueslati, Bouraoui, Zouari and Nacef, 1993; Feldman, Bacher, Campbell, Drover, Chockalingam, 1998; Butler, August, Ferdinand, Phillippes and Roccella, 1999; Chockalingam, Bacher, Campbell, Cutler, Drover, Feldman, Fodor, Irvine, Ramsden, Thivierge and Tremblay, 1998; Rojas-Fernandez, Kephart, Sketris and Kass, 1999; Wallenius, Vainio, Korhonen, Hartzema and Enlund, 1995). Rand (1993) points out that poor adherence is most common when the treatment regimen is preventive rather than curative. Also, the literature on patient adherence with life-long treatment regimens that are simple and palatable (e.g., anti-hypertensives) suggests that while these improved treatments can enhance adherence, the overall rates of patient compliance still average only 50%.

Kyngas and Lahdenpera (1999) working with patients with hypertension found that compliance with the dietary restrictions was poorest, while compliance with medication was best. Jones, Gorkin, Lian, Staffa and Fletcher (1995) concluded that low rates of continuation with a newly prescribed antihypertensive drug exist regardless of which drug is prescribed. This is also surprisingly the case where children are concerned where parental compliance is important. Grunbaum, Rodriguez and Labarthe (1993) studied parental response to identification of elevated blood pressure or cholesterol following school-based screening. It

was found that 53% had their child's cholesterol or blood pressure level re-evaluated.

Flack, Novikov and Ferrario (1996) mention that it has been estimated that within the first year of treatment 16-50% of hypertensives discontinue their anti-hypertensive medications. Even among those who remain on therapy long term, missed medication doses are common. Caro, Salas, Speckman, Raggio & Jackson (1999) found similar results. In fact Finnerty, Lawrence, Shaw and Himmelsbach (1973) found that 50% (457 of 953) found to be hypertensive on initial screening failed to keep their first verification appointment.

Mallion, Dutrey-Dupagne, Vaur, Genes, Renault, Baguet, Boutelant and Elkik (1995) did a fascinating study in France on the behavior of patients with mild-to-moderate arterial hypertension in relation to their treatment and the contribution made by the use of an electronic pillbox (Metronome). The objective of the study was to evaluate the real behaviour of patients in relation to anti-hypertensive treatment administered as a single daily dose. After a 2-week period during which no other antihypertensive was allowed to be administered, 590 patients with mild-to-moderate hypertension received 2 mg of trandolapril as a single daily dose in the morning between 7:00 a.m. and 9:00 a.m. for 4 weeks. Treatment was packaged in electronic pillboxes recording the date and time of each opening. One hundred and two patients (20%) omitted more than 20% of the prescribed doses, either consecutive doses or scattered throughout the month of treatment.

Magometschnigg (1995) quotes a similar but far more disturbing study: 389 Austrian general practitioners studied compliance in 945 hypertensives, using the Medication Event Monitoring

System (MEMS). The patients were asked to take the ACE-inhibitor Cilacapril once a day between 7.00 a.m. and 9.00 a.m. Each package opening was registered by a microprocessor located in the cover of the drug vial. In this study only 1.3% of the patients did actually open their vials between 7.00 a.m. and 9.00 a.m.

## **2.2 Stroke**

Antiplatelet therapy is currently one of the methods for preventing transient ischemic attacks and cerebral thrombosis. In 17 (10%) of the 159 outpatients, platelet aggregation was not adequately reduced because of non-compliance with their anti-platelet therapy (Komiya, Kudo, Urabe and Mizuno, 1994).

## **2.3 Cardiac Conditions**

As with hypertension, much of the non-compliance in cardiac conditions are with preventative medicine and therefore the risk is potentially greater. Luepker (1993) notes that adherence to cardiovascular treatment regimen is a major problem that limits the potential success of therapeutic advances.

Detry, Block, De Backer and Degaute (1995) found that cardiac patient compliance with therapy is often poor and, what is more, overestimated by the treating physician. In a study of adherence to aspirin in the prevention of myocardial infarction, Glynn, Buring, Manson, LaMotte and Hennekens (1994) found that several cardiovascular disease risk factors assessed

at baseline were related to poor adherence (taking <50% of study tablets): cigarette smoking, obesity, lack of exercise, and history of angina. Perkins (1988) found that only about one third of previously smoking post-myocardial infarction patients remained abstinent at follow-up.

### **2.3.1 Heart failure**

Monane, Bohn, Gurwitz, Glynn and Avorn (1994), found that non-compliance with long-term medication regimens, such as those employed in the treatment of congestive heart failure (CHF), has been found to be approximately 50%. Non-compliance with drugs was found in 23.5% of patients with decompensated heart failure who were admitted to hospital (Michalsen, Konig and Thimme, 1998).

