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VITAL STATISTICS OF CLEFT LIP AND PALATE — PAST, PRESENT, FUTURE

P. FOGH-ANDERSEN

Cleft lip and palate belong to the most common of all congenital deformities. They seem to occur among all peoples of the earth, and have been known through thousands of years; at least a case of cleft palate has been described in an Egyptian mummy (Smith & Dawson 1924).

Nothing certain is known about the incidence at birth and the mortality of these malformations in the oldest times. The earliest statistics of the frequency are Russian, from Frobelius 1864. He found 118 cases among 180,000 children in a foundling hospital in St. Petersburg, i.e. 1:1525 or 0.7 ‰; the infant mortality was considerable in those days — 42 out of Frobelius' 118 children died on account of difficulties in nutrition — and the frequency in the living population is unlikely to have exceeded 0.5 ‰.

From the first 30 years or so of the 20th century we have some comprehensive statements of the incidence at birth, indicating figures of about 1 ‰ (France, Peron 1929, 106:100, 889, and Germany, Günther 1931, 102:102 834). This corresponds to a presumed frequency in the population of about 0.7—0.8 ‰.

In Denmark the incidence at birth was investigated in 1939 (Fogh-Andersen), 193:128,306 or 1:665 or 1.50 ‰, for live-births 1.45 ‰.

Subsequent reports from various countries suggest that the frequency is still rising, Tasmania, Rank & Thomson 1960: 1.66 ‰, Denmark, Fogh-Andersen 1961: 1.7—1.8 ‰ and most recently Finland, Gylling & Soivio 1962: 1.8 ‰.

Taking into consideration the decreasing infant mortality nowadays as well as the negligible operation mortality we should expect a frequency in the living population of the coming decades of not less than 1.5 ‰, i.e. a doubling within the last 50 years or a trebling within 100 years — figures of considerable importance from a social point of view.

Is this increase real, however? It is difficult to compare figures from different times in different countries, and the early reports of the 19th century are possibly insufficient. But as to Denmark we have exact statements from 1939 as well as for the following 20 years, demonstrating a significant increase of the incidence.

Year of birth (5-year-groups)	Number of patients operated upon		Total births (live-born) in the country		Proportion of patients operated upon per mille
1938—42	478	:	264.764	or	1.31
1943—47	638	:	466.011	or	1.37
1948—52	595	:	407.144	or	1.46
1953—57	644	:	393.457	or	1.64

The table presents the total number of Danish-born patients during the last 20 years, altogether 2,355, divided into 5-year groups according to the year of their birth. It is seen that the number of patients coming under surgical treatment rose steadily from 1.31 per mille of total live-births in the first 5-year period to 1.64 per mille, corresponding to an incidence at birth of about 1.7—1.8 ‰, in the last period. The difference between 1.31 and 1.64 per mille is statistically significant.

Simultaneously with an increase in the incidence of the affection at birth — particularly during the last decades — we have noticed a considerable decrease of the operation mortality. 20—30 years ago this was generally calculated at about 2—4 % — in some places still higher — whereas now it is less than ½ % in most of the large specialized units. In Denmark, where the surgical treatment of the cleft formations is 100 % centralized in one hospital in Copenhagen, we have during the last 6 years performed more than 1200 operations for clefts of the lip and palate in infants aged between two months and two years with only three postoperative deaths — a mortality of between 0.2 and 0.3 per cent. 20 years ago the Danish mortality was about 2 %, that is nearly 10 times higher. The explanation seems rather simple, being first of all due to the improvement of anaesthesia. The fatal hyperpyrexia of former times — most likely caused by anoxia — is nearly unknown to-day. Furthermore, better preoperative paediatric control combined with a finer, atraumatic technique of surgery have contributed towards reducing the frequency of complications.

While we have thus sufficient explanation of the falling postoperative mortality, the cause of the steadily increasing incidence of cleft formations at birth is not evident.

To elucidate this problem it is necessary to state the facts which at present we believe to know regarding the aetiology of these malformations.

