CHAPTER 2

REVIEW LITERATURE

Part 1 Pain

1.1 Pain definition

As the definition of International Association for Study of Pain (IASP), pain is “an unpleasant sensory and emotional experience associated with actual or potential tissue damage” (Merskey & Bogduk, 1994). Pain is classified to acute pain, cancer-related pain and chronic nonmalignant pain. As the classification of period, the pain is divided in transient pain, acute pain and chronic pain.

1.2 Pain source

Pain can come from many site of body (Boissonnault, 1995; Fouquet, 2003; Goodman & Synder, 2000). It can be classified as the following:

1. Cutaneous pain is the pain from the body structure located in the skin and subcutaneous tissue. The point of pain can be clearly localized.

2. Somatic pain is divided in deep somatic, somatovisceral and somatoemotional (psychosomatic) pain (Bergman, Herrstrom, Jacobsson, & Petersson, 2002).

2.1 Deep somatic pain is pain from the injured structure located in the body such as periosteum, cartilage, neural tissue, muscle, tendon, ligament, joint capsule, and vessels.

2.2 Somatovisceral pain is pain from internal organ muscle pain. This pain interferes to the function of that organ and induces the symptom example; diarrhea, vomit or retch.

2.3 Somatoemotional (psychosomatic) pain is pain from the abnormal mood or stress.

3. Visceral pain is pain from visceral organ in trunk, thorax or abdomen. The point of pain can not be clearly localized because the visceral organs have the multisegmental innervation but a few nerve ending.

4. Referred pain is the pain far from the injured structure. It may come from deep somatic structure or visceral organ as for example; shoulder pain from heart disorder.

1.3 Classification of pain

Pain can be classified in many aspects. (Duarte, 1997; พงศ์การดี เจาฑะเกษตริน & คณะ). It can be classified by neurophysiologic mechanism, temporal aspects, regional affected and etiology.

Neurophysiologic mechanism classification

1. Nociceptive pain is the somatic or visceral pain. This pain occurs from noxious stimuli stimulating to nociceptor. The nerve impulse will propagate along the Aδ and C fiber and neural pathway to central nervous system.

2. Non- nociceptive pains are neuropathic and psychogenic pain. Neuropathic pain occurs from the irritation or disorder of neurological system. The pain character is stabbing, burning and electrical sharp pain. Psychogenic pain is the pain that can not be included in nociceptive and neuropathic pain. Its pain pattern is same as the body pain, called somatoform pain, but it does not relate or be explained by medical condition. This relates to psychological factor such as, abuse history, depression, personality disorder, and coping. Theses factors are the important role to this pain occurrence (Fauman, 1994).

Temporal aspects

Pain is divided by the periodical or chronicity of pain occurrence; acute pain, subacute and chronic pain. Acute pain is the recent onset pain relating to

the injury. Pain will spontaneously decrease according to the healing period. Normally, acute pain has the simple mechanism of pain, easy to diagnosis. The direct treatment to the injured area or cause of pain can resolve the problem effectively. Chronic pain is the pain continues for 3 months (IASP) or longer than 6 months (APA). Or it continues for longer than normal healing period.

For regional affected and etiology categories, they are classified by the pain site of body and the cause of pain respectively.

1.4 Chronicity of pain

Pain serves as an important alarm that warns us of threatened or ongoing tissue damage. The ability to sense pain keeps us alive and functioning. However, if pain is not resolved in the early state, it will be continue to subacute and chronic pain (Aronoff, 1999). Shipton divided chronic pain as; the malignant pain, central pain and peripheral pain causing from injury or disease, chronic pain from chronic disease e.g. diabetes mellitus or joint arthritis, and unknown cause chronic pain (Shipton, 1999).

The transition from acute to subacute pain

The transition from acute to subacute pain involves the initiation of two distinct types of sensitization: peripheral, or inflammatory, and central. Both type of sensitization usually occur together. The peripheral sensitization is the events that play out within the injured tissue itself beginning shortly following the injury. The inflammatory mediators sensitize nociceptor endings in the skin and deep tissue. It causes them to generate sensory impulses in response to stimuli. The results are tenderness of skin on light touch, soreness and aching of deep tissue on movement. Central sensitization is an abnormal degree of amplification of the incoming sensory signal in the central nervous system (CNS), particularly spinal cord. The trigger central sensitization cause a temporally increase in the synaptic strength of preexisting but previously subliminal spinal synaptic terminals. This drives the amplification of postsynaptic spinal neurons that signal pain to a conscious brain.

The transition from subacute to chronic pain

The time at which a prolonged pain be called chronic varies greatly with the specific condition and according to the physical status and age of patient. However, if acute and subacute pain relief is not obtained with in the normal healing period, it will turn to chronic. As the definition of IASP, chronic pain is the pain continues for 3 months (IASP). But as the APA chronic pain is the pain continues longer than 6 months (APA).

Whether or not the transition to chronicity involves a specific change in the underlying pain mechanism, this transition may be accelerated or exacerbated by behavioral responses of subacute pain. It will induce prolonged and exaggerated inactivity or by adopting an abnormal posture or gait. If these disability and pain maintain over time, they will contribute the emotional and cognitive response. The patients decrease the activity of daily living, the mobility or activities. They have functional dysfunction, autoimmune dysfunction and easy to suffer from disease. Sometimes they have the problem of insomnia or food taking, dependency on medication, care taker and health care system. Beside this, they will suffer from impaired interpersonal functioning, feel hopelessness or depression. It is very difficult to solve these problems with one dimension of health care (Johnson, October 1997; Niv & Synadino, 2005; Raj, 2000; Wall & Melzack, 1989). So, it is better to prevent the chronicity of pain.

1.5 Musculoskeletal pain: MSP

Pain can occur from the several system of body. Musculoskeletal system is the one of common source of pain. Brattberg et al reported that 21.8% of 321 samples were musculoskeletal pain (G. Brattberg, Parker, & Thorslund, June 1997). Musculoskeletal pain may result from the disease in musculoskeletal system such as neoplasm, congenital anomalies and metabolic disease. It may come from the degenerative or injury of the tissue of the body i.e. periosteum, cartilage, neural tissue,

muscle, tendon, ligament, and joint capsule (Fouquet, 2003). Clinical sign and symptom of MSP from musculoskeletal system disease differs from MSP from degenerative or injury (table 2.1) (Goodman & Synder, 2000; Lewis, 1992; Loth, 1996; Meadows, 1999). For the site of musculoskeletal involvement, ICD-10 (International Statistical Classification of Disease and Related Health Problems, tenth revision) presents the pain site of musculoskeletal system by quoting the site as following: (World Health Organization, 1992)

0 Multiple sites
1 Shoulder girdle: clavicle, scapula, acromioclavicular joints, glenohumeral joints, sternoclavicular joints
2 Upper arm: humerus และ elbow joint
3 Forearm: radius, ulna และ wrist joint
4 Hand: carpus, fingers, metacarpus และ joints between these bones
5 Pelvic region and thigh: buttock, femur, pelvis, hip (joint) และ sacroiliac joint
6 Lower leg: fibula, tibia และ knee joint
7 Ankle and foot: metatarsus, tarsus, toes, ankle joint และ other joints in foot
8 Other: head, neck, ribs, skull, trunk, และ vertebral column
9 Site unspecified

Table 2.1
Sign and symptom of musculoskeletal pain from musculoskeletal system disease and degenerative change

Sign and symptom of MSP from musculoskeletal system disease	Sign and symptom of MSP from degenerative change
1. History, cause and nature of symptom History and cause often does not clear and not associate to symptom. It cannot tell the cause or process of symptom.	1. History, cause and nature of symptom History is quite clear. It can show the mechanism of injury or the related factor.

Table 2.1
Sign and symptom of musculoskeletal pain from musculoskeletal system disease and degenerative change (cont.)

Sign and symptom of MSP from musculoskeletal system disease	Sign and symptom of MSP from degenerative change
2. Pain characters Deep aching, throbbing, cutting, or gnawing feeling may appear in unilateral or bilateral area.	2. Pain characters Pain is localized. Pain character are aching, cramping pain, dull, sore, heavy, or hurting. It often occurs in unilateral pattern.
3. Pain pattern and pain duration There is no certain pain pattern. It depends on the duration, severity and nature of disease in each time. Pain is commonly constant, severe pain and night pain.	3. Pain pattern and pain duration Pain may be constant or intermittent pain. It depends on the onset, acute or subacute or chronic state.
4. Aggravating factors The activities and postural change do not always effect to the symptom.	4. Aggravating factors Movement, activities, or postural change always associate to sign and symptom.
5. Reliving factors Rest, postural change or movement is not able to diminish pain. Sometime it may shortly reduce pain but not for long time.	5. Reliving factors Rest or avoidance of aggravating factor can reduce pain.
6. Symptom provocation and reduction The physical examination of musculoskeletal system does not always effect to the symptom.	6. Symptom provocation and reduction The physical examination of musculoskeletal system; palpation, stretching test, movement test, isometric

Table 2.1
Sign and symptom of musculoskeletal pain from musculoskeletal system disease and degenerative change (cont.)