### **2.3.2 Cardiac rehabilitation**

Despite empirical evidence that cardiac rehabilitation programs can play a significant role in enhancing recovery following a primary cardiac event and in enacting secondary prevention measures, attendance rates remain remarkably low (Halm, Penque, Doll and Beahrs, 1999; Harlan, Sandler, Lee, Lam, Mark, 1995; Kamwendo, Hansson and Hjerpe, 1998; King and Teo, 1998; Moore, Ruland, Hashkow and Blackburn, 1998). It could be that the women felt that such a program paled in importance compared to their busy schedule, or, simply, as is the final conclusion of this study, a need to put the whole traumatic experience behind then, not to be reminded of it on a regular basis. (Shemesh, Rudnick, Kaluski, Milovanov, Salah, Alon, Dinur, Blatt, Metskor, Golik, Verd and Cotter, 2001).

### **2.3.3 Heart transplant**

Poor medical compliance has been held responsible for a large proportion of deaths occurring subsequent to post-operative recovery in heart transplant patients (Dew, Kormos, Roth, Murali, DiMartini and Griffith, 1999) De Geest, Abraham, Moons, Vandeputte, Van Cleemput, Evers, Daenen and Vanhaecke, (1998) found that although in absolute numbers cyclosporine compliance in their sample was high, minor deviations from dosing schedule were associated with an increased risk for acute late rejection episodes in heart transplant recipients.

### **2.3.4 Endocarditis**

A working party of the Netherlands Heart Foundation has formulated guidelines for the prevention of bacterial endocarditis, which are simple and uniform in order to encourage maximum compliance (van der Meer, 1995). Gutschik (1995) maintained that in the treatment of bacterial endocarditis the maintenance of healthy gums and teeth was of major importance. His investigations, however, reported poor levels of compliance.

### **2.3.5 Hypercholesterolaemia**

Marquez Contreras, Casado Martinez, Lopez de Andres, Coresprieto, Lopez Zanolano, Moreno Garcia, Martin de Pablos and Marin Fernandez (1998) talk about the need to improve therapeutic compliance in cases of hypercholesterolaemia. Rand (1993) worked on non-

adherence with therapy in on heterozygous familial hypercholesterolemia. Tonstad, Silvertsen, Aksnes and Ose (1996) found that although low dose colestipol effectively reduces low density lipoprotein cholesterol levels, only a minority of adolescents with familial hypercholesterolaemia adhered to the new formulation for one year.

Langner , Rowe and Davies (1994), reported similar results.

## **2.4 Respiratory Conditions**

The Lung Health Study Research Group studied long-term metered-dose inhaler adherence in a clinical trial in chronic obstructive pulmonary disease (COPD). Self-reporting confirmed by canister weight classified 48% of participants at 1 year as showing satisfactory or better adherence (Rand, Nides, Cowls, Wise and Connett, 1995). In long-term home nebulizer therapy for COPD; Turner, Wright and Mendella (1995) found 50.6% of patients to be adherent, and 49.4% non-adherent. Hatton, Allen, Vathenen, Feely and Cooke (1996) studied compliance with oral corticosteroids during steroid trials in chronic airways obstruction. Excluding those who defaulted whose compliance must be questionable, eight (26%) patients did not fully comply with the trial. Barjhoux, Pepin, Deschaux-Blanc, Kulpa, Cornette, Desrues, Girault, Gauzere, Bedicam and Greil (1994) found that only 45% of the patients managed daily oxygen therapy at home superior or equal to the prescribed 15 hours and were categorised as compliant. Diaz Lobato, Garcia Tejero, Gomez, Alvaro and Villasante (1996) found that compliance was low with portable oxygen therapy in the Madrid area. Dekker et. al. (1993) found that 30% of patients receiving pulmonary medication in general

practice were considered to be compliant. Lojander, Maasilta, Partinen, Brander, Salmi and Lehtonen (1996) found Nasal-CPAP to be an effective therapy for obstructive sleep apnea syndrome. but compliance was a problem.

#### **2.4.1 Asthma**

Adherence to an asthma-management program involves a number of areas: medication, appointment-keeping, prevention, and applying an emergency plan of action. Barriers to adherence may exist in one or all four of these areas, leading to ineffective control of the asthma (Deenen and Klip, 1993; Leickly, Wade, Crain, Kruszon-Moran, Wright and Evans, 1998). Creer and Levstek (1996) found compliance to treatment regimens in asthma to be generally poor. This could be due to the fact that most of this is preventative and prophylactic and administered by the patient him/herself.

