

COMMISSION OF THE EUROPEAN COMMUNITIES — ECSC

# **Traumatology and Rehabilitation**

## **Burns**

Research on Industrial Medicine, Health and Safety (position  
at January 1, 1968)

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LUXEMBOURG, 1968





# Traumatology and Rehabilitation

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Research on Industrial Medicine, Health and Safety as at  
1 January 1968



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## FOREWORD

In assuming the responsibilities formerly exercised by the High Authority, the Commission of the European Communities declared itself prepared to continue activities started within the terms of the Treaty that set up the ECSC. The promotion of research has therefore continued, in respect of all the projects in operation.

The purpose of the present document is to describe the current status of projects now in operation within the industrial injuries programmes listed under A. (b) "Traumatology and rehabilitation" in Annex I. This Table will enable readers to situate these projects in the general perspective of ECSC's activities for the promotion of research in industrial medicine, health and safety.

The principles guiding the action of the Commission of the European Communities, and its methods, continue to be as set out in detail in the publication entitled "Policy of the High Authority for the promotion of study and research on industrial medicine, health, and safety".<sup>(1)</sup> For readers not having access to this document, the principles and methods may be summarized as follows :

- a) The health and safety of workers will be promoted by acquiring and disseminating knowledge applicable :
  - (i) to the prevention of industrial diseases and accidents ;
  - (ii) to the treatment of their manifestations and consequences ;
  - and
  - (iii) to the rehabilitation of workers disabled by them.

To this end, exchange of views and experience and original research and investigation will be sponsored and assisted.

- b) Research and other necessary activities will be financed by funds from the Communities levy, under financial plans for programmes extending over several years, each programme directed to a specific field of research.
- c) Close co-operation will be maintained with relevant employers' and workers' organizations and with government departments in preparing the programmes, carrying them out, and making known their results.

F. VINCK  
Director-General

<sup>(1)</sup> Publications Department of the European Communities, Luxembourg, 1966.





## CONTENTS

	Page
<i>Research programme : " Traumatology and rehabilitation "</i> . . . . .	11
Head injuries . . . . .	11
A. Neurophysiological research on post-traumatic coma . . . . .	11
B. Research on the " acute " stage as a whole . . . . .	13
C. Long-term research directed towards rehabilitation . . . . .	14
Spinal injuries . . . . .	16
A. Spinal injuries without neurological complications . . . . .	16
B. Spinal injuries with cord involvement . . . . .	17
Chest injuries . . . . .	18
Injuries of the locomotor system . . . . .	19
A. Morphological and physiopathological aspects . . . . .	19
B. Rehabilitation of amputees and provision of prostheses . . . . .	22
C. Biomechanics . . . . .	26
<i>Research programme : " Burns "</i> . . . . .	29
Systemic effects of burns . . . . .	29
A. Immediate effects . . . . .	29
B. Intermediate effects . . . . .	30
Tissues directly affected by burns . . . . .	31
A. Natural history of the burn wound . . . . .	32
B. Interaction between graft and recipient area . . . . .	32
Allogeneic grafts . . . . .	33
A. Donor selection ; preparation and storage of skin . . . . .	33
B. Measures to facilitate grafts acceptance . . . . .	34
Long-term results . . . . .	35



## Research programme

### “Traumatology and rehabilitation”

Six new projects were approved in 1967,<sup>(1)</sup> additional to the 31 already approved in 1966. For the research programme as a whole, 1967 was devoted to completing preliminary work and to testing methods and techniques ; many projects, however, reached full development and are already producing results.

#### Head injuries

In the research now in progress, head injury patients are being studied from three different points of view :

- a) Post-traumatic coma ; research directed towards diagnosis, using neurophysiological methods ;
- b) The “ acute ” stage as a whole (coma, return of consciousness, the phase immediately following return of consciousness) : metabolic changes in the brain and throughout the body, psychological problems associated with recovery of consciousness ; research directed fundamentally towards treatment ;
- c) Global evolution of patient reaction, from the accident to completion of rehabilitation : neurological and neuropsychiatric aspects, gradual development of aptitudes, rehabilitation.

Common to these three lines of research is the clinical application of their objectives.

#### *A. Neurophysiological research on post-traumatic coma*

Impairment of consciousness in patients in post-traumatic coma lacks the recuperative effect of normal sleep and appears to be unrelated to the day and night cycle. However, it occurred to Dr. Bergamasco that prolonged electroencephalographic (EEG) recording might show that night sleep does occur in some of these patients and that such evidence might have prognostic significance. That this is in fact so he has confirmed in patients in coma of recent onset in whom there was no indication for neurosurgery and whom he followed by EEG from the first or second day after head injury until they died or recovered consciousness.

<sup>(1)</sup> High Authority Decision dated 21 February 1967.

The all-night records of some of them revealed a pattern of cerebral electrical activity very different from that seen by day and characterized by the presence of typical sleep phenomena (spindles, K-complexes, sharp waves at the vertex, etc.). Where such activity becomes progressively organized to full reproduction of the normal sleep stages the clinical course is very often favourable. It is unfavourable (death or persistence of coma) where the night record differs little from the day record and never shows characteristic sleep phenomena.<sup>(1),(2),(3)</sup>

These initial conclusions have been amply confirmed by other work from the same research group, as will now be described.

Re-examining the case-histories of 100 comatose patients in whom EEG recording had been begun less than 48 hours after injury, Dr. Nquet reached the same conclusions as Dr. Bergamasco. His series of cases was larger, and statistical analysis brought out the additional determinant role of age. The sleeping EEG pattern was found in 49 patients, of whom 39 were under 40 ; of those under 40, the outcome was favourable in 34. The other type of EEG pattern was found in 51 patients, of whom 30 were over 40 ; of the 51, 42 died. The morphology of the " other type " of record was variable and appeared to depend on the complications attendant on the injury.

Professor Perria has made 20 ten-hour continuous EEG recordings in patients with post-traumatic coma in whom the duration of unconsciousness ranged from four weeks to 28 months. He has observed a correlation between depth of coma as evaluated clinically and the presence of a more or less complete sleep pattern in the EEG. Even in coma of long standing the presence of sleep manifestations and their gradual organization into the characteristic pattern of physiological sleep gives reason to hope that consciousness will be recovered.

In cases of long survival, coma may emerge into a peculiar clinical condition (called the " apallic syndrome " by Kretschmer, " akinetic mutism " by Cairns, and " coma vigil " by Alajouanine) in which the patients are non-responsive, but keep their eyes open, change their direction of gaze, making sucking and chewing movements, and have rest periods resembling sleep. Professor Perria's group have shown that the advent of the apallic syndrome may be heralded by the unexpected appearance of transitory runs of alpha rhythm in the EEG ; as the apallic syndrome sets in, the EEG tracings made during the rest periods begin to show stages 2 and 3 of normal sleep ; later, when the syndrome has reached full clinical development, stage 1 and (sometimes later) stage 4 appear, dominated by fast electrical activity.<sup>(4)</sup> The evolution described here is that seen in cases which subsequently proceed to recovery.

This step-by-step reappearance of the normal sleep stages in patients whose cerebral lesion has become stabilized and oedema and other perifocal reactions have

<sup>(1)</sup> Bergamasco, B. *et al.* : Il ciclo nictemerale nel coma. Possibilità prognostiche. Riv. Pat. nerv. ment., 87, 312-318, 1966.

<sup>(2)</sup> Bergamasco, B. *et al.* : Registros poligrafiche notturne in soggetti in coma post-traumatico. Boll. Soc. ital. Biol. sper., 43, 322-323, 1967.

<sup>(3)</sup> Bergamasco, B. *et al.* : EEG sleep patterns as a prognostic criterion in post-traumatic coma. Electroenceph. clin. Neurophysiol., 24, 374-377, 1968.

<sup>(4)</sup> Rosadini, G. and Gentilomo, A. : Quadri EEG di sonno nella sindrome apallica. Riv. Neurol., 37, 469-476, 1967.

had time to subside suggests a progressive reorganization of activity in one after another of the cerebral structures responsible for the EEG phenomena of sleep. These findings, considered together with the results of experimental research in animals, are leading to new working hypotheses on the location and identification of the lesions which produce coma.

At the present time, in head injury patients in whom immediate operation is not indicated, the whole clinical course is dominated by the question of exactly where, and exactly how severe, the injury is. In some cases a focal epileptogenic lesion makes its presence felt as time goes on. In general, it is in the days and weeks immediately following the injury that EEG gives its most useful indices. Prolonged recordings are needed, and these can be made at the bedside if a portable apparatus is available. Certain precautions must be taken as regards therapy, for some tranquillizing drugs (benzodiazepines) promote the appearance of low-amplitude fast activity which may consistently mask the specific patterns for which the observer is on the alert.

#### *B. Research on the "acute" stage as a whole*

Professor Toennis and his co-workers are actively probing certain aspects of the acute stage of severe brain injury—cerebral oxygen consumption, the reaction of the respiratory regulatory centres to variations in the blood gases, and the effects of treatment designed to compensate the respiratory handicap.

