Psoriasis is a well known chronic, non-contagious skin disorder since ancient times. The word “Psora” is a Greek word meaning “To itch”. It is notorious for its chronicity in its natural course and difficulties in the management. Although great efforts have been tried in medical researches for decades, it is still not curable and its exact aetiology remains unknown.

Prevalence in Chinese

In Western literature, it is well reported that 1-3% of the Caucasian population have psoriasis. Though it is a common skin disease, the prevalence reported in Chinese is lower than that of Caucasians. From the limited resources available, it is estimated that psoriasis occurs in about 0.1-0.3% of the Chinese population.\(^1\)

In 1984, a nation-wide screening of psoriasis had been conducted in 24 regions (53 centres) of China, involving a coverage of 6,617,917 population. About 11,393 cases of psoriasis (0.123% among the population studied; range from <0.1% to >0.3%) had been reported. Interestingly, the prevalence is highest in the Northeast provinces and lowest in the Southern ones where there is more sunshine. It is also higher in cities than the villages.

In Hong Kong, the prevalence is estimated to be approximately 0.3% of the total population.\(^2\) It is the 5th leading new cases of skin disorders in public dermatology clinics, with more than 600 new cases annually.

Immuno-pathogenesis of Psoriasis

Despite its unknown aetiology, there have been breakthroughs in the understanding of the immuno-pathogenesis of psoriasis in recent years. It is now almost certain that psoriasis is a T-lymphocyte mediated inflammatory dermatosis with hyper-proliferation of keratinocytes in genetically predisposed subjects (Diagram 1). It is regarded as one form of immune-mediated inflammatory diseases (IMID), which is a term designated for organ-specific diseases in which cells and cytokines of the adaptive immune system cause tissue inflammation or destruction.

Until recent years, it was believed that IMID was either mediated by Th1 T-cells (which is stimulated by IL-12) or TH2 T-cells. The former subset includes psoriasis, rheumatoid arthritis, multiple sclerosis and inflammatory bowel diseases, while the latter subset includes atopic dermatitis and asthma. A new pathogenic concept in IMID however is developed upon the discovery of a new T-cell lineage in 2005. This new cell lineage is called Th17 T-cell, which is defined by the production of IL-17, and stimulated by IL-23. This subset likely includes psoriasis, rheumatoid arthritis, multiple sclerosis and inflammatory bowel diseases. IL-12 and IL-23 are structurally related with a common 40kD subunit (p40), which leads to the development of a new group of biologics called anti-P40 (anti-IL12/23) that blocks both the Th1 and Th17 pathways.

Co-morbidities of Psoriasis

The traditional belief about psoriasis is that it is a cutaneous disease without visceral involvements, albeit 10-30% of the patients have joint involvements. This concept is challenged in recent few years when more and more systemic co-morbidities had been reported. When the term “psoriasis and co-morbidities” is searched in Medline, more than 200 articles can be retrieved over the past two decades. It is one of the hottest research topics in dermatology in the past 5 years, as shown by the numerous publications from different countries and different indexed journals. The possible co-morbidities of psoriasis reported in literatures are summarised in Table 1. Three important areas which may have impacts on medical health are worth mentioning here.

- Cardiovascular diseases (hypertension, myocardial infarction), cerebrovascular and peripheral vascular diseases
- Metabolic syndrome (obesity, diabetes mellitus)
- Non-alcoholic fatty liver
- Autoimmune diseases (Crohn’s disease, ulcerative colitis, multiple sclerosis)
- Lymphoma, melanoma, non-melanoma skin cancers
- Depression, suicide
- Smoking, alcoholism
- Osteoporosis

Table 1. Possible co-morbidities of psoriasis reported in literatures
1. Cardiovascular Diseases

Gelfand JM, et al. had published an article on JAMA in 2006 concerning the risks of myocardial infarction in patients with psoriasis.7 They had conducted a population-based cohort study using data collected by general practitioners participating in the General Practice Research Database in the United Kingdom from 1987-2002. A total of 556,995 control patients and patients with mild (n = 127,139) and severe psoriasis (n = 3,837) were studied, and controlled for traditional cardiovascular risk factors (diabetes mellitus, history of myocardial infarction (MI), hypertension, hyperlipidaemia, smoking). They found that the adjusted relative risks of MI are 1.54 (1.24-1.91) and 7.08 (3.06-16.36) respectively in mild and severe psoriasis as compared with controls.

Xiao J, et al. had published another article in J Eur Acad Dermatol Venereol in 2009 about the prevalence of myocardial infarction in patients with psoriasis in central China. Data were collected from the medical records section of five hospitals in the Mainland between 1999 and 2007.4 After adjusting for systemic therapies and other known cardiovascular risk factors in addition to age and sex, they found that the odds ratio (OR) of having an MI were 1.72 (95% CI, 1.29-2.30) and 2.01 (95% CI, 1.45-2.79) respectively in mild and severe psoriasis.

Related to the cardiovascular co-morbidities, Ludwig RJ, et al. had published an article in Br J Dermatol in 2007 concerning psoriasis as a possible risk factor for the development of coronary artery calcification (CAC).5 They found a significantly increased prevalence (59.4% vs. 28.1%, P = 0.015) and severity (CAC score according to Agatston 3.7 vs. 0.0, P = 0.019) of CAC in patients with psoriasis vs. controls. Multiple linear regression calculations identified psoriasis as a likely independent risk factor for CAC.