The problem is no less in childhood asthma where the parents, especially of the younger child, have the responsibility for administering treatment. Poor compliance was found to be a major factor causing referral of asthmatic children to the emergency room (Ashkenazi, Amir, Volovitz and Varsano, 1993). Zimmerman, Bonner, Evans and Mellins (1999) found that despite receiving primary care for childhood asthma at a major metropolitan university hospital, 83% of the sample he used were classified as pre-compliant. Gibson and Edwards (1995) found that compliance with inhaled prophylactic therapy was poor in preschool children with asthma where medication was administered under parental supervision. Chmelik and Doughty (1994) found that compliance with the asthma protocol during the fifth week



occurred only in 40% of patients. Randolph and Fraser (1998) found non-adherence in teen asthma to be epidemic. As discussed elsewhere, non-adherence in adolescence is part of the whole concept of adolescent rebellion and emancipation.

## **2.5 Diabetes**

An estimated 20 million Americans suffer from diabetes (Skaer, Sclar, Robison, Chin, Gill, Okamoto and Nakahiro, 1993). Patients with non-insulin-dependent diabetes mellitus (NIDDM) comprise approximately 90% of the diabetic population. An estimated 10-30% of patients with NIDDM withdraw from their prescribed regimen within 1 year of diagnosis, and of the remainder, nearly 20% administer insufficient medication to facilitate an adequate reduction in blood glucose. Beckles, Engelgau, Venkat-Narayan, Herman, Aubert and Williamson (1998) did a population-based assessment of the level of care among adults with diabetes in the U.S. Only 3% of insulin users and 1% of non-users met all five of the American Diabetes Association standards in the previous year. Kamiya, Ohsawa, Fujii, Nagai, Yamamouchi, Oshida and Sato (1995) did research on 570 diabetic outpatients using written questionnaires. The results revealed that approximately 30% of the patients did not implement the prescribed exercise regimen. Thompson, Cummings, Chalmers and Newton (1995) identified insulin error or manipulation in 42% of young adults. Diabetic ketoacidosis occurs more frequently in the young adult population than in any other age group. Abnormal insulin treatment behaviour is likely to be the major cause of ketoacidosis in this age group. In a study by Weissberg-Benchell, Glasgow, Tynan, Wirtz, Turek and Ward (1995), it was found that within the 10 days before their clinic visit, many adolescents admitted to engaging

in various mismanagement behaviors, with 25% admitting to missing shots. They point out that parents tended to underestimate adolescent mismanagement.

## **2.6 Antibiotics**

Antibiotics pose a particular problem , as disturbances in the taking of them not only lead to non-effectiveness of the treatment but to the patient building up an immunity to that particular antibiotic or class of antibiotics thus restricting and sabotaging future antibiotic treatment.

Where there has been sporadic compliance with several antibiotics at different times, a potentially dangerous situation could exist as very few antibiotics would be eventually effective for that particular patient.

Grob (1992) found that compliance with antibiotic regimens was poor in the community and he felt that this problem had become increasingly relevant as more patients were discharged early from hospital while still on medication.

Sclar et. al. (1994) studied compliance with short-term regimens of oral antibiotic therapy and found mean compliance rates of 80%, 69%, and 38% for administration once a day (QD), twice a day (BID), and three times a day (TID), respectively. al-Shammari, Khoja and al-Yamani (1995), looking at short-term antibiotic therapy among patients attending primary health centres in Riyadh, Saudi Arabia, found results suggesting that approximately two thirds of patients were compliant with their medications. Sunakawa, Akita, Iwata, Sato and Fujii (1995) carried out a survey in Japan to investigate compliance among children given oral

antibiotics in an outpatient setting. They found that approximately one-quarter of patients did not take their full course of antibiotics. They point out that the percentage in general falls when looking at maintenance or prophylactic antibiotics.

### **2.6.1 Prophylactic antibiotic therapy**

In splenectomized patients who are at risk of overwhelming infection and are advised to take life-long prophylactic oral penicillin; Keenan, Boswell and Milligan (1999), found that 58% of patients did not take their penicillin on the day studied. Goldstein and Sculerati (1994) in their research on compliance with prophylactic antibiotics for otitis media in a New York City clinic, found that less than half of the children attending an inner city clinic complied with maintenance medication. Berkovitch, Papadouris, Shaw, Onuaha, Dias and Olivieri (1998) found that compliance with prophylactic antibiotic therapy in children with sickle cell disease was highly variable and its evaluation problematic. Smyth and Judd (1993) assessed compliance with antibiotic prophylaxis after urinary tract infection in children, using a parent questionnaire, and a urine test for antibacterial substances. In (97%) cases, parents reported giving the antibiotics every day but only (69%) of urine tests were positive. Malfertheiner (1993) found problems in patient compliance with antibiotic therapy in *Helicobacter pylori* treatment.