The elaboration of methods for continuous monitoring of blood gas tensions by means of intravascular electrodes has encountered technical difficulties. Work to solve the technical problems is going forward, and meantime determinations continue to be made on blood samples. The results obtained at the end of 1967 were machine-processed. Although the statistical analysis was not complete on 31 December 1967, it may be stated now that a fall in the partial pressure of oxygen ( $P_{O_2}$ ) in the arterial blood is frequent, and calls for correction by appropriate therapy.

Partial pressure of respiratory gases was estimated in the cerebrospinal fluid (c.s.f.) at the same time as in the blood. Good correlation was found between the  $P_{O_2}$  in the c.s.f. and the  $P_{O_2}$  difference between arterial blood and venous blood taken from the bulb of the jugular vein. The  $P_{O_2}$  values in the venous blood showed a wide range of scatter. It is concluded that the values found in the c.s.f. give a good indication of the quantity of oxygen actually delivered to the brain. The partial pressure of carbon dioxide in the C.S.F. corresponds, in general, to that found in the blood from the jugular vein. Estimations of pH are as yet too few for conclusions to be drawn.

Blood gas analysis has made it possible to study the effect of assisted respiration (by the Bird respirator\*Mark 8) in patients with acute head injury. Assisted respiration generally causes a rise in the  $P_{O_2}$  of arterial blood and in the arterial-venous  $P_{O_2}$  difference, but the rise is not uniform. The benefit obtained is less pronounced in the presence of respiratory disease. In bronchitis, for example, with their high airway resistance, the apparatus must be set for weak airflow, expiration perhaps being assisted by a negative pressure of 2 to 5 mm of water. Since the machine is pressure-cycled, not volume-cycled, the risk of hypoventilation persists under these conditions, and constant surveillance is essential.



These questions of partial pressures of gases in the C.S.F. and the effects of assisted respiration in acute head injury are discussed in a paper which is at present in the press.<sup>(5)</sup>

Another therapeutic problem still with us is cerebral oedema. Corticosteroid hormones capable of bringing water out of the cellular milieu have sometimes proved beneficial, but often ineffective. The pituitary gland reacts to excess corticosteroid by increased secretion of antidiuretic hormone, which is a corticosteroid antagonist. Professor E. Bernard-Weil, of Professor David's team, has suggested that in addition to substances such as adrenocorticotrophic hormone (ACTH) or hydrocortisone a whole posterior-pituitary extract be given, in the hope that by inhibiting the secretion of antidiuretic hormone it will eliminate the anticorticosteroid effect. The method has already given encouraging results, and it may be that its effectiveness will also be tested by the other centres taking part in this research programme.

Professor Laine's team have been studying the blood sugar content immediately following brain injuries. Slight increases, to rates of between 1.20 and 1.80 gr. per litre, have been found after comparatively mild injuries; in serious cases on the other hand the rate practically always went above 1.80. Not one patient showing a rate over 2.40 gr. per litre survived, which would suggest that glycaemia is a helpful pointer for purposes of prognosis.

The rise in glycaemia is not accompanied by any significant variation in cortisone and insulin. There does, however, appear to be a direct relation between the glycaemia and the content of lactic, pyruvic and alphaketoglutaric acid in the blood, from which it is deduced that the hyperglycaemia occurring is connected with the metabolic effects of the injury and does not mean that a particular area of the brain is affected.

### *C. Long-term research directed towards rehabilitation*

This is a forward-looking research with unpredictable results. Its aim is to find out to what extent better treatment and rehabilitation will help injured persons back to professional and social activity.

In 1967 a systematic study of 80 cases of recent head injury was started as part of the triple research by Professor Gomirato, Professor Jochheim, and Dr. Naquet. The clinical data are being recorded in accordance with a pre-established scheme to permit of statistical analysis in common. It has not yet been decided how many cases are to be admitted to the final sample, for the investigators may continue recruitment during 1968 and time must be allowed for observation. A preliminary review of cases treated and difficulties encountered was made at the end of 1967. The inception of the research which Drs. Venema and Greebe planned to carry out on the same subject has been delayed.

### *Moderate and major brain injuries*

During the first weeks following complete recovery of consciousness, the results of psychological tests of total efficiency lie at the lower limit of normal.

<sup>(5)</sup> Frowein, R.A. and Karimi-Nejad, A.: Gasdrucke und Veränderungen der Säure-Basen-Verhältnisse im Liquor cerebrospinalis sowie Ergebnisse der assistierten Beatmung im Stadium nach Hirnverletzungen.

Personality tests also show massive regression, in which defence systems are disturbed and old conflicts re-lived. The patients are anxious, and their anxiety persists throughout their stay in hospital (Dr. Naquet). All the investigators stress the decisive part that enlightened medicopsychological treatment could play during recovery of consciousness, as a counterpoise to anxiety (due to lack of affectionate interest and to a reaction against hospital loneliness), and as an aid to restoration of full mental function. To satisfy these requirements, however, more psychiatrists and medical psychologists would be needed than are at present available.

A second critical period occurs when the rehabilitation process is terminated and return to work has to be faced. Professor Jochheim has been able to get most of his less seriously and some of this more seriously injured patients taken back by their former employers ; having first undergone preliminary training for a sufficient period at the rehabilitation centre, the man can often, after a reinitiation stage, be returned to the same job as he was on before. During this stage work-performance checks and medico-psychological supervision are still essential. Factory doctors, appropriately briefed, can make a major contribution to this work of resettlement. More serious difficulties, partly connected with the present unfavourable economic situation, arise if change of employment has to be considered ; these difficulties can be reduced with the help of the employment exchange's labour counsellor for the seriously injured. Where the sequelae are grave and persistent the man may well have to be on " non-competitive " work for anything from six months to two years before the permanent loss of capacity can be accurately assessed.

#### *Minor brain injuries*

The clinical evolution of minor brain injuries seems to differ in different countries. Thus, the incidence of post-traumatic neurosis and of so-called " subjective " symptoms (vertigo, non-neuralgic head pains, manifestations of neurasthenia) was higher in 200 cases of old head injury reviewed by Professor Gomitato in Italy than in a similar series observed by Professor Jochheim in Germany. *A priori*, the investigators attribute these differences to the different methods of allocating statutory compensation, and the repercussions of these methods on rehabilitation. In Germany, the compensation due under liability arrangements is decided expeditiously and once for all : the anxious thus know where they stand and are reassured in consequence, and return to work then completes the " normalization " of relations between the erstwhile patient and society. The statutory accident insurance on the other hand entitles to a monthly allowance calculated on the basis of the loss in capacity as such, irrespective of return to work.

The problem, however, is also a medical one. In mild injuries, severity assessments made by different physicians are liable to be at variance so that the patient reaches the conviction that his case " baffles the doctors ". Diagnosis, and classification according to " gravity ", are especially difficult in a condition which may present three aspects :

- a) pre-accident changes (thus, as Professor Gomitato has shown, cervical arthrosis or latent vestibular asymmetry may contribute to the onset of vertigo) ;

- b) organic changes directly due to the accident ;
- c) secondary changes due to the individual patient reaction.

The research now in progress will make it possible to correlate the "immediate" picture (based on previous history, direct trauma, and objective assessment of clinical evolution) with the "delayed" one (duration of hospitalization and of absence from work, results of rehabilitation, late subjective complaints and sequelae). It will also indicate points that should be observed and investigations that should be performed in the immediate phase because of the assistance they give in predicting the subsequent course.

In order to satisfy normal statistical requirements, to have standards of comparison, and to prepare the way for the classification of patients who have been studied in homogeneous groups, a pilot study in a large number of patients will have to be carried out first. Such a pilot study is being conducted at Esch-sur-Alzette by Dr. Muller ; it aims at achieving satisfactory grading of 2200 head injury patients treated in the past, and the work is already well advanced.

### Spinal injuries

Current research in this field is concerned with two types of lesion :

- a) injuries confined to the bony vertebral column and producing no neurological complications ;
- b) injuries affecting both bony vertebral column and spinal cord.

#### A. Spinal injuries without neurological complications

Injuries of the *cervical spine* are being studied by Professor Junghanns and Professor Decoux.

Professor Junghanns is reviewing 500 x-ray reports from cases of recent head injury. Concomitantly, the Forensic Medicine Institute of Cologne University is conducting a serial examination—including radiography and vertebral arteriography and with interest focused especially on head injury cases—of all cervical spines that become available at necropsy. In addition, 30 patients who had sustained whiplash injury to the cervical spine were submitted to an initial clinical and radiological review in 1967 and will be re-examined periodically.

To find a means of differentiating minor traumatic lesions from developmental anomalies, Professor Junghanns is studying variations in vertebral body shape by serial measurements on radiographs, 200 of which have now been processed.

A manual procedure for examination of the cervical spine has been suggested.<sup>(6)</sup> The patient being in the supine position, the observer notes the range of maximal rotation of the head to right and to left, with the neck (i) in forward flexion, (ii) in extensions, and (iii) between flexion and extension. The results expressed in de-

<sup>(6)</sup> Hinz, P. and Erdmann, H. : Zur manuellen Untersuchung der Halswirbelsäule in der Gutachterpraxis. Z. Orthop., 104, 28-37, 1967.

grees, provide an index of neck stiffness due to soft tissue lesions invisible radiographically.

Professor Decoux is investigating the functional anatomy of the cervical spine [in co-operation with the Anatomy Department of Lille University (Professor Minne)] and conducting a radiological study of the site and amplitude of vertebral column motility in normal subjects. His group have also devised and put into practice a new operation for vertebral body consolidation by anterior bone graft.