Sign and symptom of MSP from musculoskeletal system disease	Sign and symptom of MSP from degenerative change
	resisted test or functional test is able to provoke or reduce pain.
7. Comorbidity symptom Frequently, symptom of other system will occur with musculoskeletal system such as fever, fatigue, weight loss, exhaustion or insomnia etc.	7. Comorbidity symptom Normally, no side symptoms appear.

As the above mention, musculoskeletal pain can be developed to chronic if it is not stop by early intervention. It is becoming increasingly apparent that certain mechanism may permanently establish the pain signal in the central nervous system. Consequently, it is much more difficult to turn off if the pain is allowed to persist for and indeterminate period. Chronic pain and its associated disability have a social effect of major proportion. The disruption of employment, family and society interactions, and individual integrity is enormous harmfulness.

In 1989, Brattberg et al reported that 40% of 666 complete respondents age 18-84 reported obvious pain. It showed that pain problem of more than 6 months duration was far more than short-lasting problem. Pains in the neck, shoulder, arms, lower back and legs were most frequent (G. Brattberg, Thorslund, & Wilkman, 1989 May). Picavet and Schouten studied 3,664 Dutch samples aged 25 years and over, they found that 74.5% reported musculoskeletal pain during the past 12 months. Point prevalence of musculoskeletal pain was 53.9% and 44.4% reported pain lasting longer than 3 months. The ranking of most frequently reported pain sites (based on point

prevalence) was lower back, shoulder, neck, knee, wrist/hand, higher back, hip, elbow, ankle, foot. Furthermore, it showed that there was higher prevalence in women than men in all age group and majority of pain reported pain at more than one site pain. Seventeen to twenty seven percent reported the use of medicine during the last year. (Picavet & Schouten, 2003 Mar). This finding was the same as the study of Brattberg et al. They found that women tended to report severe pain more than men, wholly pain in back, hip and extremities (G. Brattberg et al., June 1997).

From the national health and nutrition examination survey in non-institutionalized civilian population of United Stage 25-74 years, it was found that 14.4% was chronic musculoskeletal pain patients (G. Magni et al., 1990). In 1993, this survey was repeated again and it showed that 32.8% of 2,341 samples suffered from chronic musculoskeletal pain. In pain group, there were significantly more female, older people and people with low income (G. Magni, Marchetti, Moreschi, Merskey, & Rigatti-Luchini, 1993). This finding was agreeed with the reviewing study of Harkness et al presenting that there was higher proportion of musculoskeletal pain in female (Harkness, Macfarlane, & Silman, 2005). A cross sectional survey of Bergman et al in 2,425 Swedish subjects completing questionnaire showed that the age and sex adjusted prevalence of chronic regional musculoskeletal pain (CRP) was 23.9% and of chronic widespread musculoskeletal pain (CWP) was 11.4%. And this pain associated with sociodemographic factors. Odds ratio (OR) for CWP showed a systematic increasing gradient with age and was highest in the age group 59-74 yrs (OR 6.36, 95% CI 3.85-10.50) vs age group 20-34 yrs. CWP was also associated with female sex (OR 1.91, 95% CI 1.41-2.61), being an immigrant (OR 1.83, 95% CI 1.22-2.77), living in a socially compromised housing area (OR 3.05, 95% CI 1.48-6.27), and being an assistant non-manual lower level employee (OR 1.92, 95% CI 1.09-3.38) or manual worker (OR 2.72, 95% CI 1.65-4.49) vs being an intermediate/higher nonmanual employee. OR for CRP showed a systematic increasing gradient with age and was highest in the age group 59-74 yrs (OR 2.22, 95% CI 1.62-3.05) vs age group 20-34 yrs. CRP was also associated with being a manual worker (OR 1.63, 95% CI 1.19-2.23) vs being an

intermediate/higher nonmanual employee (Bergman, Herrstrom, Petersson, Svensson, & Jacobsson, 2001).

Von Korff et al reported that the site-specific 6 month prevalence rates of musculoskeletal were 41% of back pain. Thirty seven percent of 1,016 samples were recurrent pain and 3.6%, 1.8% and 2.7% were severe and persistent pain with no activity limitation day, with 1-6 activity limitation days and more than 7 activity limitation days respectively (Von Korff et al., 1990; Von Korff, Dworkin, Resche, & Kruger, 1988). Elliott et al surveyed chronic pain (pain longer than 3 months) by postal self-completion questionnaires consisting of pain questionnaire and chronic pain grade questionnaire in 5,036 patients age 25 and over. Sixty one percent completed questionnaire. Fifty percent self reported chronic pain with women more likely than men. Back pain and arthritis were the two most commonly reported causes of chronic pain. And they found that 15.8% (228 patients) had pain graded as most severe (grade IV) (Elliott, Smith, Penny, Smith, & Chambers, 1999). While the other study found that 30% of 3,664 samples reported the limitation in daily life due to their musculoskeletal pain. The highest percentage (24.4%) with work leave was found for low back pain. (Picavet & Schouten, 2003 Mar).

1.6 Pain mechanism

1.6.1 Traditional Specific theory

Tissue injuries trigger the release of chemicals that give rise to an inflammatory reaction that in turn triggers pain signals to the brain. These signals, in form of electrical impulses, are carried by thin unmyelinated nerves called nociceptor (C fibers) that synapse with neurons in the dorsal horn of spinal cord. From the dorsal horn, the pain signal is transmitted via the spinothalamic tract to cerebral cortex, where it is perceived, localized, and interpreted (figure 2.1) (Brookoff, July 2000 ; Kaplan & Tanner, 1989; ราตรี สุดทรวง & วีระชัย สิงหนิยม, 2545).

Pain signal are transmitted to the brain by 2 main pathways. The lateral system (A) is made up of long thick fibers that transmit information about the onset of injury, precise location and intensity. They carry a rapid flow of pain signals to the thalamus to stimulate an immediate antinociceptive response. The medial system (B) is composed of phylogenetically older fibers. They carry slower signals and probably transmit information related to the persistence of injury and level of response induced.

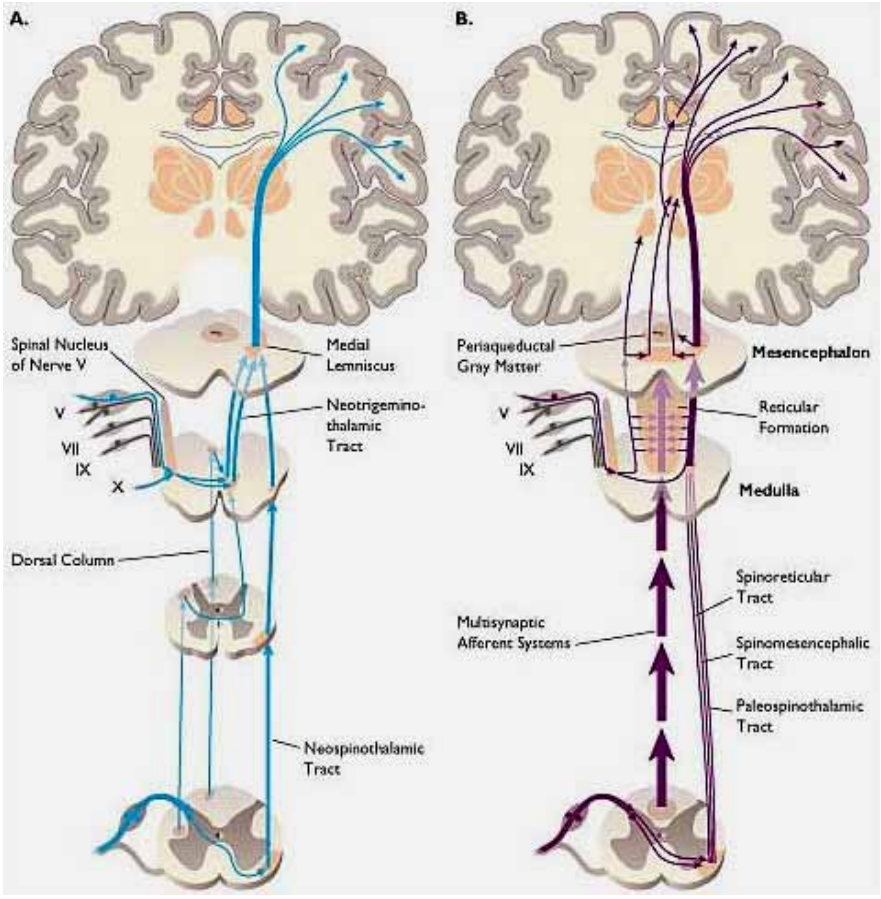

Figure 2.1

Spinothalamic tract pathway A) Neospinothalamic tract for fast pain B) Paleospinothalamic tract for slow pain (Brookoff, July 2000)

This complex nociceptive system is balanced by an equally complex antinociceptive system. Pain signal arriving from peripheral tissue stimulate the release of endorphins in the periaqueductal gray matter of the brain and enkephalins in the nucleus raphe magnus of the brainstem. The endorphins inhibit propagation of the pain signal by binding to μ-opioid receptors in the presynaptic terminals of nociceptors and the postsynaptic surfaces of dorsal horn neurons. The enkephalins bind to delta-opioid receptors on inhibitory interneuron in the substantia gelatinosa of the dorsal horn. It causes release of gamma-aminobutyric acid (GABA) and other chemicals that dampen pain signals in the spinal cord.