## **2.7 Haemodialysis and renal transplant**

As has been seen above there has been non-compliance with relatively minor conditions and

also very serious and life threatening conditions, not only with preventative medicine but with actual treatment. Non-compliance with haemodialysis and renal transplant has almost immediate dire and serious consequences:

Non-compliance is known to be an important cause of late graft failure after renal transplantation (Hilbrands, Hoitsma and Koene, 1995). Warady, Mudge, Wiser, Wiser and Rader (1996) report on a transplant allograft loss in an adolescent patient as a result of medication non-compliance. Poor compliance with dialysis is a significant cause of dropout and morbidity (Latham, 1998; Amici, Viglino, Virga, Gandolfo, Da Ran, Bocci and Cavalli, 1996; Bame, Petersen and Wray, 1993)

Interestingly, Lin, Ko, Tsai and Chen ( 1995), found a higher rate of compliance in Chinese patients, as did Bleyer , Hylander, Sudo, Nomoto, de la Torre , Chen and Burkart (1998) in Japanese and Swedish patients.

## **2.8 Tuberculosis**

Tuberculosis has resurfaced as a "global emergency" in recent years not only in terms of increase in number of cases world-wide but also the emergence of the deadly multidrug-resistant tuberculosis. The World Health Organisation (WHO) has issued a call for the global community to step up its vigilance against the disease (Enarson, 2000). There were an estimated 8.3 million new tuberculosis cases in 2000 and the global burden of tuberculosis is growing. (Corbett, Watt, Walker, Maher, Williams, Raviglione and Dye, 2003).

Tuberculosis occurs mostly in the low income countries, over 90% of all cases arising there and over 95% of deaths from the disease occurring there (Enarson, 2000). However even in countries like the United States of America there has been a resurgence of the disease which is seen as a constant threat to the nation's health (Buchanan, 1997). Estimates of the global impact of tuberculosis indicate that it is the most frequent cause of death in the world from a single agent in young adults and that at least 20 million people have died unnecessarily from the disease in the 10 years preceding 2000 (Enarson, 2000).

Corbett et.al. (2003) point out that the increasing global burden of tuberculosis is linked to HIV infection and that the HIV pandemic presents a massive challenge to global tuberculosis control. Not only does HIV increase the risk of reactivating latent tuberculosis but it also increases the risk of rapid progression of the disease.

One of the most important causes of the world-wide increase in tuberculosis is non-compliance with control programmes (Pilheu, 1998; Rideout and Menzies, 1994). Tan (1995) points out that chemotherapy is the most powerful tool in the fight against tuberculosis and should be used with utmost care and under stringent conditions. It is not enough just to prescribe the correct medication, but more importantly, the patient must be closely monitored for compliance and progress. He stresses that any facility that provides for the treatment of tuberculosis must have a good working mechanism to detect the treatment defaulter and take immediate remedial action. Only then can a high standard of control of the disease be maintained and the prevention of the emergence of drug-resistant organisms (Tan, 1995).

There is also the twin problem of delay in seeking treatment, another potentially serious aspect

of non compliance, in fact life threatening in many conditions.

Rubel and Garro (1992) working in the treatment of tuberculosis found that fewer than half those beginning treatment completed it. One hundred and two (102) subjects at Mistassini Lake, Quebec, Canada who were prescribed preventive treatment between 1981 and 1991 were interviewed, of whom 33.7% were judged to have been compliant (Rideout and Menzies, 1994). Similar results were found by a number of different authors (King, Dorner, Hackett and Berry, 1995; Wong, 1995; Tansuphasawadikul, Poprawski, Pitisuttithum and Phonrat, 1998).

Non-adherence with the treatment of tuberculosis in children can be disastrous (Starke, 1999). Alperstein, Morgan, Mills and Daniels (1998) studied compliance with anti-tuberculosis preventive therapy among 6-year-old children. In the subsample of 44 children, only 59% attended all follow-up clinic visits, and 54% collected all 6 months of isoniazid prescribed.

Patient compliance in Africa, which has been a major problem in tuberculosis control before the HIV epidemic, has now become even more difficult as HIV patients are more prone to infections of any type (van der Werf, 1994). Wilkinson and Moore (1996) working in the Hlabisa Hospital, KwaZulu-Natal, found that HIV-positive patients with tuberculosis were three times more likely to fail to complete treatment than HIV-negative patients. (A tentative suggestion is given here with reference to one of the patients from a similar cultural background, interviewed for this study : As soon as the patient had been diagnosed with breast cancer she stopped taking her medication for high blood pressure as if the need for it had been taken away by the seemingly life threatening illness. It is possible that the same is true in the

mind of the patient with the dual diagnosis of HIV and tuberculosis).