Drs. Cremona, Marchal, and Waegele at Algrange are taking a special interest in the *lumbar spine*. In a systematic radiological investigation of the vertebral column performed in 1967 in 820 heavy workers they found abnormalities in one third and major abnormalities [spondylolisthesis or retrolisthesis<sup>(7)</sup>] in 40. Television was used in this screening operation and proved satisfactory ; it enabled movement of the spine during flexion and rotation of the body to be observed, and at the same time restricted the use of films to severe lesions requiring a permanent record. In the hope of throwing fresh light on the pathology of the vertebral column in miners, these workers are analyzing case-histories made accessible by the administration of the Miners' Relief Fund.

A job analysis in relation to vertebral column stress has been carried out at two steelworks and an iron mine. It was based upon chronometry and weight of loads moved, and led to a general grading of jobs by order of heaviness. It is to be completed by an analysis of the work postures and movements specific to different occupations. The objective is to compile lists of jobs which are compatible or incompatible with the commonest lesions and abnormalities.

#### *B. Spinal injuries with cord involvement*

While one research group are engaged upon two projects concerning the respiratory and circulatory problems of paraplegis, another are investigating the peripheral circulation, its regulation, and its influence on tissue metabolism.

##### *Respiration and general circulation*

Professor Rehn and Professor Meinecke, and likewise Dr. Houssa, devoted the first months of their research activity in this field to setting up their equipment and working out methods and techniques. The experimental work proper began too recently for even partial or interim results to be available as yet.

##### *Metabolic effects of the state of the circulation in paralyzed areas*

Professor Decoux's associates have begun a systematic radiological study, at the Berck Heliomarine Treatment Centre, in paralytics of long standing. In an analytical review of the records (including whole skeleton radiographs) of 126 paraplegic patients, Dr. Maury found that 60% had ectopic ossification (which in 66% took the form of giant osteomata) situated in the hip and/or knee regions (in half the cases in both of these regions). Ectopic ossification around the elbow.

<sup>(7)</sup> Respectively, forward and backward displacement of one vertebra upon the vertebra below.

was seen in quadriplegic patients, but there were not enough of these for a valid assessment of incidence. Scrutiny of the 126 case histories provided evidence that such ossification is unrelated to bed-sores, to the state of the urinary bladder, or to cerebral trauma. It emerged that the patients with osteomata had been immobilized for longer periods than the others, that osteomata were more frequent in lesions of the cervical or thoracic segments of the vertebral column than in the lesions of lower segments, and that they may begin, or undergo reactivation, in response to local injury or even several years after the onset of paralysis. Their physiopathological interpretation and the elaboration of measures to prevent them therefore call for elucidation of their circulatory and metabolic aspects, and upon these research is now beginning.

In June 1967 Professor Decoux and Dr. Maury held a meeting with other research workers (Professor Benassy and Grossiord of Paris and Dr. Chantraine of Liège) who, although not in receipt of ECSC grants, are interested in infra-lesional blood supply and its relation to neurogenic osteogenesis. The meeting provided an opportunity to compare viewpoints and apportion to work. To consolidate this co-operation other meetings are planned.

### Chest injuries

The research directed by Dr. Zannini is concerned mainly with *mild chest injuries* (contusions, rib fractures, and a small number of cases of haemothorax) and aims at eliminating their sequelae (muscular atrophy, rigidity at the costovertebral joints, and adhesions) by starting breathing exercises early. Therapy begins by encouraging relaxation, overcoming antalgic postures (superficial respiration), and restoring regular diaphragmatic breathing and is completed as soon as possible by postural bronchial drainage and mobilization of the entire thoracic cage and the auxiliary muscles of respiration. In the cases of haemothorax these measures promoted re-expansion of the lung and no sequelae were encountered.

Dr. Lageze's research is concerned chiefly with *severe chest injuries*. The first step was re-examination of some 50 comprehensive case-histories of patients who had had at least one "costal flap" <sup>(8)</sup> <sup>(9)</sup> and who had continued to suffer from functional sequelae (in the form of diminution of the respiratory volumes and hypoxaemia) although their bony lesions were consolidated. When such hypoxaemia was subsequently studied in patients with recent injuries, it was found that it did not always respond to respiratory re-educational measures; bronchspirometry disclosed the presence of persistent hypoventilation in the injured area, leading to reduction in respiratory exchange.

<sup>(8)</sup> French *volet costal*, i.e. the unstable segment or "flap" functionally disunited from the chest wall in "flail chest" or "stove-in-chest".

<sup>(9)</sup> Lepêtre, M.: Indications et résultats de la rééducation respiratoire des grands traumatismes du thorax après le traitement chirurgical. Thesis, Faculty of Medicine, Lyons, 1967.



## **Injuries of the locomotor system**

To allow for new research initiated in 1967 the arrangement of the subject matter in the following account is somewhat different from that used in the document setting out the status of work as at 1 January 1967.

### *A. Morphological and physiopathological aspects*

#### *Bone and cartilage*

Professor Lacroix and his associates, using their technique for labelling bone with fluorescent substances, have continued their analysis of the events in fracture repair and are preparing an illustrated document describing them in detail. The following aspects received special attention in 1967 :

- a) the resorption of bone at the fractured surfaces by special mechanisms not necessarily depending on osteoclasts ;
- b) the haematoma which forms in the fracture gap ; calcium is deposited in it and it undergoes invasion and incomplete breakdown but survives in part until the fragments unite ;
- c) the two stages in the development of callus, namely, (i) the formation of a bony revetment at some distance from the fracture line and (ii) the formation of a cartilaginous mass which advances from the bony revetment towards the fracture line to meet its fellow growing across from the other fragment.

These studies have confirmed that the periosteum plays a dominant part in callus formation, a fact which explains why certain osteosynthetic procedures such as the application of encircling bands may prove disastrous clinically while others prove satisfactory ; these procedures do not all breach the periosteum in the same way.

Under normal conditions the periosteum forms bone. The fact that after a fracture it sets about forming cartilage, which is important in callus formation, indicates that the fracture has not only caused structural damage but has also resurrected developmental powers latent in certain tissues, in the present case in periosteal cells. How and why this happens is one of the general biological problems posed by the ability of all living organisms to preserve their internal organization during tissue repair. As a possible explanation of the phenomenon when it occurs in bone, Professor Maurer has considered an interaction between the tissues inside and outside the bone, which the fracture has brought into contact with each other. With this tentative hypothesis in mind he has conducted the following experiments.

In one animal a bone marrow graft was placed against the cortex of a bone stripped of its periosteum but otherwise intact, while in a second animal a similar graft was inserted between the periosteum and the bony wall ; osteogenesis at the graft site was more abundant in the second animal than in the first.

In two groups of animals the central part of a long bone was removed, the periosteal sheath being preserved intact, and the two extremities maintained by an external support. In the first group the cut surfaces of the bone ends were left open ; in

the second group they were covered over with an impermeable membrane occluding the marrow cavities. Osteogenesis in the space between the ends was abundant in the animals of the first group, nil in those of the second.

These experiments, and others conducted by the same investigator, show that bone marrow cells are necessary for periosteal osteogenesis. Bone marrow cells may provoke similar reactions in other types of connective tissue, in which case bone formation is less prominent.

It is known that during embryological development the tissues of different quality which contribute to the formation of an organ exert a reciprocal influence upon each other and that such influence plays a decisive part in the proper organization of body structures. This "presence effect" of tissues is probably connected with the release of inducer substances. Professor Maurer's observations include a hypothesis that phenomena of the same type may again come into play in adult life to govern the regenerative processes which are active in tissue repair.

Continuing their research on turnover in adult bones, Professor Lacroix and his associates have found that remodelling in normal adult bone is maximal in certain well-defined parts of the long bones (in particular, of the tibia). Such areas are situated near the joints, which are the sites of election of post-traumatic osteoporosis.<sup>(10)</sup> In a confrontation between the radiographic appearances of osteoporotic zones and the clinical evolution of fractures, Professor Decoulx has noted that diffuse extension of the bone rarefaction in the latter is an indication that pseudoarthrosis will develop at the fracture site and may call for surgical intervention.<sup>(11)</sup>

Other researchers, also seeking to define the data of completion of consolidation, are investigating the problem by non-radiological methods. Professor Maurer, for example, is experimenting clinically with ultrasonics. In their work on osteosynthetic procedures, Professor Hernandez-Richter and Struck have chosen as criterion of consolidation the resistance of callus to mechanical stress, and are using an apparatus devised for estimating this resistance in the living animal: the bone segment selected (hind leg of rabbit or dog) is submitted to a progressively-increased, laterally-applied load, and the load needed to bring about a constant degree of bending (0.1 - 0.5 - 1 mm) is measured. The reliability of these *in-vivo* measurements has been checked in isolated bone removed after sacrifice of the animal.<sup>(12)</sup> Initial trials on fractured bone in process of consolidation (rabbit, conservative treatment) indicate that the rigidity of callus undergoes maximal increases between the 20th and 35th days after fracture, being about one-third of that of normal bone by the 20th day and about 80% by the 35th.