2. Metabolic Syndrome (diabetes mellitus, hypertension, hyperlipidaemia & obesity)

Sömmer DM, et al. had published an article about the prevalence of the metabolic syndrome in patients with moderate to severe psoriasis in Arch Dermatol Res. in 2006.2 They had investigated a total of 581 adult patients hospitalised for plaque type psoriasis as compared to 1,044 hospital-based controls. A distinct pattern of chronic disorders was found to be significantly associated with psoriasis, including type II diabetes mellitus [odds ratio (OR)=2.48], arterial hypertension (OR = 3.27), hyperlipidaemia (OR = 2.09), and coronary heart disease (OR = 1.95). The combined presence of these conditions together with obesity, known as the metabolic syndrome, was clearly more prevalent in psoriasis patients (OR = 5.29).

In the cross-sectional study on association between psoriasis and the metabolic syndrome by Cohen AD, et al., published in J. Dermatology in 2008,7 it had demonstrated that psoriasis was associated with the metabolic syndrome (OR = 1.3, 95% CI = 1.1-1.4), ischaemic heart disease (OR = 1.1, 95% CI = 1.0-1.2), diabetes mellitus (OR = 1.2, 95% CI = 1.0-1.3), hypertension (OR = 1.3, 95% CI = 1.2-1.5) and obesity (OR = 1.7, 95% CI = 1.5-1.9). This study included 16,851 patients with psoriasis and 48,681 controls.

3. Lympho-proliferative Diseases

Gelfand JM, et al. had studied on the risks of lymphomas in psoriasis and published in J Invest Dermatol. in 2006.8 Their study used large population-based cohort data collected from the General Practice Research Database in the United Kingdom (1988-2002), involving 153,197 psoriasis patients and 765,950 control patients without psoriasis. The adjusted relative risks in Non-Hodgkin’s lymphoma, Hodgkin’s lymphoma, T-cell lymphoma and all lymphomas in severe psoriasis were 0.73, 3.18, 10.75 and 1.59, indicating that there is higher risks of lymphomas in patients with psoriasis.

Possible Mechanistic Links Between Psoriasis and its Co-morbidities

The link between chronic inflammation and metabolic and vascular disorders is now increasingly recognised. It is postulated that proinflammatory cytokines (such as tumour necrosis factor-alpha) involved in the immune-mediated or inflammatory pathway may contribute to atherogenesis, peripheral insulin resistance, and hypertension. Macrophages and adipocytes also share common features such as expression of cytokines, FABPs, and nuclear hormone receptors, which may contribute to obesity.9

Many studies had reported that various IMIDs, including psoriasis, are at higher risks of developing systemic co-morbidities. IMIDs may cause these co-morbidities through shared genetic risks, common environmental factors, or common inflammatory pathways that are co-expressed in IMIDs and target organs.10

As mentioned in previous paragraphs, psoriasis is now classified as an IMID of the skin with T-cell mediated pathogenetic pathways and involvement of various inflammatory mediators. This may similarly predispose to the increasingly reported associated co-morbidities. The potentially systemic nature of the inflammatory processes in the pathogenesis of psoriasis has thus led to the postulation that it may be considered as a systemic disease, rather than a pure cutaneous disease.

Is Psoriasis Really an Independent Risk Factor for These Co-morbidities?

Despite increasing reports from difficult countries supporting the association of these co-morbidities of psoriasis, there were skeptical views about their true causal relationship. Nijsten T and Wakkee M. had written an excellent and critical commentary in J Invest Dermatol. 2009 Jul issue about the complexity of the association between psoriasis and its co-morbidities.11

Although these studies did involve very large data base, their designs were not without shortcomings and pitfalls. Most of them are observational studies which were not primarily designed for the detection of these co-morbidities. Diagnostic bias and detection bias were unavoidable.

Moreover, many confounding factors may be involved in these co-morbidities, as illustrated in Diagram 2. For example, psoriasis itself may lead to impaired health-
related quality of life (HRQOL) such as depression, anxiety and stress, which may result in an unhealthy life style leading to alcoholism and chronic smoking. The presence of arthropathy may lead to lack of exercise. The well known side-effects of some systemic antipsoriatic drugs may also count, such as acitretin may cause hyperlipidaemia and cyclosporine may cause hypertension. All these confounding factors may contribute to the cardiovascular diseases and metabolic syndrome. Conversely, obesity and smoking may increase the risk of developing psoriasis as reported, while drugs like lithium in treating manic-depressive illnesses and certain beta-blockers in treating cardiovascular diseases may also induce psoriasis.

Despite many studies that had supported the association of these co-morbidities, there are also inconsistencies in the findings in other studies.12

Finally, although in the supporting papers, most of the reported associations had reached statistical significance after statistical analysis, as they had involved very large data base, it is essential to know that statistical associations do not equate to causal relationships, and do not always have clinical relevancy.

Diagram 2. Schematic overview of possible confounding factors influencing the association between psoriasis and its co-morbidities (Modifie from Nijsten T and Wakkee M)11

**Conclusion**

Although there are increasing reports that psoriasis may have significant systemic co-morbidities, judging from the present evidences, causality has not yet been proven. Whether there is true causal relationship between psoriasis and these co-morbidities is still uncertain and open to debate. Upgrading psoriasis to an systemic disease obviously will have significant impacts on the management of this chronic disease, such as more aggressive treatments, routine screening of the co-morbidities, and possibly healthcare resources reallocation. Therefore, until more well proven evidences are available, it is still more appropriate to regard psoriasis as a cutaneous disease at the moment. Nonetheless, psoriasis is definitely more than skin depth in its impact on the affected patients, in view of its physical and psychosocial impairments. It also reminds dermatologists the need to manage patients holistically as a whole, rather than just focusing on their skin.

**References**