## **2.9 HIV/AIDS**

Ekstrand and Chesney (2002) point out that the difficulty of enlisting patient adherence has been viewed as the most serious problem confronting medical practice with literature reviews estimating that only 1/3 of patients correctly follow physicians' directions. Scheduled appointments have been reported as missed 20-50% of the time, with approximately 50% of patients not taking their medications as prescribed. The increased attention to adherence in HIV/AIDS has reinvigorated the field of non-adherence studies and highlighted the role for social and behavioural scientists in the prevention and treatment of all diseases. Successful long-term treatment of HIV/AIDS requires at least 95% adherence to HAART (highly active anti-retroviral therapies) in order to prevent emergence of drug-resistant HIV variants that lead to regimen failure and limit options for future therapy (Chesney, 2003). Molassiotis, Nahas-Lopez, Chung, Lam, Li and Law.(2002) discuss this further, pointing out that sub-optimal treatment can lead to drug failure and facilitate selection of one or more resistance mutations; once the selection begins , it is difficult or impossible to stop resistance even with optimal treatment. Such resistance could create new strains of the virus, creating a dangerous public health situation and decreasing the success of available HIV treatments. They note further that failed HIV treatments present major cost implications for health care services, especially as a limited number of HIV-infected patients can have access to the expensive antiretroviral medication.

Ballester (2002) discusses the very sobering fact that though important advances in the field of pharmacological treatment of HIV infection patients have been produced, with the development of new and more potent antiretroviral drugs, researchers and clinicians report a high rate of problems related with adherence that invalidate benefits derived from medical advances. It is therefore of vital importance to study the problem of non-compliance as the psychological element in treatment is negating success.

Golin , Liu, Hays, Miller, Beck, Ickovics. Kaplan and Wenger (2002) found that on average, subjects took 71% of prescribed doses with over 95% of patients achieving sub-optimal (<95%) adherence with their HIV/AIDS medication. Simoni, Frick, Lockhart and Liebovitz, (2002) did interviews with a random sample of 50 primarily indigent, African American and Puerto Rican men and women at an outpatient (HIV) clinic in the Bronx, New York. Analyses revealed a generally high rate of adherence according to self-report data (i.e. on average, participants reported taking 85% of their medications over the last 3 days). However, adherence to the correct number of pills, dosing schedules, and special instructions was more problematic.

"The issue of adherence with medication is even more complex in the HIV patients compared to other chronically ill patients , as it is not uncommon for patients to receive as many as 30 or more tablets per day. These complex regimens require that patients remember which tablets to take , at what time and with what food, which might in itself be very difficult for many people living with HIV" (Molassiotis et.al., 2002, p.302).



### **2.9.1 HIV in Women**

Sixty-three HIV-positive women who were prescribed at least one antiretroviral drug in the last month were interviewed in their homes. Sixty-seven per cent reported taking all prescribed antiretroviral medication doses. One-third took a sub-optimal dose putting themselves at increased risk of treatment failure and the selection of resistant HIV strains (Durante, Bova, Fennie, Danvers, Holness, Burgess and Williams, 2003). Another study of adherence to medication in women with HIV was done by Erlen, Sereika, Cook and Hunt (2002). They found that adherence ranged from 60% to 75%. Murphy, Greenwell and Hoffman (2002)'s results are more serious. They studied HIV symptomatic or AIDS diagnosed women who had a young well child. Very poor rates of adherence to their antiretroviral drugs, too, were found, ranging from 43% (pill count assessment) to 56% (self-report of 3-day adherence to dose).

### **2.9.2 HIV in Childhood and Adolescence**

Steele and Grauer (2003) found that, consistent with much of the paediatric adherence literature, adherence to antiretroviral medications among children and adolescents appears to be frequently sub-optimal. Another study by Van Dyke , Lee , Johnson , Wiznia , Mohan, Stanley, Morse, Krogstad and Nachman (2002) of children with HIV found that overall, 70% of children reported full adherence and 30% reported non-full adherence. In fact, Murphy, Wilson, Durako, Muenz, and Belzer (2001) found adherence to be a serious problem among HIV-positive adolescents.

HIV treatment demands a compliance rate which far exceeds that described in the literature for any other medical condition. Researchers and staff at treatment centres are calling urgently for appropriate interventions to improve compliance, in fact, to eliminate non compliance totally.

## **2.10 Genitourinary Conditions**

Women discharged from a municipal emergency department with the diagnosis of pelvic inflammatory disease were surveyed by telephone about their compliance with a standard 10-day regimen of doxycycline. Of the 386 women who completed the survey, 31% reported complete compliance; 28% reported that they did not fill their prescriptions for doxycycline (Brookoff, 1994). In their investigation into the default rate at the Fife colposcopy clinic: Patterson , Roworth and Hill (1995) had findings which suggested that there are two distinct groups of defaulters: those who default initially but subsequently re-attend, and those who default completely.

Vanhegan and Wedgwood (1999a) found that in their data collected on young people there was a very low level of genitourinary medicine clinic attendance by the referred Brook Advisory Centre clients. Only 28.9% of adolescent males returned to the clinic for their scheduled follow-up care appointments for sexually transmitted diseases (Weinman, Smith and Buzi, 1996).