Injuries to limbs often have articular repercussions. In order to study the development of post-traumatic arthrosis, Professor Monteleone induces hip-joint dislocation in guinea-pigs and analyzes its consequences for the metabolism of articular cartilage. An attempt is being made, with the aid of radioisotopes, to identify the

<sup>(10)</sup> Dhem, A.: Le remaniement de l'os adulte. Paris, Maloine, 1967.

<sup>(11)</sup> Decoulx, P.: La raie d'ostéoporose de Lacroix. Acta orthop. belg. In the press.

<sup>(12)</sup> Struck, H. and Hernandez-Richter, J.: Tierexperimentelle Untersuchungen über die Belastung des Knochens *in vivo* - eine neue Messmethode. Langenbecks Arch. klin. Chir., 379, 468-470, 1967.

metabolic pathways by which mucopolysaccharides are synthesized in damaged cartilage.

#### *Nerves and muscles*

Professot Scaglietti has undertaken a long-term follow-up study of 1200 cases of peripheral nerve injury treated between 1943 and 1965. The patients are being re-examined and the findings compared and classified in such a way as to bring out the pathological and functional evolution of the lesions, the general clinical aspects, and the features peculiar to individual nerves and to specific types of trauma.

When a nerve is divided, scar tissue forms in the gap between the severed ends. While the scar is undergoing organization, nerve fibres in the proximal segment regenerate and grow down in an effort to bridge the gap and re-enter the conducting pathway represented by the distal segment. The nerve fibres of latter, cut off from their parent cell bodies, degenerate and are absorbed ; their sheaths (sheaths of Schwann) become invaded by endoneural connective tissue and thus lose the ability to guide the down-growing regenerating fibres. The ultimate outcome depends (i) on the amount of scar tissue blocking the passage of the regenerating fibre and (ii) on whether the regenerating fibres advances faster than the sheaths are destroyed, or *vice versa*.

These phenomena are being studied (i) on operation specimens which include the scar tissue and the cut ends of the injured nerve and (ii) (with the necessary reservations) in experimental animals.

Professor Scaglietti's group have demonstrated that the sheaths of Schwann in the distal segment retain their normal appearance during the first two months after the injury ; thereafter they undergo gradual change and are completely obliterated by the 12th month. Their rate of destruction seems to be related to the structure of the nerve concerned, in particular to the amount of connective tissue present, which varies from nerve to nerve and increases with age. In a middle-aged person, some 53% of the surface exposed on cross section of the radial nerve consists of nerve tissue, the remainder of connective tissue ; the corresponding proportion of nerve in the peroneal nerve is only 15 to 20%.

If a lesion affects not only a nerve trunk but also the corresponding cell bodies in the spinal cord, nerve regeneration cannot take place. Thus, in certain lesions due to violent traction on the upper limb, in which the brachial plexus is stretched and its roots avulsed at their attachment to the cord, the limb is permanently and irretrievably paralyzed and palliative therapy alone can be practised. These research workers were anxious to find a way of distinguishing between such irreparable lesions and those which although near the spinal cord spare it and are therefore amenable to operative repair. The methods available for pre-operative diagnosis are imprecise, as has been confirmed by a surgical review conducted in 56 of Professor Scaglietti's patients, and a working hypothesis based on anatomical considerations was therefore adopted.

After emerging from the vertebral column, each spinal nerve divides into a ventral and a dorsal ramus. If cervical spinal nerves are avulsed where their roots attach

them to the cord, the resultant paralysis affects both the muscles supplied by the ventral rami (that is, the muscles of the upper limb) and those supplied by the dorsal rami (two nuchal muscles, semispinalis capitis and multifidus). If, on the other hand, the lesion affects the ventral rami only, or the brachial plexus, which is formed from the ventral rami, the muscles of the upper limb alone will be paralyzed. Diagnosis based on electromyographic examination of the two deep muscles mentioned above was confirmed at operation in two patients. This research activity continues.

Concomitantly with the work just described, which is centred on lesions of peripheral nerve trunks, research has been proceeding since 1967 on the functional state of the muscles and nervous pathways in the vicinity of bone fractures.

The research activities of Drs. Desenfans and Chantraine in this field are oriented towards functional re-education. No later than a week after the injury, in patients in whom the supportive measures employed allow access to and early mobilization of the affected limb, they direct their attention primarily to the muscles, in particular those that are traumatized. After investigating these muscles' innervation by charting strength-duration curves, they fatigue them by repeated electrical stimulation and attempt to elicit the phenomenon of post-tetanic exhaustion. This latter test, used by Desmedt in studying myasthenia, may be of value in assessing function in damaged muscle. If alteration in strength-duration curves points to damage to nerves or to their terminal fibres, their conduction velocity and distal latency are determined. The patients are examined periodically, and it is hoped that these investigations will assist both prognosis and treatment in different types of fracture.

Using histological and electrophysiological methods, Professor Mosinger and Dr. De Bisschop are studying injuries to small nerve fibres and their effects on the muscles in the fracture zone in patients with delayed consolidation. The nature of this investigation is such that it takes place at a certain time interval after the trauma.

Dr. Dumoulin is focusing his interest on wrist and hand injuries ; these are often accompanied by painful neurovegetative complications which are difficult to treat. His initial results seem to confirm and explain the relief produced by surgical and medical procedures (local hydrocortisone infiltration, iodine ionization) which decompress the nerves traversing the carpal tunnel.

When sensory nerves are compressed in part of their course (by, for example, perilesional oedema) they show a slowing of conduction time from the periphery towards the central nervous system. Decompressive treatments bring conduction time back to within normal limits, but it remains to be seen whether this normalization is always followed by clinical improvement. It will be possible to reach a definite conclusion when more cases have been observed.

## *B. Rehabilitation of amputees and provision of prostheses*

### *Simple osteoarticular lesions*

Dr. Desenfans has been directing his attention to functional rehabilitation in :

- a) disorders of the semilunar menisci of the knee after operation ;

- b) dislocations of the knee and disorders of the ligaments of the knee joint ;
- c) fractures in the region of the knee (patella, tuberosities of tibia, condyles) ;
- d) extra-articular fractures of the femur.

The central theme of his research is stiffness at the knee joint—to prevent it if possible, to overcome it if necessary, and to restore the full range of movement which is indispensable in many occupations, especially those connected with the mining industry. Keeping this objective before them, Dr. Desenfans' team conduct systematic reviews of the practical experience gained in each type of lesion and at each phase of treatment and selected the most effective methods accordingly. Methodological criticism is not drawn from the experience of one research group only, since colleagues from other rehabilitation centres have an opportunity to contribute their views at meetings held periodically. Several problems have received new technical solutions, two examples of which, concerning fractures of the femur, will now be described.

A special suspension cradle has been devised to permit weightfree mobilization of the knee immediately after osteosynthesis of the femur. The leg and foot rest on a hammock of adjustable length, attached at its distal end, on each side, to the arms of a rigid stirrup articulating above with a Balkan beam. At its proximal end, near the knee, the hammock is supported by two cords, with weights attached, stretched over pulleys. The leg can thus move in the long axis of the bed, a range of from 90°-flexion to almost complete extension being possible at the knee joint ; rotation of the thigh, on the other hand, is precluded.

The raised position of the limb promotes drainage from the operation site. The apparatus is applied as soon as the patient leaves the operating theatre, is kept on permanently throughout the first three to four days, and subsequently is used at night only.

Quadriceps exercises—of which resisted extension of the leg is the chief element—are essential to prepare the patient for walking and resumption of the upright position. Impressed by criticism of the " Colson chair ", in which the resistance applied has an undesirable centripetal component in the axis of the leg, the researchers have invented a " direct graded-resistance chair " : the patient sits in an adjustable chair, the hollow of the knee well supported ; leg extension is opposed by graded weights applied to the front of the instep by means of a mobile arm oscillating around a horizontal axis which coincides with the articular axis of the knee. Leg and knee being otherwise unimpeded, the patient can relax his leg completely after each movement.

In performing this research, which they plan to extend to the other joints of the body, the investigators have come to view physical rehabilitation as an integrated process made up of many elements which range from teaching the patient to overcome his disability and helping him to relearn the actions specific to his occupation to last-minute re-training preceding resumption of work. Their most recent report summarizes the general principles and the methodological foundation of their approach. The work will be continued in 1968, on aspects peculiar to different lesions and different occupations.



At Heidelberg Professor Costa is continuing his research into the fitting of artificial limbs immediately after amputation. His patients are divided into three groups : (a) those in whom the stump and its joint are put in plaster of Paris bandages immediately after amputation and a provisional prosthesis fitted within 24 hours ; (b) those treated likewise, except that the prosthesis is not applied until three weeks later ; and (c) those in whom the stump has become infected and the prosthesis is not fitted until the infection has cleared up. When this research is concluded, the results will be compared with those obtained by traditional methods, before 1966.

It is already becoming evident that immediate fitting shortens treatment significantly without disadvantage to the patient. At the same time it has made it necessary to revise fitting procedures as regards both the socket (to allow for the special condition of the stump) and the distal part of the prosthesis. To hasten production of the latter, prefabricated parts are used, and arrangements have had to be made for these to be manufactured.

Stump volume is liable to vary, because of oedema or muscular atrophy, in all lower limb amputees, so that the socket, even when made by moulding, has to be readjusted many times.