There is no doubt that some congenital malformations are caused by exogenous influences during embryonic life, whereas others are genetically determined. Most likely the majority of congenital deformities are due to a combination of exogenous factors and a gene-pattern, predisposing more or less to congenital malformations in general or to single, specific malformations.

Cleft lip and palate was originally presumed to be of exogenous origin — psychic shock during pregnancy etc. Numerous observations of familial occurrence suggested, however, the influence of a hereditary element. Systematic family investigations in various countries, especially in Denmark (Fogh-Andersen 1942) left no doubt that heredity is the main factor in the aetiology of cleft formations — at least of cleft lip with or without cleft palate. A familial occurrence of clefts was demonstrable in 37 % of these cases. Among cases of cleft palate alone a familial occurrence was found in only 19%, indicating a possible influence of exogenous factors in this type of cleft.

The Danish observations have in all essentials been confirmed later in various countries. During the last years, however, some writers have suggested the possibility of a somewhat greater importance of exogenous factors. This hypothesis is based on the results of animal experiments, especially in U.S.A., which showed that deficient diets — especially deficient in vitamins — fed to pregnant rats might give defective offspring with cleft formations and other congenital deformities (Warkany and co-workers). The stated experiments have already given rise to some "experimental series" on humans — with and without supplemental vitamin intake during the first trimester of pregnancy to mothers who had previously born a cleft lip and/or cleft palate child (Lyndon Peer and Conway 1958); the results have not been convincing so far, however.

A question of current interest is the sad one of the thalidomide-embryopathies demonstrated within the past year. Cleft lip and palate do not seem to belong to the thalidomide syndrome, to judge from the literature, and some uncertainty still prevails regarding these malformations, which are mostly of a very complex nature, but their occurrence has at least shown that certain substances — as for instance thalidomide — may have a marked teratogenic effect in humans. Moreover, it deserves notice that the Danish material from 1942 already suggested that cleft lip and palate combined with other malformations — "multiple malformations" — most often occurred sporadically, without a family history, being therefore possibly due to unknown exogenous factors.

The question now suggests itself: Is the rising incidence of cleft lip and palate at birth most likely to be genetically determined, or is it caused by an exogenous influence?

It is generally accepted that the frequency in a population of any hereditary affection — irrespective of the manner of inheritance — will remain constant through generations, provided there is a balance between a certain reduction of the relative fertility and a certain frequency of mutation. The increasing survival on account of the decreasing mortality in infancy in connection with essentially better cosmetic and functional results of surgery, primary as well

as secondary, will inevitably have caused an increase of the effective fertility (though still less than the average fertility in the population). We cannot say whether the frequency of mutation has changed, but there is no special reason to believe that it has decreased, anyhow.

Consequently we must reckon with a certain rise of the incidence at birth simply by the increasing fertility. On account of a predominantly recessive type of inheritance and, in addition, failing "penetrance" or expression of the gene in the "dominant" families with relatively rare "direct" inheritance, it is likely, however, that a perceptible increase of the affection in the population on a purely genetic basis will take a considerable number of generations.

Accordingly the demonstrated raised incidence at birth during the last decades may perhaps be due in part to exogenous factors — still on the assumption of an unchanged frequency of mutation. In this connection, however, it deserves attention, that the rise in frequency is equally distributed over the different groups of cleft formations, more especially it is not higher for the group of isolated cleft palate, the type of cleft which seems to be familial in no more than one-fifth of the cases.

It is as yet impossible to pronounce with certainty on the nature of exogenous factors that might be active here. An increasing insufficiency of the food, in respect of nutrients and minerals as well as vitamins, is very improbable — at least in Denmark. With the thalidomide catastrophe in mind and with our knowledge of the enormous abuse of tablets of nearly all kinds which has taken place during the last few decades in most civilized countries — particularly sedatives, hypnotics, and psychopharmacologic agents — we cannot exclude the possibility that certain drugs or other substances taken by the pregnant woman during the first months of pregnancy might interfere with the embryonic development — no matter whether such interference is intensified by a hereditary predisposition to malformations or not.