## **2.11 Ophthalmic Conditions**

In one hundred glaucoma patients who were being followed in a setting emphasizing correct usage, fifty-nine reported they had not used their eye-drops precisely as prescribed (Patel and Spaeth, 1995). In Bour, Blanchard and Segal (1993)'s study of patients with primary open-angle glaucoma, they found that sixty-eight per cent of these patients confirmed strict compliance with the treatment prescribed. Gurwitz, Glynn, Monane, Everitt, Gilden, Smith and Avorn (1993) found substantial non-adherence to be common in the elderly suffering from glaucoma.

Gower, Stein and Turner (1994) found the incidence of non-compliance to be 55%, 84%, and 91% for three lens care system regimens. Up to 80% of contact lens complications can be traced to poor patient compliance with recommended lens care guidelines (Ky, Scherick and Stenson, 1998).

## **2.12 Neurological Conditions**

Researchers have found problems in compliance with anti-epileptic medication (Cramer, Vachon, Desforjes and Sussman (1995); Gomes M da & Maia Filho H de, 1998). In Sri Lanka, Seneviratne, Gunatilake, Adhikari and De Silva (1998) found that of the patients with epilepsy interviewed, 24.8% were presently driving a vehicle, and of them 51% were riding a motorcycle. In Nigerian epileptics, Ogunniyi, Oluwole and Osuntokun (1998) found that (25.5%) were compliant with therapy. A very high default rate of over 88% was noted in

cerebral palsy (CP) patients attending a child neurology service, in Nigeria. (Iloeje & Ejike-Orji, 1993). On a less serious but potentially debilitating note, Steiner, Catarci, Hering, Whitmarsh and Couturier (1994) give the warning that if migraine prophylaxis does not work, one should think about compliance.

### **2.13 Psychiatric Conditions**

Compliance with conventional antipsychotic medication is often poor, with many patients discontinuing treatment only a few months after commencing therapy. This is a great contributor to recidivism, or the "Revolving door syndrome" (Naber, 1999; Delaney, 1998). In depressed patients treated with fluoxetine or amitriptylin, studied by Demyttenaere, Van Ganse, Gregoire, Gaens and Mesters (1998), 37% had an adherence of less than 70%.

Leung and Heimberg (1996) found problems with homework compliance in the cognitive-behavioral treatment of social phobia.

In substance abuse after-care group therapy participation levels are often low (Lash and Blosser, 1999).

### **2.14 Dental and Peridontal**

In the dental situation particularly, the aspect of post traumatic stress and stressful situations are relevant. It is widely accepted that children and in fact people of all ages tend to avoid the

dentist due to trauma or pain that has been experienced, even vicariously from friends or siblings. Blinkhorn (1993) found that compliance with dental surgery based health education programmes was often disappointing.

Supportive periodontal therapy is needed for the success of periodontal therapy. It is known, however, that cooperation is poor and a matter of concern (Novaes, Novaes, Bustamanti, Villavicencio, Muller and Pulido, 1999 and Tan, Powell and Seymour, 1992).

## **2.15 Health Practices**

In terms of preventive services, Ornstein, Musham, Reid, Jenkins, Zemp and Garr (1993) point out that despite an emerging consensus as to which preventive services are appropriate, a minority of patients receive them.

Hand-washing is one of the most important control measures for preventing the spread of bacteria. Guinan, McGuckin-Guinan and Severeid (1997) have documentation that adults and health care workers have a compliance rate of only 50% with this basic control measure.

Preventive measures in eating habits should in principle be able to curb the incidence of Travellers Diarrhea but compliance of travellers is usually poor (Castelli, Beltrame & Carosi, 1998). One of the major problems faced by eye injury prevention programs in the military is the low compliance among individual soldiers with eye armor use (Wong & Seet, 1997).

Pregnant women are not always careful with their health and with various risk factors

(Dujardin, Clarysse, Criel, De Brouwere & Wangata, 1995). Many women continue to smoke and drink during pregnancy despite the warning labels (Jones-Webb, McKiver, Pirie and Miner, 1999; Hankin, Firestone, Sloan, Ager, Sokol and Martier, 1996). In studies among pregnant women in Indonesia with an iron-supplementation program, it was concluded that compliance was a major problem (Schultink, van der Ree, Matulessi & Gross, 1993; Ridwan, Schultink, Dillon & Gross, 1996).

van Valkengoed, Boeke, van den Brule, Morre, Dekker, Meijer and van Eijk (1999) studied systematic home screening for Chlamydia trachomatis infections of asymptomatic men and women in family practice by means of mail-in urine samples. They found that 33% of invited males (1809/5464) and 50% of females (2751/5541) sent in the study material.