Professor Merle d'Aubigne's associates prepare their moulds with the patient lying down, on a stump which has been elevated for at least 20 minutes.<sup>(13)</sup> They have found that if an elastic bandage is applied to the stump there may be reactive oedema when it is removed. In the hope of eliminating the need for adjustments to the socket they are experimenting with different degrees of pressure applied while taking the moulds.

After fitting, stump shrinkage continues because of muscular atrophy, which is greater in some areas than in others ; a stable state is reached some six months after the amputation. The research workers are experimenting successfully with a pneumatic lining which, by taking up play in the socket when the stump shrinks, eliminates the need for a fresh mould. This lining is not circular and its purpose is not to protect bony prominences but to make up for variations in stump volume. Professor Pierquin's team at Nancy and Professor Merle d'Aubigne's at Valenton are working in this field.

At Nancy, Dr. Paquin and Mr. Fajal have successfully developed a prototype prosthesis rapidly adaptable to any amputee irrespective of height and amputation level. A limited number of sets of prefabricated parts may have to be manufactured. Clinical experimentation is in progress and is affording an opportunity to review structural details and the suitability of the material used. The difficulty of effecting a stable junction between parts in resin and metal respectively has been overcome by incorporating Duralumin laminae in the plastic material ; other combinations are being tried. During this research a new knee mechanism has been developed.

<sup>(13)</sup> Maurer, P. *et al.* : Moulage du moignon de jambe pour prothèse de contact. *Rev. Chir. orthop.*, 52, 639-644, 1966.

Continuing his work on tubular framework prostheses, Dr. Kuhn has constructed a knee equipped with a braking device, and this is at present undergoing clinical trial.

A new line of research aims at defining the load supported by the lower limbs during ambulation in normal subjects and in leg and thigh amputees. Using a special dynamometer incorporated in the sole of the shoe, Professor Groh and his co-workers have measured the forces active in the foot during impact of the heel on the ground, during the phase of vertical projection of the centre of gravity, and during impulsion imparted by the ball of the foot.<sup>(14)</sup> In amputees, the vertical components of these forces and the braking components (heel impact) are the same in both limbs, but the propellant force imparted by the ball of the foot is less on the side of the prosthesis. Since the absolute values recorded in amputees are below those in normal subjects, no overload seems to be produced at the joints. Still to be explored are the effects of lateral displacements of the body's centre of gravity, which might lead to overload on the pelvis and the vertebral column.

#### *Upper limb amputees*

From an analysis of the results of rehabilitation in 150 upper limb amputees treated at the Gondreville Rehabilitation Centre,<sup>(15)</sup> it emerges that some 50% wear their appliance permanently and, of this 50%, some 90% work. Of the remaining 50%, 25% wear their appliance only occasionally (and then chiefly for cosmetic reasons) and the others have given up wearing it altogether. It is noteworthy that amputees who work prefer occupations calling for as little bimanual activity as possible.

These results are the outcome of intensive efforts in the equipment and functional re-education of amputees. However, medical and technical concepts in this field are advancing very rapidly ; amputees should be enabled to benefit from these advances, and the author of the Gondreville analysis is of opinion that even more can be returned to active work than is now the case.

Professor Cotta is so pleased with the results of immediate fitting in lower limb amputees that he is considering trying it in upper limb amputees too. Dr. Marquardt believes that the myoelectric prosthesis opens up new prospects in the equipment of bilateral amputees. His medical-social survey of such subjects has not as yet proceeded beyond cases studied before 1966 ; it will not be resumed until after completion of a technical study on myoelectric control of externally- (electrically- or pneumatically-)powered prostheses. In order to endow movement with sensibility, Dr. Kuhn is trying to develop a device which will inform the amputee of the force expended by his prosthesis when it grasps an object.

It is in terms of the patient, of his amputation, of his personality, and of the movements he is called upon to make in his daily life and work, that Dr. Lescoeur, in a synthetic study, considers the various ways in which hand function can be replaced. He believes that the choice of a permanent prosthesis should be based upon expe-

<sup>(14)</sup> Schales, H., Groh, H., Bauman, W., and Kubeth, F. : Über die Abstoßkräfte des Fußballens bei Gang und Lauf. *Ergonomics*, 10, 683-697, 1967.

<sup>(15)</sup> Herment, J.P. : Thesis, Faculty of Medicine, Nancy, 1966.

rience gained in wearing a trial one, and his work in 1967 has been centred mainly on the development of trial prostheses.

A prosthesis aimed at replacing hand function must have an appropriate terminal device or tool. Seeking to combine cosmetic acceptability, functional polyvalence, and lightness in an artificial hand suitable for real work Dr. Kuhn has created a three-finger mechanism operated by a single traction cable ; the thumb opens first, and at a certain point in its course mobilizes the index ; the third (or middle) finger is rigid and serves for vigorous pulling or pushing movements. Large objects can be grasped between the thumb and the two fingers, and flat or thin ones between the index and middle finger.

Finally in this field, attention should be drawn to the introduction of plastic jackets which can be moulded individually into the body of an injured or disabled person. Dr. Kuhn has found that the distribution of pressure so obtained prevents pressure sores in patients required to spend long periods in the lying or sitting position.

### C. *Biomechanics*

In contrast to the function of the kidneys and of other organs whose role is to maintain constancy of composition in body's milieu intérieur, the global function of the locomotor system—movement—is directed entirely towards the exterior. A movement is normal when it is well controlled and when it is accomplished with speed and efficiency, speed and efficiency which have no precise limits and are always perfectible. Limb movement is angular ; it concerns reciprocally articulated masses submitted to forces which are variable in time, and whose points of application are multiple. It is therefore difficult to express limb movement as an equation, but it can be filmed and its acceleration can be measured. Knowing the weight of the body and the weight and length of the limb segments, the investigator can attempt to estimate the mechanical load transmitted to the bones and joints. This information would be useful in the prevention of joint lesions, in orthopedic surgery, and in rehabilitation, but it calls for the ability to process a very considerable mass of numerical data within a limited period of time.

In the context of a new research activity, Professor Groh is trying to solve this problem, which is primarily a problem of method.

A test subject moves about against a background of location lines ; attached to certain parts of his body are guide lights and piezoelectric acceleration pick-ups arranged in threes (along three orthogonal axes). The data " displacement of luminous points " are recorded on film by two cinematographic cameras. The data " acceleration " are amplified and transmitted by a portable radio emitter to an oscillograph, which takes its time-marking from the camera shutters. A television camera takes up the oscillographic tracings and the filmed pictures. The acceleration and displacement curves are synchronized and correlated by an analogue converter which records the data on punched tape. They can then be interpreted by an appropriately programmed computer.

While waiting for the apparatus to be finally assembled, Professor Groh has conducted preliminary research, first on the use of cinematography for movement

analysis,<sup>(16)</sup> and subsequently on radio transmission of accelerometric data. The latter investigation included an estimation, in 30 subjects, of the force of impact to which the body is subjected during walking and running over different types of terrain. Forces of 30 g were found at the boot heel and 15 g at the calcaneum ; they were transmitted to the interior of the body at a speed of 30 m per sec but were quickly absorbed and fell to 1 to 2 g in the pelvis and 0.5 to 1 g in the head.

<sup>(16)</sup> Weiss, R., Baumann, W., and Groh, H. : Über die Beinbewegung beim Lauf. Z. Biol., 115, 407-417, 1967.





## Research programme "Burns"

In implementation of this programme 43 research projects were submitted to the European Communities Commission, which referred them for consideration by the consultative committees. As a result of the consultations, 23 can begin in 1968. Their subject matter is set out in the following pages.

### Systemic effects of burns

Although a burn is a local aggression its effects are not confined to its local manifestations—blisters and eschars—but are also *general*. The general effects may be of great severity, both at the time of injury and until complete healing of the local lesion.

#### A. Immediate effects

The present research deals with four aspects of burns :

- a) the wound, considered as a factor in pathogenesis : it is the starting point of nervous impulses, of products of tissue degeneration, and of bacterial toxins, and is the site of fluid loss (by exudation, evaporation, and oedema),
- b) the circulatory deficiency, due to a dramatic fall in the volume of circulating blood as the result of (i) stagnation of large quantities of blood in paralyzed sectors of the circulation, (ii) invasion of the intercellular spaces by fluid extravasated from the vessels, and (iii) cellular oedema ;
- c) oxygen lack in the internal organs ;
- d) the functioning of the internal organs under the conditions outlined above.

At Amsterdam Dr. Goris plans to conduct a trial with three methods of local treatment of the burn wound in pigs subjected to 50% (second degree) burns : (i) conservative "exposure treatment" (i.e. the burned area is left exposed to the air) ; (ii) wet dressings (0.3% chloramine solution) ; and (iii) primary excision of the burned tissue followed by autograft. The intention is to observe the course of shock under each of the three treatments and to compare healing time and functional results. A specific objective is to determine the extent of primary excision which the circulatory deficiency will allow.

At Munich Professor Werle is studying the pathogenic factors of oedema, with special attention to capillary permeability. Burns, he believes, may foster the for-

mation of amine-like substances (kininins) which increase capillary permeability, and he plans to combat their effects by administering kinin-antagonists.