Spinal interneurons release dynorphin, which activates kappa-opioid receptors and leads to closure of N-type calcium channels in the spinal cord cells. These actions normally relay the pain signal to the brain. Following the release of enkephalins, spinal cord cells release other small molecules, including norepinephrine, oxytocin, and relaxin. These molecules also inhibit pain signal transmission.

1.6.2 Gate control theory

Gate control theory is the idea that physical pain is not a direct result of activation of pain receptor neurons, but rather its perception is modulated by interaction between different neurons. Without any stimulation, both large and small nerve fibers are quiet and the inhibitory interneuron blocks the signal in the projection neuron that connects to the brain. The "gate is closed" and therefore there is no pain. With pain stimulation, small nerve fibers (C fiber) become active. They activate the projection neurons and block the inhibitory interneuron. Because activity of the inhibitory interneuron is blocked, it cannot block the output of the projection neuron that connects with the brain. The "gate is open", therefore there is pain (figure 2.2 A).

But if non-painful stimulation by touch or pressure, large nerve fibers (Aβ fibers or Aα fibers) are activated primarily. This activates the projection neuron and it also activates the inhibitory interneuron which then blocks the signal in the projection neuron that connects to the brain. The "gate is closed" and therefore there is no pain (figure 2.2 B). Since the C fiber, the Aβ fiber also has an excitatory connection on the

projection neuron itself. Thus, depending on the relative rates of firing of C and Aβ fibers, the firing of the nonnociceptive fiber may inhibit the firing of the projection neuron and the transmission of pain stimuli (Kandel, Schwartz, & Jessell, 2000; Kaplan & Tanner, 1989; University of the West of England, 2004).

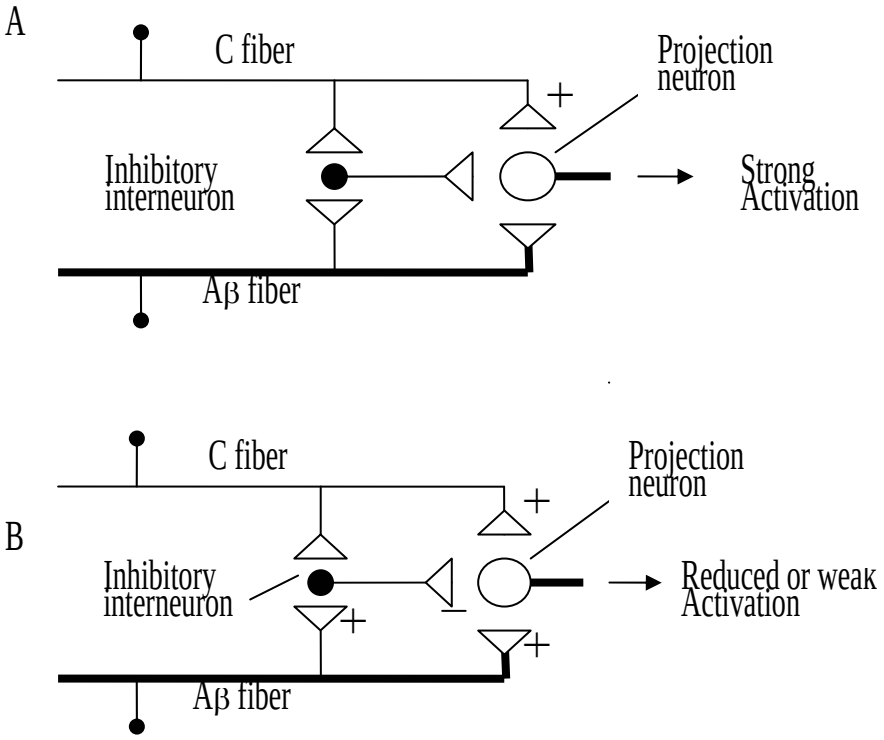

Figure 2.2

Gate control theory: - inhibition, + excitation

A) closing the gate B) opening the gate

1.6.3 Patterning theory

This theory based on the hypothesis that the perception of pain represents a temporal or spatial summation of the skin sensory input at the dorsal horn cells. While pressure alone is not perceived as painful, continual pressure may be quite painful. Pain also frequently occurs when the pattern of nerve impulses is disrupted by disease or injury. This concept is pain as having a cybernet effect. Initial peripheral stimulation transmitted centrally via the dorsal column of the spinal cord becomes self-sustaining.

Neuronal spinal cord firing is sustained, forming a loop or a reverberating circuit (engram). It no longer requires peripheral stimulation for pain perception. Phantom limb pain is the example of this phenomenon(Kaplan & Tanner, 1989; Wall & Melzack, 1989).

1.7 Chronic pain pathways (Brookoff, July 2000 ; Whitten & Donovan, 2005)

Chronic pain is not just prolonged version of acute pain. As pain signals are repeated generated, neural pathways undergo physiochemical changes that make them hypersensitive to the pain signal and resistant to antinociceptive input. The main neurotransmitter used by nociceptors synapsing with the dorsal horn of the spinal cord is glutamate, a versatile molecule. This molecule can bind to several different classes of receptors that most involved in the sensation of acute pain. AMPA (alpha-amino-3-hydroxy-5-methyl-isoxazole-4-propionic-acid) receptors are always exposed on afferent nerve terminals. In contrast, NMDA (N-methyl-D-aspartate) receptors are involved in the sensation of chronic pain. They are not functional unless there has been the persistent or large scale release of glutamate. Repeated activation of AMPA receptors dislodges magnesium ions that act like stoppers in transmembrane sodium and calcium channels of the NMDA receptors complex. The conformational change in the neuronal membrane makes these receptors susceptible to stimulation. This change is the first step in central hypersensitization and marks the transition from acute to chronic pain.

Activation of NMDA receptors can also cause neural cells to sprout new connective endings. This neural remodeling can add new dimensions to old sensations. The emotional component of pain may be increased. For example, if the new connections channel more of the pain signal to the reticular activating system of the brain. When that occurs, the signal's pathway into the cerebral cortex is more splayed and the pain signal more diffuse and difficult to localize. Furthermore, if the uncontrolled pain prolongs for months or year, it will have spread beyond the originally affected organ or dermatome.

1.8 Pain assessment

Pain assessment is detected by self report or observation of behavior. There are many scales for pain assessment. Some scales measure only pain intensity but some measure many dimension of pain (Abram & Haddox, 2000; Aronoff, 1999; Shipton, 1999). However, the assessment mostly is paid attention in pain intensity.

Pain intensity evaluation

The visual analogue scale (VAS) is common scale for pain evaluation because of their high sensitivity to pain change (Gramling & Elliott, 1992 Jan). Pain intensity is measured by put the mark on the line long 10 centimeters. The numeric is represented for this line is 1 to 10. The meaning of the pain intensity along the line is at the left end of line means “no pain” that equals 1 and at the right end of line means “pain as much as possible” that equals 10.

Another scale pattern is widely used is verbal descriptor (category) scales. They are pain rating scale such as mild, discomfort, distress, horrible, or excruciating. These scales are easy to assessment because it use the felling of person under word meaning. Beside, some scales use the numeric rating scale and graphic rating scale for pain evaluation.

Multidimensional pain evaluation

Mc Gill Pain Questionnaire is the example of pain measurement evaluating many dimension of pain. It presents pain intensity, pain character, pain pattern, and pain site. It provides quantitative information that can be treated statistically, and is sufficiently sensitive to detect differences among different methods to relieve pain (Ronald, 2005).

However, pain assessment in acute and chronic stage is quite difference. Aim of acute pain measurement is pain severity and duration for treatment planning. Because of simple problem of acute stage, pain assessment is simple too. But for chronic pain, not only the pain dimension or complication from pain but also the social and psychological sequelae that accompanying the pain have to be evaluated.

So the aims of assessment in chronic condition are pain dimension, physical disability or physical dysfunction in activity daily living, working, family and social interaction, and even psychological problem.

At the present, there is development of many questionnaires evaluating many dimension of problem, such as Oswestry Low Back Pain Disability Questionnaire. It measures the functional status and disability. It points to the activity daily living but not point to social or psychosocial dimension. For Roland-Morris Disability Questionnaire, it is developed from sickness impact profile with 136 questions. The aim of this scale is the assessment of the health status of chronic disease patient not for musculoskeletal problem. Million Visual Analog Scale (MVAS) is composed of 15 questions. It addresses the disability and physical function in chronic low back pain patient.

Anagnostis et al studied the psychometric properties among Pain Disability Questionnaire (PDQ) developed for all site of musculoskeletal pain, MVAS, Oswestry Low Back Pain Disability Questionnaire and Roland-Morris Disability Questionnaire (Anagnostis, Gatchel, & Mayer, 2004) . It is found that Test –retest reliability coefficients of PDQ, Oswestry, MVAS, and Roland-Morris were 0.94-0.98, 0.83-0.99, 0.92-0.97 and 0.72-0.91 respectively. And Cronbach's alpha coefficient of PDQ was 0.96. And the responsiveness of the PDQ as measured by Cohen's effect size statistic, ranged from 0.85 to 1.07, better than another questionnaires.

