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## MELANIEN — WAARDEVOLLE BIOLOGIESE INSTRUMENT

Die melanien-inhoud van die vel verdeel ons bevolking in drie geneties-verskillende rasse, naamlik Blankes, Kleurlinge en Bantoes. Aldrie hierdie rasse het ewe veel melanosiete (d.w.s. melanien-produserende selle) maar as gevolg van 'n verhoogde melanosiet-stimulerende hormoon-aktiwiteit (M.S.H.-aktiwiteit), is die melanien-produksie van melanosiete meer aktief in donkerder individue.[1] Ons laat dit aan die politici oor om die probleem van een vaderland vir drie rasse op te los, en ons bepaal ons by die biologiese belangrikheid van hierdie pigment.

Die pigment melanien is in die biologiese wetenskap (waarvan geneeskunde 'n toegepaste vertakking is) 'n groot unifiserende faktor. Dit snoer die belange van fisioloog en anatoom—veral dié van die biochemikus, die embrioloog en die genetikus—stewig saam om 'n klein granule wat elektronmikroskopies gesien kan word in die Golgi-apparaat van melanosiete. Deur tirosien ensiematies oor polifenoliese en kinoïede verbindings op te bou, ontstaan melanien, wat op hierdie kleurlose ‚premelanien' granule neergelê word.[2]

As gepigmenteerde marmotvel op wit marmotvel oorgeplant word, sprei die pigment in die wit area in. Billingham en Medawar[3] het 'n proses van ‚infektiewe oordrag' (van sel tot sel) gepostuleer. Dit was 'n handige analogie vir Burnet[4] om te gebruik as verklaring vir die oordra van 'n selfvermenigvuldigende, immunologies aangepaste ensiem, en dit het sy klonus-uitverkiesingsteorie help vorm. Hierdie teorie het 'n langverwagte oplewing in immunologiese denke aangewakker. Hoewel Billingham en Silvers[5] onlangs kon aantoon dat melanosiet-migrasie belangriker is as die ‚infektiewe oordrag', het die ouer teorie reeds sy vrugte op immunologiese velde afgewerp.

Ons mag dus wel verheug wees dat ons kortliks 'n paar bydraes van melanien tot die onkologie (of gewasse-leer) kan oorweeg, aangesien dit miskien belofte vir die toekoms inhou.

Die maligne melanoom met sy swak prognose is gelukkig seldsaam, maar intensiewe bestudering daarvan het baie interessante gegewens en vrae opgelewer. Die ontrafeling hiervan mag ongekende terapeutiese vrugte afwerp.

Die eerste punt van belang is dat vrouens 'n beter prognose as mans het.[6] Dit geld vir 'n oorlewing van vyf jaar, wat in een studie 25·6% vir mans teenoor 40·0% vir vrouens was, en vir genesing—wat vir mans 7·4% teenoor 28·6% vir vrouens was. Die ondersoeker het gemeen dat dit deur die verskil in weerstand tussen die geslagte verklaar kon word, maar dit is moontlik dat vroulike ydelheid 'n gepigmenteerde letsel gouer onder die dokter se aandag bring.

Daar is ook 'n verwantskap tussen diepgeleë tumore en velpigmentasie. Curth[7] verdeel dit in vier groepe wat ons nie hier volledig kan oorweeg nie. Die eerste groep behels toestande waar 'n bekende verwantskap tussen pigmentasie en tumor aantoonbaar is, byvoorbeeld Addison se siekte, kageksie en pseudo-acanthose nigricans. Eersgenoemde toestand is met pigmentasie verbonde as die byniere primêr vernietig word en is aan verhoogde M.S.H.-aktiwiteit toe te skryf. Persone met metastases toon by outopsie dat 1/3 bynier metastases het. Kageksie volg dikwels op uithongering met of sonder maligniteit en berus ook op M.S.H.-aksie vir sy hiperpigmentasie. Pseudo-acanthose nigricans verskyn in vet persone sonder endokriene afwykings maar kan ook dikwels met hipofisêre tumore gevind word.

Die tweede groep, waaronder die Peutz-Jeghers sindroom, is 'n geneties bepaalde toestand waar geen direkte verband tussen die pigmentasie en dermtumore aantoonbaar is nie. Hier word tumor-neiging en pigmentasie oorgeërf as dominante eienskap maar met wisselende mate van samehang.

Maligne acanthose nigricans verskyn in 17% van gevalle vóór die kanker, in 22% ná die kanker maar in die orige 61% verskyn velletsel en tumor gelyktydig. As die tumor verwyder word, verdwyn die velletsel dikwels maar by verskyning van metastases herhaal ook die velletsel. In hierdie groep is die hele meganisme nog onseker, hoewel die verwantskap tussen tumor en pigment seker is.[7]

Ten slotte is daar 'n vierde groep waar 'n waarskynlike verwantskap met diepgeleë tumore vermoed word, maar waar dit nie bewys is nie, nl. unilaterale naevus verrucosa, vitiligo en urtikaria pigmentosa.[7]

Vir die sitostatiese terapie is dit miskien belangrik om daarop te let dat die polifenoliese en kinoïede intermediêre stowwe (in die opbou van melanien) aan 'n sitotoksiese klas stowwe behoort.[8] Tydens sy melanogenese is die melanoom dus gedurig onderhewig aan sitotoksiese produkte. Daar is egter getuienis dat hul remmende aksie op die sulfhidriel-afhanklike ensiem-sisteme, deur die ensiem glutatioon-peroksidase verhinder word.