The anti-inflammatory activity of epsilon-aminocaproic acid was described in the course of earlier research work by Professor Trabucchi's group.<sup>(17)</sup> In the hope of finding a more active preparation Professor Bertelli plans to synthesize and experiment with new substances in the same chemical series.

Professor Benichoux at Nancy is going to treat burned animals experimentally by hyperbaric oxygen in air-tight chambers. Buffer fluids (such as a solution of Tham) and antibiotics will also be given in order to assess their effects on oedema and on oxygenation of the blood.

Professor Vanlerenberghe at Lille plans to study the effects on the liver—as a water-excreting organ and a viscus which plays an important part in the regulation of metabolism—of the circulatory derangement provoked by burns.

### B. *Intermediate effects*

After primary shock has passed off, the burned patient is still in precarious internal equilibrium. Infection of oedema fluid in the vicinity of the burn, circulatory disturbance in the viscera, damage to the viscera themselves, negative protein balance combined with difficulty in satisfying nutritional requirements, and weakening of the body defences against infection are the principal elements in a condition of ever-present danger.

From among this array of problems the investigators have selected for their two principal avenues of research (i) the metabolic response in the burn syndrome and (ii) resistance to infection.

These two subjects are connected. The emergence and diffusion of new strains of micro-organisms, pre-selected by antibiotics, resistant to most of these, and often virulent (the most frequently encountered being staphylococci and, more recently, pseudomonas)—are obliging the medical profession to revise hospital arrangements for the control of infection in patients with sepsis, to seek means for reinforcing the body's natural biological defences, and to study more closely the cellular and metabolic forces which subserve these defences in normal subjects and burned patients.

Prompted by earlier research<sup>(18)(19)</sup> which demonstrated the primary role of infection in mortality from burns, Professor Decoulx is re-examining the sources, the modes of transmission, and the causes of generalization of infection in burned persons. This work will embrace the preventive value of air decontamination measures, the problems raised by balneotherapy, the early diagnosis of septicaemia, and the therapeutic usefulness of antibiotics.

<sup>(17)</sup> Donati, L. *et al.* : Sull'effetto protettivo di alcuni farmaci nei riguardi della lesione locale da ustione. *Atti Accad. med. lombarda*, 79, 1964.

<sup>(18)</sup> Decoulx, P. *et al.* : Causes de la mort semi-tardive des brûlés. *Soc. Méd. milit. franc. Bull.*, 57, 196-209, 1963.

<sup>(19)</sup> Decoulx, P. *et al.* : Les moyens de défense antibactériens chez les brûlés. *Presse méd.*, 72, 257-260, 1964.

Professor Krauss's associates at Freiburg-im-Breisgau are interesting themselves in the reticulo-endothelial system, which plays a major role in the body's defence against infection. Its efficiency can be appraised from the rate with which a suspension of particles of labelled albumin is cleared from the blood stream. This test will be performed in burned animals artificially infected with pseudomonas and the results correlated with the values for basal metabolism and skin evaporation. The ultimate aim is to find out whether certain drugs liable to depress the activity of the reticulo-endothelial system are contra-indicated in burned subjects, and if a case could not be made for recommending substances which stimulate its activity.

At Bochum, Professor Rehn and Dr. Hierholzer will concentrate on infection by staphylococci, with special attention to the production of antibodies active against these organisms and the relation of such production to clinical condition. As in the research directed by Professor Krauss, non-specific protective factors (phagocytosis) will also be considered.

At Düsseldorf, Professor Staib has noted important variations in the alpha amino acids of the plasma and of the liver during the month following infliction of a burn.<sup>(20)</sup> He now plans to undertake quantitative determinations of the amino acids and to follow up their metabolic fate by labelling with radioactive carbon.<sup>(14C)</sup> This will demonstrate the changes which burns bring about in the normal processes of protein synthesis and breakdown.

### **Tissues directly affected by burns**

After the slough has been removed, either by spontaneous separation or by surgical intervention, the burn wound is found to be the site of proliferating and highly vascular connective tissue (granulation tissue), which becomes covered and stabilized by epithelial cells derived partly from the edge of the wound and partly from foci of regeneration. If epithelialization does not take place spontaneously (because the burn is too extensive or too deep) the surgeon applies skin graft to the granulation tissue. The grafts he uses are prepared from skin taken either from uninjured parts of the patient's body (autografts) or from another person, living or dead (allogeneic grafts, also called homografts). The stabilization of the wound depends on the relation which develops between the graft and the recipient area, a relation which is complex and as yet not fully understood; this problem is common to both types of graft and will be discussed here. The ultimate form of the epithelial covering, and the patient's recovery, depend on the reaction between graft and host, a problem which will be discussed in the next section of this report.

<sup>(20)</sup> Kroener, H. et al. : Adeninucleotide und freie Aminosäuren in der Rattenleber sowie Aminosäure und Corticosteronspiegel im Serum von Ratten nach Verbrennungen. Z. klin. Chem. klin. Biochem., 5, 81-83, 1967.

### *A. Natural history of the burn wound*

Immediately after infliction of a thermal injury, examination of the burned area may reveal tissue which is hardly damaged at all and which will heal spontaneously, or irreversible lesions with total tissue destruction, the depth and extent of which may be difficult to determine at that early stage. Professor Mon-saingeon considers that in some cases ("intermediary" burns) the affected tissues die only secondarily, as the result of a sequence of events which are little understood but which there is reason to hope are not irreversible. If this process could be influenced it might be possible to limit the damage, with decisive effect on patient survival. It would be rational to suppose that tissues not directly destroyed by heat but lying within an oedematous enclave with a poor blood supply may suffer oxygen lack. The respiratory state of such tissues can be assessed by measuring their oxidation-reduction potential with very fine electrodes implanted in them before infliction of an experimental burn. Using this method, the research workers propose as a first investigation to ascertain the local effects of certain general therapeutic measures (such as fluid replacement and administration of various drugs) which are practised immediately after receipt of a burn.

Professor Comel and Mian are to investigate enzymatic activity in the tissues of burned areas; specifically, in fragments of superficial tissue removed from the margin of the necrotic zone, in the granulation tissue, and in parts which are the site of cutaneous regeneration. Enzymes studied will include proteases (the agents which break down high molecular weight proteins) and oxidases and dehydrogenases (which play an important part in tissue respiration). The results of this work will guide the choice of local treatment of burns.

### *B. Interaction between graft and recipient area*

Since patients with very extensive burns often have little skin left that would be suitable for autografting, surgeons have had to make such skin as is available cover as large a burned surface area as possible. Surface coverage can be increased three- or fourfold if a graft is cut into a criss-cross pattern (mesh-graft) or into small separate bits (micrograft).

Dr. Colson's research project concerns micrografts, the use of which offers full scope to the proliferative capacities of the epithelial cells. Starting from the micrograft these cells spread, enter into contact with the granulation tissue, and establish a two-way relation with it, the granulation tissue providing the nutritional and supportive conditions which enable epithelial mitosis to proceed, and the spreading lamina of epithelium keeping the connective tissue proliferation under control. The research workers want to find out the conditions which, in the long term, will produce connective tissue with the properties of normal dermis rather than, as is liable to happen, a fragile, atropic integument, incapable of performing the functions of normal skin.

The aim of the research proposed by Dr. Hermans of Beverwijk is to increase further the mitotic potentialities of the epidermal cells by applying suspensions of skin cells to the wound. In his working hypothesis he stresses the advantage of using the deep layers of the skin to prepare the suspensions. The experimental part of the research will be carried out in pigs, whose skin has many points of similarity

with that of humans. If the results are encouraging, the method will be applied in humans.

Professor Grignolo is taking up a special problem, that of corneal grafts in burned patients. By definition, corneal grafts are allogeneic (homologous). The normal cornea has no blood vessels and graft rejection therefore does not occur in normal subjects. Burns, however, provoke a vascular reaction in the pericorneal conjunctiva and this may lead to rejection. Professor Grignolo and his co-workers will use light and electron microscopy to observe the very fine changes which take place in the anterior chamber of the eye after burns and after corneal grafts ; their aim will be to determine the causes of these changes and to consider remedies.

### **Allogeneic grafts**

As a result of improved treatment, most burn deaths now occur during the secondary or the tertiary stage. They are attributable directly or indirectly, to the fundamental difficulty of making up for the loss of a large part of the body's skin surface. If it became possible for the entire burned area to be covered, systematically and at an early stage, with grafts possessing the properties of normal skin the therapeutic advance would be a decisive one. For this purpose, autografts are certainly the most suitable biological material, since they present no compatibility problem, but a patient's resources in healthy skin may, as we have seen, be poor. The expedients described above for extending the surface area which an autograft can cover solve some of the problems but are limited in scope. Allogeneic skin, on the other hand, is potentially available in unlimited amount, but if reserves for routine use are to be built up, it is necessary :

- a) to devise a system for labelling skin, as is done for blood (blood groups) and to find an economical method of storage ; and
- b) to overcome the immunological reactions which lead to graft rejection.

#### *A. Donor selection ; preparation and storage of skin*

Clinical experience, acquired mainly in organ transplantation, shows that the histocompatibility barriers are less rigid in man than in most animals, and suggests that selection of the most compatible donor available for any one graft recipient would reduce the speed and degree of immune rejection. How, then, should donors be selected ?