Besides this, there were the development of questionnaire for pain measurement, SF-36 bodily pain scale and Graded chronic pain scale. Both questionnaires measure pain severity, pain dysfunction and psychosocial dimension. There were the differences of reliability, validity, advantage and disadvantage between both scales (Von Korff, Jensen, & Karoly, 2000). SF-36 bodily pain scale was developed to evaluate general health status. The questions is consisted of pain intensity, physical function interfered with 4 weeks. This measurement is appropriate to collect the normative data. Its disadvantage is that the questions do not associate to pain intensity and cannot evaluate the chronicity and persistence of pain. Test –retest reliability

coefficients was 0.78 and Cronbach's alpha coefficient was 0.79-0.96. For graded chronic pain scale or graded classification of chronic pain, it was developed for measurement of the chronic pain severity, repeated pain and pain dysfunction in community context. Cronbach's alpha coefficient in back pain was 0.74 and in temporomandibular pain was 0.71. This scale was used in various population and difference context in many studies, the reliability and validity were good (Von Korff, Ormel, Keefe, & Dworkin, 1992).

Part 2 Depression

2.1 Depression

The International Statistical Classification of Diseases and Related Health Problem, Tenth Revision (ICD) categorized the psychological condition as the following: (World Health Organization, 1992; ปราโมทย์; สุคนิชย์ & มาโนช; หล่อตระกูล, 2541)

F00-F09 Organic, including symptomatic, mental disorders
F10-F19 Mental and behavioral disorders due to psychoactive substance use
F20-F29 Schizophrenia, schizotypal and delusional disorders
F30-F39 Mood (affective) disorders
F40-F48 Neurotic, stress-related and somatoform disorders
F50-F59 Behavioral syndromes associated with physiological disturbances and physical factors
F60-F69 Disorders of adult personality and behavior
F70-F79 Mental Retardation
F80-F89 Disorders of psychological development
F90-F98 Behavioral and emotional disorders with onset usually occurring in childhood and adolescence
F99 Unspecified mental disorder

Mood disorders or mood (affective) disorders are group of symptom with mood becoming unhinged continuously for weeks or months. Mood disorder is classified as depressive disorder and bipolar disorder. Depressive disorders come in difference forms, major depression, dysthymia, and atypical depression. Depression or depressive disorder is a syndrome (group of symptoms) that reflects a sad mood exceeding normal sadness or grief. More specifically, the sadness of depression is characterized by a greater intensity and duration and by more severe symptoms and functional disabilities than is normal. The symptoms are characterized not only by

negative thoughts, moods, and behaviors, but also by specific change in bodily functions. The functional changes are called neurovegetative signs (Panzarino, 2004; The Royal College Of Psychiatrists Of Thailand, 2004; อรพรรณ; ทองแตง, เกษม; ตันติผลาชีวะ, & สุดสบาย; จุลกทัพพะ, 2004).

2.2 Diagnostic Criteria for major depressive episode (DSM-IV) (American Psychiatric Association, 1994; Hales & Yudofsky, 1999; ปราโมทย์; สุคนิชย์ & มาโนช; หล่อตระกูล, 2541)

A. Five (or more) of the following symptoms have been present continuously 2 week period and present a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure. It does not include the clear symptom due to a general medical condition or mood-in congruent delusion or hallucination.

1. Depressed mood most of the day, almost every day. This is indicated by own patient or by other's observation.

2. Marked decrease of interesting or pleasure in all activities. This occurs most of the day, almost every day. This is indicated by own patient or by other's observation.

3. Significant weight loss without diet control or weight gain (e.g. a change of more than 5% of body weight in a month). Or there is decrease or increase in appetite almost every day.

4. Insomnia or hypersomnia almost every day

5. Psychomotor agitation or retardation almost every day. This is indicated by other's observation, not subjective feeling.

6. Fatigue or loss of energy almost every day.

7. Feeling of worthlessness or excessive or inappropriate guilt almost every day (not merely self-reproach or guilt about being sick).

8. Decrease of concentration or the ability to think or decision almost every day. This is indicated by own patient or by other's observation.

9. Recurrent thought of death (not just fear of dying), recurrent thought of suicide without a specific plan, or a suicide attempt.

B. These symptoms do not meet the criteria of mixed episode (both depression and mania)

C. These symptoms cause the patients with clinical significant distress, impairment in social, occupation, or important functions.

D. The symptoms do not directly result from physiological effects of substance e.g., medication or physical illness.

E. These symptoms must be cleared from the bereavement that the symptoms have not been present longer than 2 months after the bereavement.

2.3 Cause and factors related to depression (Davis, Klar, & Coyle, 1991; Panzarino, 2004; Sadock & Sadock, 2000; The Royal College Of Psychiatrists Of Thailand, 2004)

The occurrence of depression commonly relates to many factors. The combination of factors can induce or trigger depression such as, biological or genetic factor, environmental factor, chemical factors and mental factor.

2.3.1 Biological and genetic factor

Major depression seems to occur in generation after generation in some families. The one with the history of depression in family has the tendency to become depression than other without history of depression. Women are twice as likely to become depressed as men. Young adult and adult have the chance to become depress than other age group. It seems that maternal stress during pregnancy can increase the chance that the child will be prone to depression as adult, particularly if there is a genetic exposure.

2.3.2 Environmental factor

The external event or the situation in life time is the important factor

to trigger depress. A serious loss, major illness or injury, chronic illness, poor relationship in family or social, financial problem, or any unwelcome change in life patterns such as loss of job, divorce, children leaving home or retirement can trigger a depression.

2.3.3 Chemical factor

The depression appears to be associated with altered brain serotonin and norepinephrine systems. The serotoninergic system seems to play an important role in inhibition of other neurobehavioral systems. Norepinephrine was shown to be important in mediating the organism's arousal in response to meaningful environmental stimuli and was hypothesized to play an important role in learning and memory. Both of neurochemical are lower in depressed people.

2.3.4 Psychological factor

Psychological factor also contribute to a person's vulnerability to depression. The persistent deprivation in infancy, physical or sexual abuse, clusters of certain personal traits, and inadequate ways of coping (maladaptive coping mechanism) all can increase the frequency and severity of depression, with or without inherited vulnerability. Negative thinking also mediates the effects of parental bonding, everyday stressors, and self-esteem on depressive symptoms.

Depression is often occurred as episode, recurrent, or even chronic condition. The study of the prevalence in USA during 1981-1991 showed that mood disorder is very high prevalence. Life time prevalence of major depressive disorder in men and women were 5-12% and 10-25% respectively. It was found in young adult and middle age more than elderly and childhood (Sadock & Sadock, 2000). In Thailand, Department of Mental health, Ministry of Public Health reported that the rate of depression per 100,000 persons in 2004, 2005 and 2006 were 149.9, 140.55, and 185.98 respectively (Ministry of Public Health, 2004). In 2001, Preecha et al studied the prevalence of psychiatric disorder in 2,948 Thai population aged 15-60 years from Bangkok. The questionnaire modified from Diagnostic Statistical Manual of Mental

Disorders-4thedition and the Composite International Diagnostic Interview was used to interview the samples and then diagnostic. The result showed that the lifetime prevalence of manic depressive episode was 19.9% (ธรณินทร์ กองสุข et al., 2549 อ้างจาก นันทิกา ทวิชาชาติ และคณะ, 2544; ปรีชา อินโท et al., 2544). After that, in 2004 the prevalence of psychiatric disorder in 11,700 Thai populations aged 15-59 years selected by stratified three-stage cluster sampling from 4 region of Thailand and by stratified three-stage cluster sampling from Bangkok was studied by community based - mental problem screening and audit evaluation and Mini International Neuropsychiatric Interview (M.I.N.I.). The study revealed that the point prevalence of major depressive episode in term of ICD-10 was 3.2%; 2.5% for male and 4% for female (ธรณินทร์ กองสุข et al., 2549 อ้างจาก พรเทพ ศิริวนารังสรรค์ และคณะ, 2547; พรเทพ ศิริวนารังสรรค์, ธรณินทร์ กองสุข, สุวรรณา อรุณพงศ์ไพศาล, พันธ์นภา กิตติรัตนไพบูลย์, & อัจฉรา จรัสสิงห์, 2547)

The National Institute of Mental Health Collaborative Study of the Psychobiology of Depression (NIMH-CS) reported that 54% of patients with major depression recovered within the first 6 months of entry into the study. For 18% of those who were still depressed after 1 year recovered between then. As the study of Oquendo et al, it was found that 78 of 185 subjects with depression had once again incurred at the end of 2 years. (Treichel, 2004).

By using the Beck Depression Inventory (BDI) to screen for depression in the 1,250 general Spanish population aged 18 to 64 years, the study reported that 3.52% of subjects had the BDI score of $\geq$ 13 (probable case) but only 2.56% of subjects with was diagnosed a depressive disorder (Lasa, Ayuso-mateos, Vazquez-Barquero, Diez-Manrique, & Dowrick, 2000). From the study of Ovuga et al by using BDI in 2005, it was found that 36.4% of 939 respondents aged 18 and over had the BID score of 10-19 and 17.4% had the score of 20-39 (Ovuga, Boardman, & Wasserman, 2005). While Ansseau et al found that point prevalence of major depression was 11.0% and was significantly more frequent in women than in men. In addition to those founding, they reported the significant association between depression and several socioeconomic

factors such as living alone, low level education and unemployment (Ansseau et al., 2007).

