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VAN DIE REDAKSIE : EDITORIAL

THE ASSESSMENT OF PAIN

Pain is a subjective phenomenon. Its assessment is difficult because one person cannot feel the pain of another person. The investigator has therefore to depend on the patient or the experimental subject for his description of pain, in order to assess its intensity and determine the efficacy of therapy. There are investigators who believe that the assessment of analgesic drugs can only be properly made in man, and that much of the data obtained from studies on laboratory animals are of doubtful value. However, the use of animals excludes many of the problems arising in clinical trials in man, such as suggestibility, placebo responses, and bias on the part of the observer and the patient. A doctor knows that the intensity of a patient's pain is affected by many influences, including the doctor-patient relationship.

The double-blind technique has been regarded as a sound practical control device for dealing with the possibility that conscious and unconscious bias may distort the observed effects of drugs. The administration of inactive tablets at the same time as pharmacologically active tablets is of great importance in clinical trials. The term 'dummy' instead of 'placebo' is preferred for the inactive tablet, and was defined by Gaddum as a counterfeit object intended to have no effect. It has often been assumed that the inactive drug, the dummy, and the placebo are identical, but this is not the case. Placebos have great power, exhibited not only in subjective change but manifested also in objective alteration. The effect can be produced not only by drugs but also by situations and by individuals. The effect is greater when stress is present and severer, than when it is absent. The enthusiastic physician can produce not only subjective effects but also objective effects, far greater than the sceptic.[1,2]

There is at present no electrical recording technique or any other objective index which can be correlated specifically and reliably with the perception of pain.[3] It is the subject's report or signal that marks the end point for pain, whether it be the threshold measurement or a change of quality or any other aspect.

A variety of stimuli have been used to evoke pain, and each type of stimulus has some advantages and disadvantages. Visceral pain is best elicited by mechanical and chemical stimuli, skin pain by thermal stimuli, and for direct stimulation of nerves electrical methods are most convenient. The possibility of measuring the intensity of pain has become a practical proposition as proper methods have been devised. The necessary measurement for a scale of intensity values is the measurement of 'differential thresholds', which requires determination of the smallest change in stimulus that can be recognized as evoking a change in pain intensity at least 50 per cent of the time.[3] An important distinction is to be made between intensity of pain and intensity of the stimulus.

Pain sensation is only a part of the total pain experience —broadly speaking, the combination of reactions involving consciousness. In addition to pain a noxious stimulus produces other responses; these include local tissue reactions; neural, muscular and gland activity; and the production of a state of hyperexcitability in the central nervous system sometimes manifest as hyperalgesia. Prolonged noxious stimulation of the viscera, although not painful, may induce skeletal muscle contraction; procaine injected into the muscle may relieve the contraction and abolish the pain.

Those interested in methods of assaying analgesics will obtain details of a highly scientific approach in an article by Houde.[4] The test drugs are coded, disguised and given 'double-blind' in a randomized order on demand, with appropriate standard drug controls and placebos. The selected or referred patients must be suitably cooperative to give subjective reports and evaluate their pain experience, and to assist in determining which is the best of different medications for the relief of their pain. By methods such as these the doctor becomes objective, but much study and team work is essential before controlled clinical trials can be undertaken.

1. Beecher, H. K. (1961): J. Amer. Med. Assoc., **176**, 1102.
2. *Idem* (1962): In *The Assessment of Pain in Man and Animals*, (Keele, C. A. and Smith, R. eds.), p. 159. Edinburgh and London: Livingstone.
3. Hardy, J. D. (1962): *Ibid.*, p. 170.
4. Houde, R. W. (1962): *Ibid.*, p. 202.

IMMUNO-ELEKTROFORESE

Fundamentele molekulêre bestanddele van lewende materiaal bestaan uit proteïnes. Ensieme, hormone of teenliggaampies, om slegs 'n paar te noem, neem deel aan 'n verskeidenheid van funksionele biochemiese reaksies in die liggaam wat die fisiologiese en patologiese prosesse van lewe daarstel. Ons kennis aangaande proteïnes handel hoofsaaklik oor hulle in die algemeen en nie oor individuele proteïnes as sodanig nie. Weliswaar is individuele, molekulêre strukture van proteïnes reeds gediagrammeer en bepaal, maar die aard van hul sintese of suiwer isolasie uit 'n homogene preparaat moet egter nog eksperimenteel uitgevoer word. Analitiese chemiese en fisiese metodes, of biochemiese aktiwiteit, is té onsensitief in so verre dit verskille aangaan tussen verwante proteïnes, en hulle faal ook om aan te toon, in selfs so 'n deeglik bestudeerde substans soos menslike serum, watter proteïnes almal teenwoordig is. Proteïnes besit verder die gemeenskaplike karaktertrek van spesifisiteit, bepaal deur die biologiese spesie waarvandaan dit afkomstig is. Hierdie hoë spesifisiteit, soos aangetoon wanneer teenliggaampies met 'n komplementêre stof reageer, is in skerpe kontras met die huidige fisies-chemiese tegnieke se onvermoë tot isolasie en identifikasie van proteïnes.