Professor Amiel has established, in agreement with other workers, that the genes determining most of the antigens carried by leucocytes are located at a single chromosomal locus. He considers that determination of the important leucocyte antigens of this major system, by means of sera containing leucocyte-agglutinating antibodies, should suffice for selection of the most compatible donor for a given recipient ; appropriate antileucocyte sera can be obtained from sensitized persons such as multiparous women, patients who have had multiple transfusions, and recipients of grafts. Professor Amiel will compare the results obtained by this method with those of (i) the mixed leucocyte culture technique (transformation of incompatible leucocytes when mixed together and cultured) and (ii) the matching technique de-

vised by Mathe and himself in which unrelated individuals receive successive skin grafts from both potential donors and recipients.

Since the most effective histocompatibility tests inevitably take time it would be an advantage to be able to preserve the viability of tissue to be used for transplant—in particular, in the case of burns, skin. The problem of the preservation of living skin is being investigated by Professor Clerici-Bagozzi. It is known that skin grafts can be stored at 4 °C., without serious loss of viability, for about two weeks. The research workers wish to prolong this period by appropriate storage conditions, but always within the 4 to 6 °C. temperature range.

#### *B. Measures to facilitate graft acceptance*

The rejection process is fundamentally the same for skin grafts as for kidney and heart transplants. Specific factors (transplantation antigens) present in the cell membrane of grafts arouse in the recipient a response, likewise specific, in the form of activation of immunologically competent cells which are conveyed by the blood to the graft and provoke in it a reaction leading to necrosis.

Attempts to attenuate or abrogate the rejection process, may, theoretically, be brought to bear at three levels : (i) the antigenic stimulus ; (ii) the host's response centres ; (iii) the centrifugal pathway conveying activated cells to the graft.

The antigenic stimulus can best be attenuated by reducing the disparity between donor and recipient through selection based upon the histocompatibility tests outlined above. Experimentally, graft antigens can be prevented from entering the body, but the necessary conditions cannot be brought about in burned subjects.

Host response is the subject of three research projects (Castermans and Lejeune, Hamburger and Antoine, and Traeger and Fries).

Dr. Castermans and Lejeune, of Liège, are attempting to obtain, in soluble form, preparations of transplantation antigen containing all the specific antigenic factors of an individual or, by extension, of a genetically homogenous animal strain. Biochemical identification of these substances would be of great interest, but the objective of this research are also of a practical nature.

Enough experimental data exist to justify the view that massive administration of transplantation antigens, in soluble form, would not immunize the host against a graft of the same origin, but would produce specific tolerance for such a graft. To achieve this, an extract must contain the totality of the antigenic factors, and this makes its preparation exceedingly difficult.

It has been held for some years that the "competent cells" whose specific activation leads to graft rejection belong to the lymphocyte series, and antilymphocyte sera have been obtained from animals immunized against lymphocytes of another species ; precisely how these xenogeneic (heterologous) sera act is not known, but they are one of the most effective means of combating the rejection of allogeneic (homologous) grafts. Professor Hamburger and Dr. Antoine are doing fundamental research in this field, comparing the properties of the sera (and of their immunoglobulins) obtained by immunizing experimental animals against whole lymphocytes and their particulate or soluble fractions. Xenogeneic (hete-



rologous) sera obtained by using another type of cellular element will be studied at the same time.

Professor Traeger and Dr. Fries of Lyons, who already have clinical experience with antilymphocyte serum in recipients of kidney transplants, are also attempting to separate this serum's immunoglobulins. They plan to study its modes of action in living animals (effects on the survival of skin grafts and of grafts of labelled spleen cells) and subsequently to conduct a controlled clinical trial, in collaboration with professor Creyssel's burns unit, in burned patients.

The research proposed by Dr. Voisin concerns the third level at which the rejection process is vulnerable. His idea is to protect the graft by the production of antibodies capable of blocking the targets of the rejection-provoking cytotoxic antibodies before these arrive on the scene.

### **Long-term results**

In the research outlined above, healing of burns and application of grafts are approached from the standpoint of reconstitution of the physical integrity necessary for the body's internal equilibrium. However, normal skin also has to give protection against external aggression, and to do so it needs all its inherent suppleness and strength. Any deterioration in these qualities, such as a disfiguring scar or one interfering with freedom of movement, is an obstacle to the resumption of normal living.

Professor Decoulx is studying the subcutaneous capillary network, consisting of newly-formed vessels apparently not yet possessed of normal tonus, in burned areas. When persons who have suffered lower limb burns begin to resume the upright posture cyanosis not uncommonly appears in the burned parts ; it may be severe and accompanied by small ecchymoses, and it is followed by cutaneous pigmentation. The investigators plan to study the natural history of this condition and the state of the local circulation, in particular the appearance and structure of the newly-formed vessels.

Professor Comel and Dr. Mian wish to make a systematic study of the skin covering burned areas, including the vascularity, thickness, humidity, sensitivity to pain and thermal stimuli, and secretion of sebum. The findings will be correlated with local treatments previously applied.

The factors which determine the formation of compact fibrous scars (or keloids) will be studied by Professor Bairati, through chemical analysis of the basic substance of keloid and by electron microscope observation of the fibrils and cellular elements present in keloid at different stages of its development. The treatment of these cicatricial changes being exceedingly difficult, it is hoped that the research will reveal new methods of preventing them and of preventing keloid tissue from hardening.

Finally, a retrospective review of the results of surgical repair and correction, particularly of scars following burns of the face and hands, has been considered essential. A survey is to be carried out at Milan by Professor Sanvenero-Rosselli, and will perhaps be extended later to other centres in the Community.



## I—List of research projects

### Research programme : "Traumatology and rehabilitation"

#### **Head injuries**

##### *Germany*

- 6241/21/05 Professor K.A. JOCHHEIM, Cologne  
" Rehabilitation after head injury "
- 6241/23/04 Professor W. TOENNIS, Professor R.A. FROWEIN, and Dr. KARIMI-NEJAD, Cologne  
" Effects of hypoxia on rehabilitation after severe head injury "

##### *France*

- 6241/23/08 Professor M. DAVID, Paris  
" The effect on the post-concussional syndrome of attempts at early treatment "
- 6241/21/02 Professor E. LAINE, Lille  
" Study of biological and metabolic disturbances, and of associated neuropsychiatric disorders, following head injury. Therapeutic applications. Prevention and early treatment of neuropsychiatric disorders following head injury "
- 6241/21/03 Dr. R. NAQUET, Marseilles  
" Clinical and electroencephalographic course after head injury. Recovery or a post-traumatic neuropsychiatric syndrome ? "

##### *Italy*

- 6241/32/22 Dr. B. BERGAMASCA, Turin  
" Prognosis in post-traumatic coma "
- 6241/21/01 Professor G. GOMIRATO, Pisa  
" Research in the clinical and post-clinical course of the post-traumatic neuropsychiatric syndrome, with fundamental research in biological and metabolic changes in head injury patients "

- 6241/32/01 Professor L. PERRIA, Genoa  
"Changes in the functional conditions of the encephalon in head injury patients"

*Luxembourg*

- 6241/32/12 Dr. G. MULLER and Dr. R. WIDONG, Esch/Alzette  
"Correlation between the late effects (clinical, electroencephalographic, and psychological) of head injuries and the immediate severity of trauma."

*Netherlands*

- 6241/21/06 Dr. F.B. VENEMA, Dr. H.M. GREEBE, Enschedee  
"Rehabilitation of head injury patients"

**Spinal injuries**

*Germany*

- 6241/37/13 Professor H. JUNGHANNS, Frankfurt/Main  
"Combined injuries of vertebral column and skull (and whiplash injuries)"  
6241/22/10 Professor J. REHN, Bochum  
"Injuries of vertebral column and spinal cord"

*Belgium*

- 6241/22/12 Dr. P. HOUSSA, Brussels  
"Cardiorespiratory disturbance in paraplegia"

*France*

- 6241/37/15 Professor P. DECOULX, Lille  
"The stability of the cervical spine, its mobility, its equilibrium, and its instability after trauma"  
6241/23/07 Professor P. DECOULX, Lille  
"Disorders of osteogenesis in paraplegia"  
6241/23/09 Dr. M. MAURY, Fontainebleau  
"The effects of loss of autonomic nervous regulation on the state of circulation below the lesion in patients with vertebral column and spinal cord injuries, and the possible role of such loss in the development of the para-osteoarthropathies"  
6241/33/20 Drs. E. CREMONA, J. MARCHAL, and R. WAEGELE, Aigrange  
"The vertebral column in heavy workers in mines and in iron and steel works"

## **Chest injuries**

### *France*

- 6241/31/17 Dr. P. LAGEZE, Lyons  
"The value of re-educational breathing exercises in the sequelae of severe chest injuries"

### *Italy*

- 6241/31/07 Dr. D. ZANNINI, Genoa  
"Treatment and rehabilitation in chest injuries"