The prevalence of depression in the Danish general population by using Major Depression Inventory (MDI) in April 2000 was studied by Olsen et al. The results showed that of 1,205 completed MDI participants, the prevalence of major depression was 3.3% in term of DSM-IV and 4.1% in term of ICD-10 depression. There were many factors associating to depression by univariate analysis. But for logistic regression model, traumatic events in the past year regard to personal life (OR 6.4, 95%CI 2.7; 15.5) and over consumption of alcohol (OR 3.2, 95%CI 1.5; 6.8) were significantly associated with major depression(Olsen, Mortensen, & Bech, 2004). Miller et al studied the prevalence of clinically relevant levels of depressive symptoms, they found that the prevalence of clinically relevant levels of depressive symptoms (CES-D score $\geq$ 9 on 11-item center for epidemiologic studies depression scale) in middle-aged African American was 21.1%. The factors having the largest association were lower social support, being hospitalized in the previous year, income insufficiency, decreased visual acuity and obesity (Miller et al., 2004).

2.4 Limbic System (University of Massachusetts Medical School, 2003; ราตรี; สุดทรวง, วีระชัย; สิงหนิยม, & 2545)

Limbic is the part of the brain in regard to basic instinct. It controls mood, behavior, memory and learning. In human limbic system will coordinate to other part of the brain, especially cerebral cortex, for instinct adaptation and behavior to the social context. If there is something wrong in this system, it affects to memory, learning, behavior and mood control. Limbic is the group of cells forming circle around the medial wall of cerebral cortex. It consists of: (figure 2.3)

Cerebral Isocortex, namely orbital and medial cortex of the frontal lobes, cingulated gyrus (frontal and parietal lobes), and parahippocampal gyrus (temporal lobe) that consists of pyriform cortex and entorhinal area

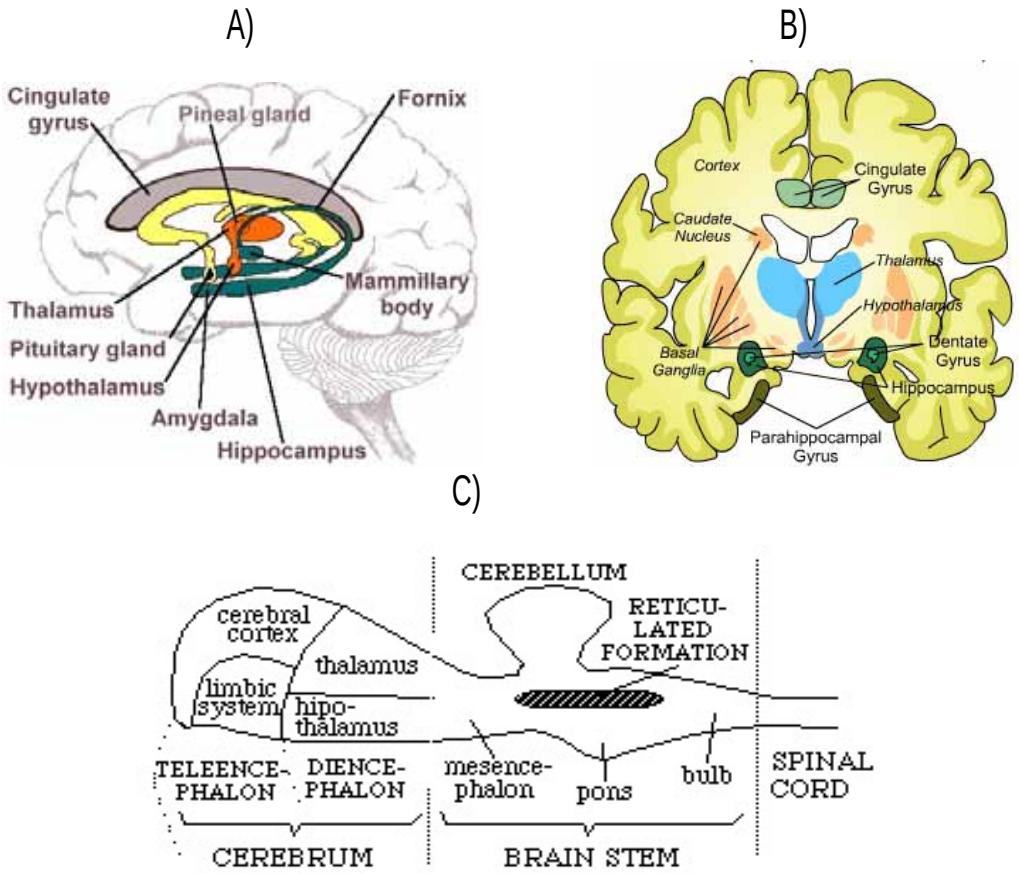

Figure 2.3

The anatomy of limbic system A) cross-sagittal section, B) cross-coronal section and C) diagram of limbic system (source: www.stanford.edu/.../basics/braintut/ab5.html, www.normandy.sandhills.cc.nc.us/psy150/brlimbic.html

Anterior perforated substance is one part in basal forebrain allocortex.

Septal and preoptic areas are the part of the brain connecting to hypothalamus and it is gray matter core of limbic system. Both structures have many cholinergic neurons of the nucleus basalis of Meynert that transmit the neuronal signal to hippocampal formation and isocortex. The experiment showed that if the septum was damaged, it stimulated the violent and fierce mood.

Hippocampal formation is the part of archicortex. It is composes of dentate gyrus, hippocampus proper, and subiculum. Hippocampus has many functions in many important systems e.g. endocrine system, memory and learning, autonomic nervous

system, and mood expression. The experiment in animal, it showed that if hippocampus nearly amygdala was stimulated, the animal will aggressive. But the animal was stimulated at hippocampus nearly septal area, it will calm down.

Septal and preoptic areas are the part of the brain connecting to hypothalamus and it is gray matter core of limbic system. Both structures have many cholinergic neurons of the nucleus basalis of Meynert that transmit the neuronal signal to hippocampal formation and isocortex. The experiment showed that if the septum was damaged, it stimulated the violent and fierce mood.

Basal ganglia consist of ventral striatum and amygdala. It controls mood behavior via hypothalamus. The stimulation to amygdala results in confusion, fearfulness, or aggressive behavior or in contrast; calm down and tameness. These behaviors depend upon the stimulated area of amygdala. Furthermore, the stimulation affects the autonomic nervous system and alters the respiratory rate, heart rate, blood pressure, and gastric juice gush in digestive system.

Diencephalon that is grouped in limbic system is mamillary body (group of cells in hypothalamus), habenular nucleus, pineal body (part of epithalamus), and anterior thalamus nucleus.

Fiber tracts that link to the limbic are Habenulointerpeduncular tract, Median forebrain bundle, Stria medullaris thalami, Stria terminalis, Diagonal band of Broca, Ventral amygdalofugal pathway. But the most important is Cingulum, Fornix, Mammillothalamic tract, and some parts of anterior limb of the internal capsule

From the study of neurophysiology, it is found that the knowledge from sensory stimulation is the role of neocortex (isocortex). And the feeling from sensory stimulation is the role of limbic system and hypothalamus that sets up the behavior patterns. So, when there is the unexpected situation, the neural signal will transmit to thalamus and then the signal will separate to 2 ways, one to cortex and the other way to hypothalamus. The signal transmitting to cortex is signal for experience knowledge. And the other transmitting to hypothalamus is for setting up of behavior pattern and expression of physical and mental simultaneous.

2.5 Hypothalamo-pituitary-adrenal axis (HPA axis) in normal condition

Blackburn-Munro (Blackburn-Munro & Blackburn-Munro, 2001) proposed the neural mechanical pattern in response to stress (figure 2.4).