At any rate, I believe that for the present we ought to advise against any kind of drugs — except vitamins — during the first months of pregnancy. This may possibly contribute to the limitation of a further rise in the incidence of cleft lip and palate in years to come.

What else are we able to do in an attempt to prevent the occurrence of cleft formations in the future? We cannot expect to attain much by eugenic measures. The empirical figures for genetic prognosis based on the Danish family investigation 1942 and later confirmed in a Canadian material (F r a s e r, 1956) do not in general indicate induced abortion or sterilization — in contrast to certain German tendencies 30 years ago ("Sterilisation aller Spaltträger"). If the parents desire induced abortion, this might be complied with, however, when the chance of cleft lip with cleft palate is great, i.e. when one parent and at the same time one or more of the children have cleft lip with or without cleft palate (risk about 15%).

In conclusion, I think we must admit that we are still far from any effective prevention of cleft lip and palate in humans, but I hope that future research on an international basis will be able to throw some light on this very important problem.

SUMMARY

Until the first third of this century the incidence of cleft lip and palate was calculated at about 1 ‰ at birth in most countries, and with the rather high mortality during early life before operation and with the operative mortality of that time we could probably estimate the frequency in the living population at about 0.7—0.8 ‰. In 1939 the incidence at birth in Denmark was found to be 1.50 ‰, among liveborn 1.45 ‰; since then it has been rising steadily, and now we have arrived at an incidence of 1.7—1.8 ‰ among liveborn children in Scandinavian countries. With the continuously decreasing mortality rate we must presume a frequency of the least 1.5 ‰ in the living population of coming decades, that is a doubling in about 50 years — a figure of great practical importance.

RÉSUMÉ

Statistique vitale du bec-de-lièvre et de la division palatine: Le passé, le présent et l'avenir

P. Fogh-Andersen

On a calculé que, jusqu'au premier tiers de notre siècle, la fréquence des becs-de-lièvre et des divisions palatines correspondait à 1 ‰ environ des nouveau-nés dans la plupart des pays; vu la mortalité importante au cours de la première enfance, avant que l'opération ait pu être réalisée, ainsi que la mortalité opératoire de l'époque, nous pouvons estimer que cette fréquence était de 0,7—0,8 ‰ environ dans la population vivante. En 1939, on enregistrait au Danemark une fréquence de 1,5 ‰ des accouchements et de 1,45 ‰ des nouveau-nés vivants; depuis, ce nombre augmente de plus en plus et nous sommes arrivés aujourd'hui à une fréquence de 1,7—1,8 ‰ parmi les nouveau-nés vivants dans les pays scandinaves. Tenant compte de l'abaissement progressif de la mortalité, il nous faut prévoir d'atteindre une fréquence de 1,5 ‰ au moins parmi la population vivante, au cours des décades à venir, ce qui équivaut à une augmentation d'environ 100 % pendant une cinquantaine d'années — ce qui est une perspective certainement très importante.

ZUSAMMENFASSUNG

Lebensstatistik der Lippen- und Gaumenspalten: Vergangenheit, Gegenwart und Zukunft

P. Fogh-Andersen

Bis zum ersten Drittel dieses Jahrhunderts betrug die Häufigkeit der Neugeborenen mit Lippen- und Gaumenspalten in den meisten Ländern ungefähr 1 ‰; die Mortalität der betroffenen Kinder war damals recht hoch, sowohl im Zeitabschnitt vor der Operation als auch infolge der Operation, und es ist anzunehmen, dass die Häufigkeit in der lebenden Bevölkerung etwa 0,7—0,8 ‰ betrug. Im Jahre 1939 fand man, dass die Häufigkeit der Neugeborenen mit Lippen-Gaumenspalten in Dänemark 1,50 ‰ war, für Lebendgeborene 1,45 ‰; seit der Zeit ist die Zahl der Neugeborenen mit Spaltbildungen stets angestiegen und beträgt gegenwärtig in den skandinavischen Ländern 1,7—1,8 ‰ der lebendgeborenen Kinder.