## **Injuries of the locomotor system**

### *Germany*

- 6241/11/07 Professor H. COTTA and Dr. E. MARQUARDT, Heidelberg  
"Myoelectric prostheses for upper limb amputees and patients with shoulder disarticulation. Early fitting of prostheses in lower limb amputees"
- 6241/13/13/1 Professor H. GROH, Saarbrücken  
"Form and degree of constraint sustained by the remaining limb in leg and thigh amputees"
- 6241/13/13/3-4 Professor H. GROH, Saarbrücken  
"Measurement, by accelerometer, of the acceleration of the human limbs and radio transmission of the results. Automatic analysis of cinematographic films and of given empirical functions (forces, acceleration, and action potentials)"
- 6241/36/14 Professor J. HERNANDEZ-RICHTER and Dr. H. STRUCK, Cologne  
"Formation of bony callus and resistance to load in para-articular fractures of the upper and lower ends of the femur, after osteosynthesis and conservative treatment"
- 6241/11/12 Dr. G.G. KUHN, Münster  
"Design for an artificial working hand, an electronic substitute for deep sensibility, a magnetic knee-control device, and individually adapted seats for the severely handicapped"

### *Belgium*

- 6241/36/06 Dr. G. BESENFANS, Montigny-sur-Sambre  
"Treatment and re-education in joint lesions"
- 6241/13/06 Dr. G. BESENFANS, Montigny-sur-Sambre  
"An electromyographic study during the consolidation of bone fractures"

6241/34/03 Dr. J. DUMOULIN, Charleroi  
" Hand injuries. Re-education "

6241/13/10 Professor P. LACROIX, Louvain  
" Physiopathologie of the sequelae of limb injuries "

*France*

6241/11/11 Dr. J. E. LESCOEUR, Saint-Cloud  
" The utilization of prostheses. Fitting techniques and re-educational methods ; utility tests ; occupational capacities of amputees equipped with prostheses "

6241/11/04 Professor R. MERLE D'AUBIGNE, Professor P. MAURER, and Dr. E. MICHAUT, Valenton  
" The fitting of prostheses in lower limb amputees "

6241/13/05 Professor R. MERLE D'AUBIGNE and P. MAURER, Paris  
" Consolidation of bone "

6241/13/02 Professor M. MOSINGER, Marseilles  
" The post-traumatic neuromuscular physiopathological disturbances related to disturbances of consolidation "

6241/11/08 Dr. J.M. PAQUIN, Nancy  
" The utilization of upper limb prostheses. Amputation levels, re-educational therapy, and early fitting of prostheses in lower limb amputees "

*Italy*

6241/36/21 Dr. M. MONTELEONE, Rome  
" An experimental study of the aetiology pathogenesis, and treatment of post-traumatic coxarthrosis "

6241/13/03 Professor O. SCAGLIETTI, Florence  
" Repair of peripheral nerve lesions "

6241/11/01 H. SCHMIDL and Professor F. ZAROTTI, Vigoroso di Budrio  
" Design of a myoelectric prosthesis and of a myoelectric control mechanism for pneumatic prostheses "



Research programme : " Burns "

**Sytemic effects of burns**

*Germany*

- 6243/11/06 Drs. G. LEMPERLE, H.E. KOEHNLEIN, and W.E. ZIMMERMANN, Freiburg-im-Breisgau  
" Changes in metabolism and in the reticulo-endothelial system in severe burns "
- 6243/15/38 Professor J. REHN, Bochum  
" Resarch on staphylococcal infection and on non-specific predisposition to inflammation in burned patients (regulation of defence mechanisms, bacteriology) "
- 6243/11/32 Professors H. HOLLMANN and W. STAIB, Düsseldorf  
" Amino acids and protein metabolism in severe experimental burns "
- 6243/11/11 Professor E. WERLE, Munich  
" Plasma loss in burned persons as the result of the pharmacological action of the biogenic kininis and amines ; therapeutic effects of their specific inhibitors "

*France*

- 6243/21/15 Professor R. BENICHOUX, Nancy  
" Changes in water and electrolytes in experimental burns treated by a combination of Tham, hyperbaric oxygen, and antibiotics "
- 6243/21/08 Professor J. VANLERENBERGHE, Lille  
" The excretin of water and electrolytes via the biliary passages in burned subjects. An experimental study in rats "

*Italy*

- 6243/11/04 Professor A. BERTELLI and E. TRABUCCHI, Milan  
" Measures for attenuating and repairing local and general damage due to burns "

*Netherlands*

- 6243/21/26 Dr. J. GORIS, Amsterdam  
" The influence of three local burns treatments upon the evolution of primary shock and upon the final functional result "

## Tissues directly affected by burns

### France

- 6243/16/29 Dr. P. COLSON, Lyons  
"Clinical, histological, and ultrastructural research on micrografts"
- 6243/11/14 Professor A. MONSAINGEON, Villejuif  
"Oxidation-reduction potential of tissues in intermediary skin burns"

### Italy

- 6243/17/16 Professors M. COMEL and E. MIAN, Pisa  
"The metabolism of the burned area ; qualitative and quantitative research on histoenzymatic activity"
- 6243/24/09 Professor A. GRIGNOLO, Genoa  
"Ultrastructural factors governing acceptance of allogeneic grafts in burns of the cornea and of the anterior chamber of the eye"

### Netherlands

- 6243/16/07 Dr. R.P. HERMANS, Beverwijk  
"Experimental and applied research on the possibility of excising large third-degree burns and obtaining healing by means of suspensions of skin cells"

## Allogeneic grafts

### Belgium

- 6243/18/34 Drs. A. CASTERMANS and G. LEJEUNE, Liège  
"Study of the factors determining incompatibility between host and allogeneic skin graft"

### France

- 6243/22/31 Dr. J.L. AMIEL, Paris  
"Evaluation of the degree of compatibility between donor and recipient of allogeneic skin grafts"
- 6243/18/35 Professor J. HAMBURGER, Paris  
"Facilitation of allogeneic grafts by the use of antitissue antibodies"
- 6243/23/21 Dr. J. TRAEGER, Lyons  
"Antilymphocytic serum and skin grafts ; their use in the treatment of severe burns.."
- 6243/23/19 Dr. G.A. VOISIN, Paris  
"Research in antibodies protecting allogeneic grafts (phenomena of immunological facilitation)"

*Italy*

- 6243/18/44 Professor I. CLERICI-BAGOZZI, Milan  
" Methods for prolonging the viability of refrigerated human skin "

**Long-term results**

*France*

- 6243/15/40 Professor P. DECOULX, Lille  
" Infection in burns. Cyanosis in burn scars "

*Italy*

- 6243/19/41 Professor A. BAIRATI, Milan  
" The nature and ultrastructure of keloid tissue "
- 6243/19/17 Professors M. COMEL and E. MIAN, Pisa  
" Functional characteristics of the burned area shortly after skin regeneration "
- 6243/19/42 Professor G. SANVENERO-ROSSELLI, Milan  
" Long-term follow-up and standardization of plastic repair procedures for severe burns of the face and hand "

**II - Recapitulatory table of research programmes on industrial**

Field and title of programme	Approved on	Financial assistance (dollar units of account, rounded figures)	
		Total allocated	Amount committed
<b>A. Industrial health and medicine</b>			
a) Physiopathology and clinical medicine			
1st programme (Industrial medicine)	5 October 1955	1,200,000	1,200,000
2nd programme (Industrial medicine)	7 April 1960	2,800,000	2,700,000
3rd programme (Physiopathology and clinical medicine)	28 April 1964	3,000,000	2,300,000
b) Traumatology and rehabilitation			
1st programme (Rehabilitation) <sup>(1)</sup>	5 December 1957	500,000	500,000
2nd programme (Traumatology and rehabilitation)	19 June 1964	1,800,000	1,100,000
3rd programme (Burns)	18 May 1966	1,500,000	6,000
<b>B. Industrial physiology and psychology</b>			
a) Human factors and safety			
1st programme (Human factors and safety) <sup>(1)</sup>	5 December 1957	1,000,000	1,000,000
2nd programme (Human factors and safety) <sup>(2)</sup>	4 November 1964	1,200,000	600,000
b) Ergonomics			
1st programme (Industrial physiology, psychology and job adaptation) <sup>(2)</sup>	4 November 1964	2,000,000	800,000
<b>C. Industrial health</b>			
a) Dust prevention and suppression in mines			
1st programme (Dust prevention and suppression in mines) <sup>(1)</sup>	5 December 1957	900,000	900,000
2nd programme (Dust prevention and suppression in mines)	21 December 1964	6,000,000	4,300,000
b) Dust prevention and suppression in the iron and steel industry			
1st programme (Dust prevention and suppression in the iron and steel industry) <sup>(1)</sup>	5 December 1957	600,000	600,000
2nd programme (Dust prevention and suppression in the iron and steel industry)	14 June 1967	4,000,000	1,000
c) Sundry research projects			
Converter gases (brown smoke)	18 July 1961	1,000,000	800,000
Converter gases (brown smoke)	19 June 1964	1,825,000	1,000,000
Atmospheric conditions in mines	16 March 1966	116,000	116,000
Defluorization of gases	16 March 1966	66,000	66,000
<b>Total</b>		<b>29,507,000</b>	<b>17,989,000</b>

<sup>(1)</sup> Part of a single financial-aid programme under the general heading of "Safety", comprising four smaller programmes.

<sup>(2)</sup> Part of a single financial-aid programme under the general heading of "Human Factors and Ergonomics", comprising two smaller programmes.











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