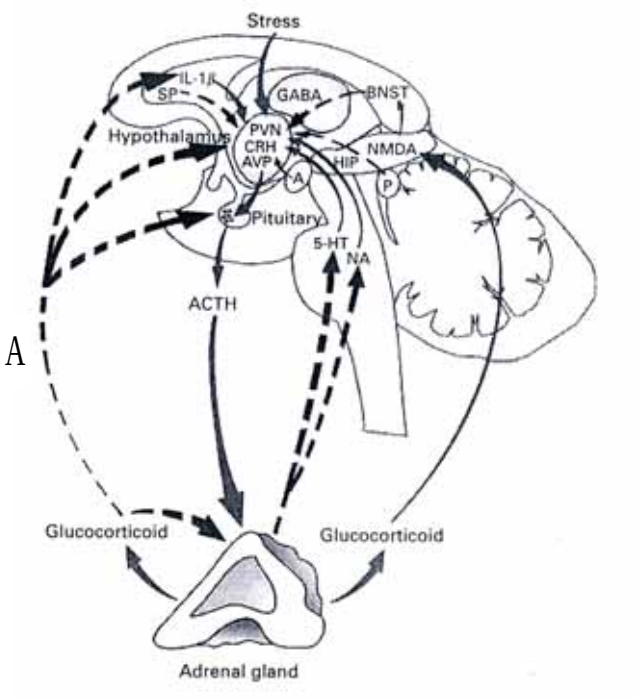

Figure 2.4

Neural mechanism of HPA axis: stimulatory pathways (thick line), inhibitory pathways (dot line), PVN:paraventricular nucleus,CRH: corticotropin-releasing hormone, AVP: arginine vasopressin, ACTH: adrenocorticotrophic hormone, HP: hippocampus, P: pineal gland, 5-HT: serotonin 5 HT, NA: noradrenergic, SP: neurokinin substance P, GR: glucocorticoid receptor (Blackburn-Munro & Blackburn-Munro, 2001)

A stressor can be defined as any stimulus that threatens normal homeostatic mechanism. Stressors are the events such as sudden changes in body temperature, prolonged undernourishment, illness, fear, worry, and pain. The neural signal from stressor transmits to hypothalamus (HPA axis) via the limbic system to activate the neurones in parvocellular division of PVN (paraventricular nucleus) containing CRH (corticotropin-releasing hormone) and/or AVP (arginine vasopressin).

CRH and AVP are then released to hypophyseal portal system and transported to anterior pituitary gland. CRH acts at the anterior pituitary gland to release ACTH (adrenocorticotrophic hormone) into systemic circulation. ACTH acts upon specialized receptors in the zona fasciculata of the adrenal cortex to initiate synthesis and release of the glucocorticoid hormone cortisol (in human and some other mammals) or corticosterone (in rat). Glucocorticoid hormone cortisol acting in the inhibitory pathway (dot line) exert a negative feedback influence at the pituitary to prevent further ACTH release, at the PVN to prevent further CRH and AVP release, and at the adrenal cortex to prevent further glucocorticoid hormone release. Additional negative feedback may be provided via both GR and the high affinity mineralocorticoid receptor acting within hippocampus (Shipton) to modulate glutamate (NMDA) stimulated activity of inhibitory GABAergic neurones within BNST (bed nucleus of the stria terminalis). The HPA axis may also be regulated by input from 5-HT (brainstem serotonergic), NA (noradrenergic neurones from the amygdala (A), by IL-1β (inflammatory cytokine interleukins-1β), all of which are in turn subject to negative glucocorticoid feedback. Additional postulated inhibitory inputs are provided by P (Pineal gland and SP (neurokinin substance).

2.6 Hypothalamo-pituitary-adrenal axis (HPA axis) in chronic stress or depression condition

Continued and prolonged stress may disturb the function of HPA axis. It results in negative feedback mechanisms are disrupted. The adaptive response of the HPA axis may then become maladaptive. From review many studies in animal with stressor e.g.: osmotic loading, dehydration, it was found that prolonged stress increased the level of CRH/CRH mRNA, AVP, corticosterone, and diminished the negative feedback. It also resulted in the cognitive deficit and behavior disturbance. The changes in HPA axis function during chronic stress in experimental animals parallel to data of clinical depression human; increase of CRH/CRH mRNA, AVP, cortisol, cognitive deficit, and behavior disturbance.

2.7 The evaluation of depressive disorder

The evaluation of the mental status can be acted by psychiatrist or by using the measurement tool. Many measurement tools have been developed to measure the physical behaviors representing to mental status. Sucheera mustered many Thai mental measurement that were developed or translated into Thai language (สุชีรา ภัทรายุตวรรตน์ , 2546) . A table 2.2 shows Thai psychological tools and their psychometric properties.
-From the comparison of all mental tools, the Heath-Related Self Report: HRSR, The diagnostic screening test for depression in Thai population of 20 items (Kasantikul et al., 1997) is appropriate to this study because 1) it is the screening test for depression in Thai population, 2) it can be used for all age range, 3) there is high sensitivity and specificity, and 4) there is the appropriate number of questions for community based-screening. The HRSR scale was modified from 39 most common depressed symptoms in Thai patients. It was developed appropriate items for depression in Thai people, pretested and then conducted for 2 years. The validity and reliability was studied in 5 medical centers in Bangkok for 405 patients aged 15-60 years. For 890 control subjects were collected from normal people in community having similar demographic distribution. The results showed that Cronbach's Alpha coefficient of HRSR scale was 0.91. Sensitivity was 90.2% and specificity was 85.3% (cut off point = 30). For cut off point = 25, Sensitivity was 75.1%, and specificity was 93.4%.

2.8 Health management for depression (Panzarino, 2004; Sadock & Sadock, 2000; The Royal College Of Psychiatrists Of Thailand, 2004)

2.8.1 Antidepressant Medications

Selective serotonin reuptake inhibitors (SSRIs) are medications that increase the amount of the neurochemical serotonin in the brain due to brain serotonin levels are low in depression.

Table 2.2
Thai mental measurement tools

Tool Developer	Measurement tool	Tool character	Measured variable	Psychometric properties	Application
Maj.Gen.Bunjong Suebsaman (Translation from A.M. McMillan)	Mental health measurement : Health Opinion Survey (HOS)	- 3 ordinal scale - 20 questions	- No mentioned - the question measures the stress condition effecting physical symptom	Cronbach's Alpha coefficient = 0.81	Community based - mental problem screening
Sucheera Phattharayuttawat, et al	Thai mental health measurement	- 5 ordinal scale - 70 questions	Five dimension of mental health i.e. somatization, anxiety, depression, psychotic, and social function	Cronbach's Alpha coefficient = 0.82-0.94	mental problem screening
Orapun Thongtang et al	Self complement survey handbook for depression in Thai elderly	- Yes or no scale - 9 questions	Depression as the diagnostic criteria of DSM-V	- Internal consistency reliability = 0.89-0.94 -Sensitivity= 2.14%, specificity = 7.56%	Community based – depression in elderly screening

Table 2.2
Thai mental measurement tools (cont.)

Tool Developer	Measurement tool	Tool character	Measured variable	Psychometric properties	Application
Duangjai Kasantikul et al	Heath-Related Self Report: HRSR, The diagnostic screening test for depression in Thai population	- 4 ordinal scale - 20 questions - self complement	Symptom of depression	-Cronbach's Alpha coefficient = 0.91 - Sensitivity = 90.2%, specificity = 85.3% (cut off point = 30) - Sensitivity = 75.1%, specificity = 93.4% (cut off point = 25)	Community based - depression screening
Brain rehabilitation group	Sadness measurement in elderly	- True or false scale (0,1) - 30 questions	Symptom of depression	Reliability = 0.93	Community based or elderly clinic based depression screening
Manote Lotrakul et al	Self complementary questionnaire for depression severity evaluation	- 4 ordinal scale - 20 questions	Depression symptom	- Cronbach's Alpha coefficient = 0.858 - Concurrent validity (spearman-Brown) = 0.7189	Depression severity evaluation

2.8.2 Electroconvulsive therapy (ECT)

ECT is used for the patients that cannot uptake or do not respond to antidepressants, or have severe depression and are at high risk for suicide. And it is effective for the patients who antidepressant medications do not provide sufficient relief the symptom.

2.8.3 Psychotherapy

There are many forms of treatment including talking therapy, cognitive/behavioral therapy, and psychodynamic therapy. Talking therapy helps the patients understand and realize their problems and resolve the problems by talking with the therapists. Cognitive/behavioral therapy will focus on the patient's disturbed personal relationships that cause depression by advising them changing the negative style of thinking and behaving that are associated to depression. They will learn how to more satisfaction and rewards through their own actions and unlearn the behavioral patterns that contribute their depression. These therapy techniques may be used for individual patient or group of patients and family. And it will be more useful when combination to social skill training for the case with social interaction problem. Psychodynamic is the technique that focuses on resolving the patient's internal psychological conflicts that are typically thought to be rooted in childhood.

2.8.4 Education for patients and family for environmental adaptation

- Always arrange the physical activity for patients
- Avoid the noisiness and poor environment that contribute depression
- Establish the familiar environment by adjusting the house environment and the person in the house
- Encourage the patient to do the easy activity by house member
- Always arrange the recreation for patients
- Don't highly expect from the patient for do everything
- Have the positive thinking to the patient, give the good speech, and should not blame them

Part 3 Chronic pain and Depression

Frequently, there is the comorbidity of chronic pain and depression. While, there is the comorbidity of acute pain and anxiety. Raj (2000) proposed three patterns of the relationship between chronic pain and depression as following: 1) Depression or personality disorder is antecedent to chronic pain, 2) Depression or anxiety is consequent to chronic pain, and 3) Coincidence of chronic pain and other condition such as somatoform pain disorder, factitious disorder that can't be explained by medical condition (Raj, 2000). Now critical to understanding of the causative relation between chronic pain and depression is the question of the chronology of pain, Rush et al reviewed many studies about the relationship of chronic pain and depression. They reported that 15 of 15 previous studies showed that depression followed the onset of pain-the so-called "consequence hypothesis", while 3 of 13 studies showed depression preceded the development of pain- the so-called "antecedent hypothesis" (Fishbain, Culter, Rosomoff, & Rosomoff, 1997; Rush, Polatin, & R.J., 2000).