In die afgelope dekade is 'n metode ontwikkel, hoof-

saaklik deur Franse navorsers,[1] wat bekend staan as *immuno-elektroforese* en wat as analiserende hulpmiddel in die studie van proteïnes groot beloftes vir die toekoms inhou. Dit berus op elektroforetiese skeiding gevolg deur serologiese identifikasie van die betrokke proteïne. Twee fundamentele beginsels wat in die afgelope 25 jaar as onafhanklike navorsingsrigtings ontwikkel het, word hierdeur saamgesnoer en benut. Tiselius het in 1937 die tegniek van elektroforese daargestel as 'n metode om serum-proteïnes met behulp van hul migrasie-snelhede in 'n elektriese veld van mekaar te skei. Veelvuldige modifikasies van die oorspronklike het sedertdien die lig gesien. Tans demonstreer eenvoudige papier-elektroforese ongeveer 8 - 10 komponente in 'n normale menslike serum, terwyl stysel-gel-elektroforese ongeveer 20 elektroforeties-verskillende sones kan aandui. Immunologies reageer hierdie fraksies egter as komplekse. Onafhanklik van mekaar het Oudin,[3] van die Pasteur Instituut in Parys, en Ouchterlony,[2] van die Karolinska Instituut, Swede, 'n metode ontwikkel om sulke komplekse te ontrafel. Beide antigeen en teenliggaam diffundeer in 'n agarmedium met die spoed van diffusie wat eweredig is aan hul onderskeie konsentrasies en diffusiekoëfisiënte. Waar antigeen en teenliggaam mekaar ontmoet, vorm 'n duidelik-waarneembare lyn van presipitasie in die agar—die aantal lyne hang af van die verskillende komplekse aanwesig. Die suksesvolle toepassing van hierdie metode lei verder tot die tegniek van immunodiffusie wat vandag gemeenplaas is in die immunochemie as 'n eenvoudige, dog akkurate en sensitiewe metode van ondersoek. Wanneer dit egter nodig is om komplekse sisteme, soos bv. menslike serum te identifiseer gee selfs hierdie metode 'n onontsyferbare reeks van presipitasielyne. Grabar en Williams,[1] van die Pasteur Instituut, kom egter met 'n nuwe benadering tot die probleem. Deur primêre elektroforese van antigene, en dus lineêre uitspreiding van die proteïenfraksies, gevolg deur presipitasie met 'n homoloë antiserum, wat lateraalwaards uit 'n trog diffundeer, het hulle die eenvoudige metode van immuno-elektroforese daargestel. In 'n normale menslike serum kan daar van 25 tot 28 fraksies aangedui word!

Namate hierdie tegniek steeds meer en meer in die gebruik kom, blyk die voordele daarvan duidelik: Die geometrie van die eliptiese lyne van presipitasie is betreklik konstant—wat die identifikasie van 'n gegewe proteïen vergemaklik. Geen maskering van spoorhoeveelhede kan plaasvind deur een of meer antigene in oormaat nie. Slegs 'n paar mikrogram van die presipitaat is nodig om 'n waarneembare reaksie te gee. Die presipitasie-reaksie is welbekend vir sy hoë spesifisiteit.

In algemene laboratoriumwerk is die toepassings van hierdie metode veelvuldig. Difterie-toksien en toksoïed, immunologies identies, is immuno-elektroforeties van mekaar te onderskei. Verskille tussen patogene en nie-patogene mikrobakterieë is reeds aangedui, terwyl interessante studies op die biologiese verwantskap tussen diere gedoen is. Vir kliniese werk is Scheidegger[4] se mikrometode baie geskik vir reeks-ondersoeke. Intensiewe studies is reeds uitgevoer oor die yster-draende β - transferrien van die plasma. Alfa haptoglobien word as 'n biochemiese indeks gebruik om verskillende indiwidue geneties te klassifiseer. Lig kan ook gewerp word op die onbekende onderliggende patologie van mïelomatose en gedissemineerde sklerose. Immuno-elektroforeties is dit selfs moontlik om te bepaal op watter tydstip ontwikkelende embriologiese weefsel biochemiese identiteit openbaar.

Met veiligheid kan voorspel word dat steeds waardevoller bydraes tot ons kennis deur immuno-elektroforese in die toekoms gelewer sal word. Tans is dit slegs 'n kwalitatiewe metode, maar wanneer dit op 'n meer kwantitatiewe basis geplaas word, sal dit 'n ongeëwenaarde hulpmiddel in die studie van proteïnes en in die geneeskunde in die algemeen wees.

1. Grabar, P. en Williams, C. A. jnr. (1953): Biochem. biophys. Acta (Amst.), **10**, 193.
2. Ouchterlony, O. (1948): Acta path. microbiol. scand., **25**, 186.
3. Oudin, J. (1948): Ann. Inst. Pasteur, **75**, 30.
4. Scheidegger, J. J. (1955): Intern. Arch. Allergy, **7**, 103.