## **2.16 Immunization**

Lopreiato and Ottolini (1996) did an assessment of immunization compliance among children in the Department of Defense health care system in the USA. They found that the overall immunization rates were 84%. However, only 50% of adolescents were up-to-date, primarily because of failure to receive booster doses of measles-mumps-rubella vaccines. Jones, Fasher, Hanson, Burgess, Isaacs, Joshi, Blanch and Byrne (1992) found that only 70% of children had received their diphtheria- tetanus-pertussis (DTP) and poliomyelitis immunization at the appropriate time, 13% had completed the schedule later than recommended and 17% had immunizations overdue by 4 weeks or more. Joffe and Luberti (1994) found that parents reported their child's immunization status incorrectly in 23% of cases.

Wilkinson, Morath, Bennett, Burgess and Isaacs (1996) worked with an accelerated schedule of hepatitis B vaccination in high-risk youth. Participants were often elusive, needing multiple attempts to establish contact. Twenty (50%) of the 40 completed three immunizations. In Kottenhahn, Rosenthal and Biro's (1996) study, however, on Hepatitis B vaccine completion among adolescents, seventy-one percent completed the series. The four-dose oral typhoid vaccine strain Ty21a should be taken every other day before meals, and kept refrigerated between doses. Rahman, Barr and Hilton (1993) studied the use of this in a New York state travel immunization facility. Non-compliance with one or more of these instructions was seen in approximately 30% of travelers.

## **2.17 Malaria**

In a stable malaria zone in Burundi, Van Bortel, Barutwanayo, Delacollette and Coosemans (1996) reported on the use of impregnated mosquito nets sold at a promotion price. They found that the purchase of a bed net did not necessarily mean that people would use them. About 30% of the bed nets bought at the promotion price could not be found and most of them were resold in the neighbouring country (Tanzania). Between 7% and 47% of the bed nets were still packed and not in use.

Reported malaria prophylaxis use by tourists to East Africa revealed that only 52% admitted to taking their chemoprophylaxis without any missed doses (Behrens, Taylor, Pryce and Low, 1998). Chatterjee (1999) found the same problem with travellers to India. In South Africa, Durrheim, Gammon, Waner and Braack (1999) found that only 30% of travellers to the

Kruger National Park reported using anti-malarial drugs both regularly as prescribed and for 4 weeks after leaving the malaria area. Froude, Weiss, Tanowitz and Wittner (1992) studied imported malaria in the Bronx in a review of 51 cases recorded from 1986 to 1991. In nine of 13 patients who received prophylaxis, there was inadequate dosing or poor compliance. Individuals born in regions endemic for malaria are at high risk of acquiring malaria on return to their countries of origin and are less aware of the need for malaria prophylaxis than are other travelers. In studying the changing pattern of imported malaria in British visitors to Kenya 1987-1990; Pryce, Behrens and Bradley (1993) found that compliance with chemoprophylaxis was poor, with only 16% of cases using currently advised regimens. Faye, Mar, Diop, Gaye, Bah, Dieng, Dieng, N-Dir and Diallo (1997) evaluated malaria chemoprevention among 359 pregnant women attending a health center in Dakar. They found that 64.6% of these patients assume compliance to antimalarial chemoprophylaxis.

## **2. 18 Geriatric**

There seem to be a particular set of problems, which will be discussed later, among geriatric patients. Levine and Tideiksaar (1995) studied personal emergency response systems and the factors associated with use among older persons. They found that less than 50% of the subscribers were found to be fully compliant. Schulz, Kruse and Meier-Baumgartner (1995) found evidence of intentional and unintentional non-compliance with pharmacotherapy in nearly three-quarters of the geriatric patients attending a German clinic.



## 2.19 Other Conditions

Non-Compliance has been reported and studied in a variety of other illnesses and conditions such as: cystic fibrosis (Conway, Pond, Hamnett, and Watson, 1996), leprosy, (Kannan and Sivaram, 1992), burn rehabilitation, (Johnson, Greenspan, Gorga, Nagler and Goodwin, 1994), and rheumatoid arthritis, (Taal, Rasker, Seydel and Wiegman, 1993), and other rheumatologic diseases (Gerster, 1993).

Non-compliance has also been reported as a major issue in growth hormone therapy (Skinner, Clayton, Addison & Price, 1995; Smith, Hindmarsh, and Brook, 1993), with children treated for amblyopia, (Woodruff, Hiscox, Thompson and Smith, 1994), and children treated nonsurgically for vesicoureteral reflux (Wan, Greenfield, Talley and Ng, 1996). In a Swedish study on compliance in teenagers with coeliac disease, good knowledge of coeliac disease and dietary treatment was found in 87% of children and dietary compliance was 81% (Ljungman & Myrdal, 1993).