Underlie comorbidity of chronic pain and depression may be contributed by the nociceptive and HPA axis interaction (figure 2.5). Central to coincidence or consequence hypothesis is the concept that the chronic stress evoked by chronic pain leads to loss of negative glucocorticoid feedback on the HPA axis (figure 2.4) and results in a positive drive on the axis and down regulation of the glucocorticoid receptor within the brain and periphery (line 1). Inflammation and nerve injury stimulate noci-responsive neurones within the dorsal horn of the spinal cord, and the relay of nociceptive information ascends to the brainstem to be gated within the hypothalamus prior to its cognitive appraisal within the somatosensory cortex (line 2). Monoaminergic neurones in the brain stem normally descend to the spinal cord to act as a break on nociceptive transmission. During chronic pain, loss of monoaminergic tone in response to glucocorticoid-induced monoamine depletion may lead to reduced descending inhibitory impulses to the spinal cord to effect an enhancement of pain sensation (line 3). Loss of glucocorticoid inhibition of pro-inflammatory cytokines leads to proliferation of

peripheral inflammatory events, contributing to pain sensitization (line 4). Although acute stress is analgesic (implying an inhibitory circuitry between the limbic and somatosensory cortices), chronic stress evoked by

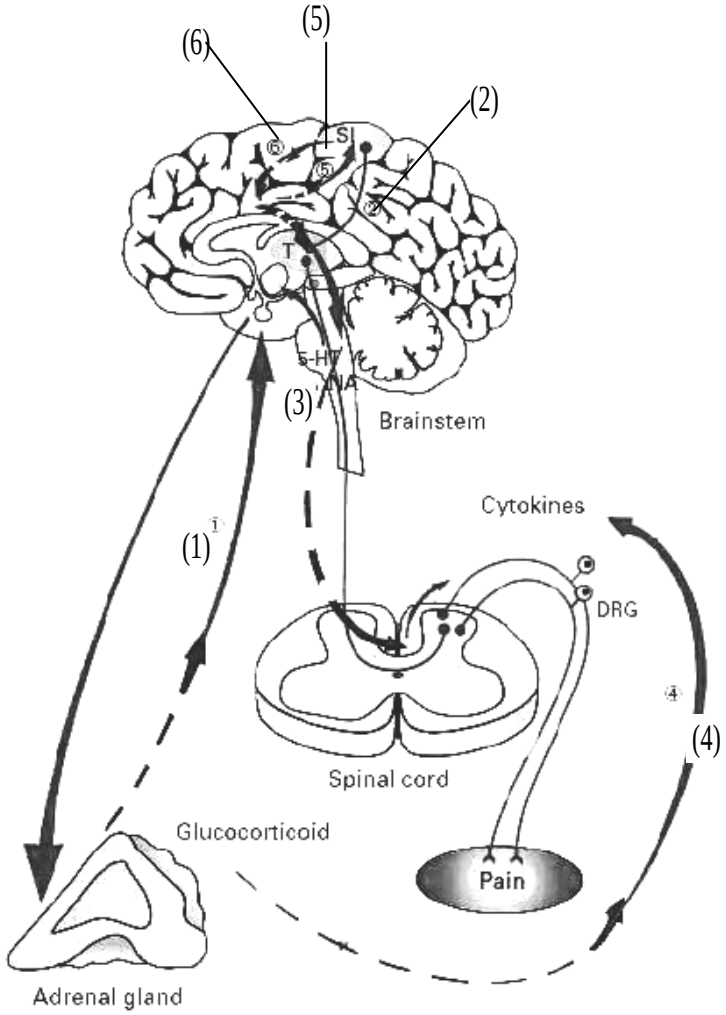

Figure 2.5

Neural mechanism interaction between nociceptive and HPA axis: DRG, dorsal root ganglion; 5HT, 5-hydroxytryptamine; NA, noradrenaline; SI, somatosensory cortex; T, thalamus (Blackburn-Munro & Blackburn-Munro, 2001)

chronic pain may lead to down-regulation of glucocorticoid-mediated activity of this inhibitory connection, leading to enhanced pain perception (line 5). Similarly, although acute pain is mood enhancing via both sympathetic and glucocorticoid routes (implying

an excitatory reciprocal link between the somatosensory and limbic cortices), chronic pain –induced down regulation of glucocorticoid-modulation of this link may lead to depressed mood (Line 6) (Blackburn-Munro & Blackburn-Munro, 2001).

There were the studies for the relation of chronic pain to depression in clinic and community context. Von Korff et al reported the result from the study of chronic pain in 1,016 patient attending at Center for Health Studies, Group Health Cooperative of Puget Sound, USA that 1) 41% of all patients was chronic back pain and almost with grade V pain level, 26% was headache, and 17% was abdominal pain; 2) pain status was not associated with age but was associated with gender, low household income, lower levels of educational attainment, and unemployment, and high family stress; 3) the percentage receiving an algorithm diagnosis of major depression measured by 60-item version of the Hopkins Symptom Checklist-Revised (SCL) increased from 2% among no-pain persons to 5% among grad II pain persons, and to 20% among grade V pain persons, 4) graded pain status was strongly associated with the number of health care visits by in the year after interview, the mean number of health care visits per year was 4.0, 4.4, 5.0, 6.8, 4.9, and 9.5 for persons with no pain, grade I pain, grade II pain, grade III pain, grade IV pain, and grade V pain respectively (Von Korff et al., 1990).

In 1990, Magni et al reported the data from NHANES I (National Health and Nutrition Examination Survey I) that 14.4% of 3,023 subjects age 25-74 years suffered from chronic pain. In pain group, there were significantly more females, older people, and people with a lower income. Mean CES-D score (the Center for Epidemiologic Studies Depression scale), percentage CES-D score of $\geq$16 (23.6%) and $\geq$20 (18.3%) in the chronic pain group was significantly higher than that of subjects without chronic pain. The variables more linked to CES-D score of $\geq$16 and $\geq$20 were female sex, lower income, race other than white, and presence of chronic pain (G. Magni et al., 1990). These findings were correspond to their epidemiologic follow-up study in 2,341 subjects aged 32-86 years in 1993 which showed that in pain group there were significantly more females, older people and lower income. The chronic pain group reported a significantly higher mean score than no-pain group on the CES-D. Logistic regression analyses

showed the variables that emerged with a significant link to a CES-D cut-off of 16 were presence of chronic pain, female sex, not being married, low income, low education, and a race other than white (G. Magni et al., 1993).

In 1993, Leino and Magni reported the data collected from 2,653 employees (white-collar and blue collar worker) of the Vaimet metal industry plants, Central Finland since 1973, 1978, and 1983. The multiple regression analysis showed that the musculoskeletal morbidity indices were used as predictors of the development in the stress symptoms of score (SSS) and the depressive symptoms score (DSS). While SSS was a good predictor of the 5-year development in both musculoskeletal symptoms and clinical findings in the men group. Although DSS showed the similar results but it was less consistent than SSS. It was discussed that this might be from the limitation of the non-specific instrument to assess depressive symptoms (Leino & Magni, 1993).

Prospective study on the relationship between depressive symptoms and chronic musculoskeletal pain in 2,324 subjects with completed data both at the NHANES I (National Health and Nutrition Examination Survey I) and its follow-up study showed that the odds ratio derived on the basis of a risk of 1 for the non-depressed subjects provided a value of 2.14 for the depressed. Logistic regression of socio-demographic variables and of chronic pain on development of depression (CES-D $\geq$16) showed that chronic pain is the variable which best predicted depression, especially neck/back pain and hip pain. On the other hand, logistic regression of socio-demographic variables and of CSE-D score on development of chronic pain also showed that depressive symptoms significantly predicted the development of chronic musculoskeletal pain. The odd ratio for the prediction of depression by chronic pain was 2.85 (G. Magni, Moreschi, Rigatti-Luchini, & H., 1994)

The cross-sectional study of data from a U.S. national household survey conducted in 1997-1998 showed that 5.71% of 9,585 respondents was depression. Of 9.79% was depression with at least 1 pain symptom of arthritis/rheumatoid, chronic back problem, chronic severe headache, or other chronic pain condition. The depressed patients with comorbid pain were and average of tens years older than those without

pain (46.6±0.7 compared with and 36.6±0.6) and were significantly more likely to be married, to have less education, and to have a much lower average annual family income than those without pain. Furthermore, the patients with pain also had much lower mental health inventory scores than those without pain. Health care use data showed that 20% of depressed patients with comorbid pain used the health service at least one time per year by using complementary and alternative medicine rather than mental health specialty (Bao, Sturm, & Croghan, May 2003).