Waar ons wel nie veel oor melanien as sulks gesê het nie, het ons probeer om sy belangrikste *gebruik* in biologie bloot te lê nl. dié van maklik waarneembare merker—ooglopend vir die klinikus; mikroskopies—maklik sigbaar; elektronmikroskopies—problematies in oorsprong. Vir die biochemikus—tergend vanweë sy inerte aard; vir die fisioloog—'n aanduiding van hipofiese aktiwiteit en eienaardig in sy respons tot humerale stowwe; vir die onkoloog—'n brug na nuwe gesigseinders.

Naas die eritrosiet, is die melanosiet seker dié gespesialiseerde sel wat die meeste internasionale kongresse in die afgelope paar jaar geniet het. Dit is egter nie 'n prestasie nie maar slegs 'n noodsaaklikheid. Albei is pigmentselle en pigment gee kleur aan ons lewe en denke!

1. McQuinness, B. W. (1963): Ann. N.Y. Acad. Sci., **100**, 640.
2. Birbeck, M. S. C. (1963): *Ibid.*, **100**, 548.
3. Billingham, R. E. en Medawar, P. B. (1947): Nature (Lond.), **160**, 61.
4. Burnet, F. M. (1959): *The Clonal Selection Theory of Acquired Immunity*. Londen: Cambridge Univ. Press.
5. Billingham, R. E. en Silvers, W. K. (1963): Ann. N.Y. Acad. Sci., **100**, 348.
6. White, L. P. (1963): *Ibid.*, **100**, 115.
7. Curth, H. O. (1963): *Ibid.*, **100**, 76.
8. Hochstein, P. en Cohen, G. (1963): *Ibid.*, **100**, 876.

## DRUGS AND HUMAN PERFORMANCE

Many drugs have been used to enhance performance, but proper studies have only been made on the effects of caffeine and the amphetamines.[1] Laboratory studies have indicated that both types of drug prolong the amount of time during which an individual can perform physically exhausting work. There has also been a suggestion that the level of the performance may be raised, but the results have not been definite. During World War II there were reports that the Germans were using methylamphetamine to prolong endurance. In military field studies it has been found that some improvement may be produced in certain tests, but the drugs did not always prevent sleep or improve performance. In studies on athletic performance amphetamine has been shown in certain studies to produce a significant improvement, even in events like the shot put.

In studies on tasks requiring relatively fine motor adjustments rather than gross muscular effort and endurance, many factors need to be considered, but certain provisional conclusions have been reached. Amphetamine appears to lower reaction time, and improve hand steadiness and coordination. Caffeine impairs hand steadiness, has equivocal effects on coordination, and can to some extent restore impaired motor performance caused by alcohol.

The report that the American astronaut, Major Gordon Cooper, was instructed to swallow his amphetamine tablets at a critical moment in his return from space some weeks ago, gives practical confirmation of the acute value of amphetamine. It is apparently regarded by the American authorities and their medical advisers as suitable for the use of spacemen under controlled conditions, and it seems to be accepted as the drug of choice when reaction time, hand steadiness and coordination are all involved, as they were in the case of Major Cooper, who had to guide his spaceship down to an exact spot on the surface of the sea, from some hundreds of miles in space, at a speed of 18,000 m.p.h., adjusting his controls at split-second timing for the desired effect. It is important, however, to remember that Major Cooper used the drug under carefully controlled conditions, and that he took it at the correct time interval before he had to carry out these complex actions. The action of amphetamine wears off fairly rapidly, leaving a state where coordination will not be enhanced and may even be deleteriously affected.

Much of the evidence is variable and contradictory, and before accepting the above conclusions individual studies should be critically analysed.[1] On the other hand a fairly definite answer can be given regarding the effects of drugs on that form of activity known as monitoring (the behavioural responses to data provided by mechanical and electronic devices). Amphetamine can sustain a high level of proficiency, restore performance that has deteriorated, and contribute something not provided by engineering design. It seems also to hasten conditioning and to increase the rate at which subjects acquire proficiency in a motor skill.

The evidence at present available indicates that intellectual performance, as judged by studies of tasks designed to assess verbal and arithmetical behaviour, is not improved by amphetamine compounds or caffeine, except possibly when fatigue or boredom has produced a decrease in normal performance. Much more work is needed to determine whether the amphetamines improve judgment; in certain studies, for example during the war, little evidence was found of adverse effects upon judgment. Others have determined that time-estimation is affected. The effects of amphetamines on mood have been studied by many investigators. Euphoria and feelings of exhilaration, an increase in energy and in the desire and capacity for work, and difficulty in going to sleep, talkativeness, and a feeling of less fatigue have been reported. With caffeine there is a tendency to produce nervousness, irritability, and disturbed sleep.

Some workers claim that these drugs enhance performance by making people more interested in their task. However it is quite likely that the amphetamines affect performance changes and attitude changes. Very significant variation in drug response has been demonstrated to occur independently of variation in attitude. There is evidence that the amphetamines, and possibly caffeine, can enhance performance, and that they can do this not merely by restoring performance degraded by fatigue, lack of sleep, or boredom.

There is no convincing evidence that these drugs impair judgment. They are relatively benign agents. The subjective effects produced by normal doses are usually favourable. But these statements refer only to the acute effects produced by the drugs. The chronic use of these drugs is regarded by some authorities as harmful, and more experimental evidence is needed. What is known so far is that there is no evidence of physical dependence, some degree of tolerance develops, and the incidence of habituation is quite low. Nevertheless the physician should keep in mind the risk of 'addiction' in patients with unstable personality. The sociological aspects of the use of amphetamines are discussed by Leake.[2]

1. Weiss, B. and Laties, V. G. (1962): Pharmacol. Rev., **14**, 1.
2. Leake, C. D. (1958): *The Amphetamines*. Illinois: Charles C. Thomas.