Nastasi, Villani, Falconi, Loguercio and Coltorti (1994) studied nutritional problems in cirrhotic patients. They found that at the long run control all patients tended to return to their previous alimentary habits, neglecting, in the course of time, the diets they had been prescribed.

In the treatment of venous ulcers, 67% of patients were found to be less than compliant (Erickson, Lanza, Karp, Edwards, Seabrook, Cambria, Freischlag & Towne, 1995). In the oral

maintenance treatment of melioidosis, only 50% of patients complied with the 20 weeks' treatment regimen and poor compliance proved the most significant risk factor for subsequent relapse (Rajchanuvong, Chaowagul, Suputtamongkol, Smith, Dance & White, 1995). In selective population chemotherapy with oxamniquine in Ethiopia, Birrie, Abebe and Ayele (1995) found that some 76% of the persons completed the total dose.

A few conditions apart from those cited above, apparently show strict compliance. Silvestri, Hufford, Durham, Pearsall, Oess, Weese-Mayer, Hunt, Levenson and Corwin (1995) found that their study population of infants at increased risk of sudden infant death syndrome had excellent compliance.

### **2.19.1 Allergen**

Many patients do not complete the recommended 3 to 5-year course of multiple allergen immunotherapy (Rhodes, 1999). Tinkelman, Smith, Cole and Silk (1995) found that there was a much higher rate of noncompliance in those who received their injections in facilities outside the allergist's office.

### **2.19.2 Hormone Replacement Therapy**

Hormone replacement therapy (HRT) is perhaps the most important development in preventive medicine in the Western world for half a century, yet long-term compliance is notoriously poor. Studd, Panay, Zamblera and Leather (1996) found that up to 75% of women

who start on HRT are reported to drop out within the first 6 months. Torgerson, Donaldson, Garton, Reid and Russell (1993) found that compliance with HRT after screening for women with low bone density was 48% for postmenopausal women and 59% for women with a simple hysterectomy.

## **2.20 General Follow up and Patient Behavior**

Kiefe and Harrison (1993) followed-up appointment-keeping in patients discharged from a General Medicine Inpatient Service. A compliance rate of 60% with first follow-up appointment was found.

An interesting result was found by Adams and Thompson (1996), in that almost half of the patients who presented to the Emergency Department and supplied home telephone numbers gave telephone numbers at which they could not be reached in follow-up, avoiding, somehow, the situation.

A study with very different and, unfortunately, unusual results was done by Murray and LeBlanc (1996). Working in Canada, they examined the percentage of outpatient clinic appointments kept after referral from the emergency department. Overall, 81.7% of appointments were kept. Orthopedic surgery had the best compliance rate (86.7%), gynecology the poorest (60.6%). They note that the compliance rate at VGH is higher than any found in studies of similar American hospitals.

## 2.21 Medicines

Thormodsen, Fonnelop, Rytter and Torisen (1997) did a study on unused medication returned to pharmacies. Drugs used in cardiovascular and respiratory diseases constituted the largest part of the medication returned, both with respect to value and to volume. A similar study, done by Kamaruzaman, (1995), on unclaimed prescriptions, found that vitamins, anti-inflammatory and antibiotic drugs were predominant.

## 2.22 Summary

The above has highlighted the extensive problem of medical non compliance which pervades every aspect of medical science and is relevant to every age group, some being more 'at risk' such as adolescence and old age. It runs across different cultures, nationalities and racial groups and even genders. There is an extensive body of research covering the problem and the cry from the medical personnel that even when a disease can be prevented, cured or controlled, some 'imp of the perverse in the patient himself' (Mennenger, 1938, p. 5) mitigates against it.

What is this 'imp of the perverse'? Is it only the patient him or herself? Is it his society, his/her family, his/her culture, his/her financial circumstances ? Is it a lack of education or understanding of that education? Is it due, as Kessels (2003) reports due to instant forgetting? Is this instant forgetting related to medical trauma? As Kessels points out, the more anxiety and stress, the more forgetting.

The call has come from researchers and staff at treatment centres working with HIV/AIDS, a call for effective interventions to improve compliance, in fact, to eliminate non-compliance completely. HIV/AIDS treatment demands a compliance rate far above that which is presented in the medical conditions here. To make any real headway with treatment as opposed to the danger of the opposite to the individual and society, successful interventions have to be offered.

In this section the extent of the problem has been highlighted in various medical fields as a background to the study of oncology and to make it clear that the problem is universal. The problem of non compliance is apparent in both life threatening and chronic disease of which cancer is both. It is shown that non compliance ranges from 15-93% but averages around 50%. It runs through the most critical of conditions to the most minor. An effective intervention and understanding in the field of non compliance in the oncology setting could well be used and researched in the general medical setting. Further research will be suggested in this direction.