In 2004, Currie and Wang studied the prevalence of chronic back pain, major depression and the association between depression and chronic back pain from Canadian community health survey in 118,533 Canadian populations. It showed that 9% was chronic back pain. The individuals with chronic back pain were on average older, less educated, and more likely to be female. Of 19.8% of chronic back pain was depression. But in total, about 1.8% of the Canadian adult population was estimated to have both chronic pain and major depression. This was more likely to be female, single, and younger group. The rate of major depression in persons with back pain increased with higher self-reported pain severity. Persons with major depression were more likely to be in the low income group. After controlling for the influence of other known risk factors, the presence of chronic back pain was the strongest predictor of major depression among all the variables examined in selected participants (Currie & Wang, 2004). The comparative study between the 20 patients with chronic pain associated with head and neck cancer and the 20 patients with chronic pain associated with temporomandibular disorder showed that there was a statistical significance correlation between the level of depression and the intensity of chronic pain (r=0.483). The levels of depression were progressively higher in accordance with the degree of severity of the chronic pain (Tesh, Denardin, Baptista, & Dias, 2004). Both studies were correspondent to the study of Benjamin et al, a population-based case-control study in random samples age 18-65 years. They also found that estimated prevalence of mental illness was 11.9%. The chance of mental problem occurring in the chronic widespread pain

patients was 3.18 times to non-chronic widespread pain patient (Benjamin, Morris, McBeth, Macfarlane, & Silman, March 2000).

A population-based, cohort study was conducted in Saskatchewan, a Canadian province. A survey was mailed to 2,184 random samples of 593,464 residents aged 20-69 years and listed in the HIRF (Health Insurance Registration File) on August 31, 1995. They were followed up survey at both 6 and 12 months. Two outcome variables; Pain onset and pain severity, and depressive symptom were measured by 7-item Chronic Pain Questionnaire and the Center for Epidemiological Studies Depression Scale (CES-D) respectively. Eleven hundred and thirty one subjects (approximate 51%) completed baseline questionnaire. Fifty two percent of 1,131 completed the 12 month follow-up period and 14% reported the onset of troublesome neck or low-back pain during the study year. Those with scores on the CES-D over 16 were almost twice as likely to develop troublesome pain as those with scores under 16 [adjusted hazard rate ratio (HRR) 1.87% (95%CI: 1.10 to 3.19)]. Those in the highest quartile of depression scores (greater than 12) had almost four times the risk of pain onset those in the lowest quartile [adjusted HRR 3.97 % (95%CI: 1.81 to 8.72)]. Using the scores of the CES-D, the crude HRR between depression and the onset of troublesome neck or low-back pain was 1.06 (95%CI: 1.03 to 1.08). This showed that depressive symptomatology was a strong and independent predictor of the onset of an episode of neck or low back pain that was intense, disabling or both (Carroll, Cassidy, & Cote, 2004).

Boersma and Linton (Boersma & Linton, 2005 Nov) studied the interrelationship between pain intensity, psychological variables, and function across three stages in the development of a chronic pain problem in 204 Swedish age 20-60 years. A total 197 subjects returned a filled out questionnaire but only 184 (90%) had completed data. Members of group 1 (N=48) had pain duration < 1 year (median 6 months), group 2 (N=47) had pain duration 1-3 years (median 2 years), and group 3 (N=89) had pain duration >3 years (median 9 years). The persons with pain duration > 3 years reported significantly higher levels of current pain intensity, more frequent pain, and lower levels of function than person with pain duration 1-3 years and <1 years. The

result showed no significant differences between the groups on the psychological variables. However, they found that depression was significantly correlated with pain intensity in the groups with pain duration < 1 year and 1-3 years.

Thirty-six thousand, nine hundred, and eighty four respondents aged 15 years or over were randomly selected from Canadian Community Health Survey data. Five disorders of psychological variables; major depressive disorder, bipolar disorder, social phobia, agoraphobia, and panic disorder, and list of chronic condition had been evaluated. The results showed that major depression prevalence in all musculoskeletal condition was higher than other psychological disorders. The prevalence of depression was lower in subjects with arthritis or rheumatism (5.0%) than in those with back pain (6.2%) or fibromyalgia (13.4%). In a logistic regression model, main effects for age and sex were significant, all of the psychiatric conditions tend to decline in prevalence with age , the mood and anxiety disorders were more common in women (Patten, Williams, & Wang, 2006).

The study in 97 female patients with diffuse musculoskeletal pain more than 3 months duration and 85 healthy controls showed numerical rating scales of anxiety and depression were significantly higher in patients than in controls. The three step multiple regression analysis demonstrated that age was not a significant predictor of numerical rating scales of anxiety and depression(Huber et al., 2007).

One thousand and twenty nine participants completing the questionnaire were included in the study of Munir et al (Munir et al., 2007). All of them were identified the chronic illness using the International Classification of Disease. Two of 17 different groups of chronic illness were musculoskeletal pain (31%) and depression/ anxiety (14.8%). Both groups were generally younger than the other participants and reported their illness symptoms to be more severe than other groups. Those with depression/anxiety reported higher level of education and higher scores in work limitation compared with all other groups, followed by those with musculoskeletal pain.

Part 4 Chronic Musculoskeletal Pain Management

It is important to have adequate management of any underlying specific musculoskeletal disorder. Such management could include disease modifying drugs and pharmacological treatment of nociceptive and neuropathic pain. Pharmacological treatment (analgesic, antidepressants, and anticonvulsants) is often of lower value than non-pharmacological intervention (physical exercise and patient education with cognitive approach, preferably given in combination within a multi-professional rehabilitation programme) when pain is non-specific, chronic or widespread (Bergman, 2007; Geffen, 2003). Standard acute pain treatment have only limited efficacy in treating chronic pain. So the variety alternative techniques are developed to treat chronic pain including behavioral intervention, physical manipulation, electrotherapy, biofeedback, psychotherapy, and exercise programme. As the pain is chronic, the focus of treatment should not be on passive treatment techniques that deny patient control over their own physical health. The focus of treatment should be on helping patients to regain control over their lives by active participation in their pain therapy programme and independent management of their pain such as self-management techniques or active modalities: exercise (Aronoff, 1999; Bergman, 2007). The health provider should be act as only a motivator, a challenger, and educator. A meta-analysis of 65 studies clearly demonstrated that patients with chronic pain who participate in multidisciplinary pain programme consistently show improvement in pain, mood, psychological functioning, return to work, and health care utilization. The multidisciplinary pain programme being useful consists of medical management and education, physical therapy and reconditioning, occupational therapy, psychiatric and psychological management, education and support group, family involvement and intervention and education, vocational rehabilitation and return to productive activities, and relapse prevention. However, program should create the individual treatment plan because it was demonstrated to be more efficacious than the package of treatment (Buse, Loder, & McAlary, 2005).

Strawbridge et al studied the result of physical activity on the risk of subsequent depression for 1,947 subjects age 50 years and older (Strawbridge, Deleger, Roberts, & Kaplan, 2002). The physical activity included frequency of long walk, exercise, sports, and swimming. The results showed that low and medium physically activity subjects were more likely to be depressed than were those with high activity. Physical disability showed a strong association with depression, since subjects who reported such impairment were four times more likely to be depressed than were subjects with no mobility impairment (OR=4.02). Female and subjects with fewer than 12 years of education were more likely to be depressed , as were those who reported financial strain or neighborhood problems. Furthermore the longitudinal association between physical activity and incident depression showed that physical activity was protective for subsequent depression.

Sullivan and others studied the result of the pain-disability prevention (PDP) program (activity structuring, activity planning, graded activity involvement, cognitive restructuring and problem solving) in the patient with musculoskeletal pain and concurrent symptoms of depression in 2007 (Sullivan, Adams, Tripp, & Stanish, 2007). They showed that PDP program which focus on the reduction of psychological barrier to return-to work was able to reduce the BDI-II score (Beck Depression Inventory-II) in the early chronic pain and chronic pain group. The pain severity moderately decreased in early chronic pain group while pain severity slightly increased in chronic pain group. However the changes in pain severity were significantly correlated with change in depressive symptoms. Furthermore, for participants in early chronic group, pain symptoms showed greatest reduction in the last 5 weeks of the program, which depressive symptoms showed greatest reduction in the first 4 weeks of program, in other word, depressive changed before pain symptoms.

The study sample of 143 individuals aged 20-67 years with chronic musculoskeletal pain (> 3 months) participated in a 57 week long multidisciplinary rehabilitation programme at a rehabilitation center in central-Norway. The multidisciplinary rehabilitation programme consisted of; period 1 intensive training,

individual exercise programme with focus on endurance, strength, mobility and relaxation technique for 5 weeks, group-based education/training in difference health related subjects, and indoor-outdoor activities everyday; period 2 continuing of period 1, individual counseling, and work ability preparing; during/after finishing the rehabilitation period, exercise group was added in the participant's local community. The data were collected at the start of programme, after 5 weeks of intensive training, at the end of 57 week programme, and at a1 year follow-up after the end of programme. The results showed that 100% completed the 3 points in time but 51% completed at the 1 year follow-up. During 57 week programme period and 1 year follow-up, pain intensity and pain experience significantly ($p<0.01$) decreased from the start of programme to the one year follow-up. During 57 week, there were significant long term improvement (trend over time) in cognitive, physiological, psychological capacity and significant reduction in both anxiety and depression score measured by the Hospital Anxiety and Depression Scale (HADS). Furthermore, functional health status significantly increased on the variables feeling, daily activities, social activities, and overall health from baseline to the end of the 57th week of programme. But one year after the programme compared to the 57th week, the participants reported a decrease in physical fitness and social activities (Lillefjell, Krokstad, & Espnes, 2007).