Im Hinblick auf die ständig sinkende Mortalität kann angenommen werden, dass die Frequenz der Lippen- und Gaumenspalten in den kommenden Jahrzehnten in der le-

benden Bevölkerung wenigstens 1,50 ‰ betragen wird; das bedeutet eine Verdoppelung im Laufe von 50 Jahren, eine Steigerung von grosser praktischer Bedeutung.

RESUMEN

Una estadística vital acerca de la fisura de labio y paladar del período pasado, presente y futuro

P. Fogh-Andersen

Hasta el primeratercio de este siglo la incidencia de la fisura de labio y paladar se calculó aproximadamente a 1 ‰ en nacimiento en la mayoría de los países y con demasiado gran mortalidad durante el período inicial de la vida antes de la operación y en cuanto a la mortalidad operatoria de aquel tiempo quizás podamos estimar la frecuencia por lo que se refiere a la población viva aproximadamente a 0,7—0,8 ‰. En 1939 la incidencia en nacimiento en Dinamarca hizo 1,50 ‰, entre los recién nacidos vivos 1,45 ‰; desde aquel tiempo ha sido aumentándose permanentemente y actualmente la incidencia hace 1,7—1,8 ‰ entre los recién nacidos vivos en los países escandinavos. Con la mortalidad que va disminuyéndose sin cesar tenemos que suponer una frecuencia de al menos 1,5 ‰ en la población viva de las décadas futuras, es decir, esto significa una dobladura dentro de aproximadamente 50 años — una cifra de una gran importancia práctica.

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ETIOLOGY OF BILATERAL CLEFT LIP AND PALATE

W. PORADOWSKA, M. JAWORSKA

In our material of 450 children with cleft lip and/or cleft palate operated on during the period of eight years (1953—1961) we have been able to get full family histories in 51 cases of bilateral cleft lip and palate (group I) and in 286 cases of the remaining types of clefts (group II). It seems unquestionable that bilateral cleft lip and palate should result from exceptionally unfavourable conditions of embryonic development. A thorough analysis of our material has fully confirmed our suggestions. Since this particular group of defective children has not yet been subjected to a separate etiological evaluation, it seems of value to report our results.

We attempted to compare the incidence of some factors in these two groups of facial clefts. According to other investigators (3, 6), those factors repeat themselves with such frequency in the histories taken from mothers of abnormal children that they may be considered of definite significance.

Retrospective inquiries are of limited value since it is likely that mothers more readily recall unusual events in pregnancy when the child is abnormal (1). We have attempted to overcome this difficulty by comparing our cases of bilateral cleft lip and palate not with the sample of births from the general population but with other types of defect from our material. Mother's reaction by no means depended on the type or severity of an anomaly but on other factors like psychosocial adjustment, intellectual level etc. On the other hand, it shoud be stressed that she could not have known of the organogenetic significance of the early months of pregnancy and there was nothing in our questions to suggest it.

MATERIAL

1. Familial incidence of cases in group I was much higher than in group II — 21.6 per cent and 8.8 per cent respectively. We are tempted to suggest that heredity plays a greater role in the etiology of the former group.

2. The most impressive item of all is the incidence of psychological factors. 47.1 per cent of mothers of group I and 35.7 per cent of group II were severely disturbed with depressive and anxiety states. Family conflicts, alcoholism of the husband, death or disease of close relatives were common findings.

3. The factor next in importance was undernourishment with/or persistent vomiting. Its incidence was found to be equal in both groups — 35.3 per cent and 35.2 per cent respectively.

4 and 5. Acute, infectious diseases (influenza, rubella etc.) occurred in 31.4 per cent in the group I and in 16.4 per cent in group II. Poor health during pregnancy (chronic diseases like anaemia, heart and kidney diseases or gynaecological disorders) also represented a significant item in both groups, particularly in group I — 19.6 per cent, in group II — 15.0 per cent.

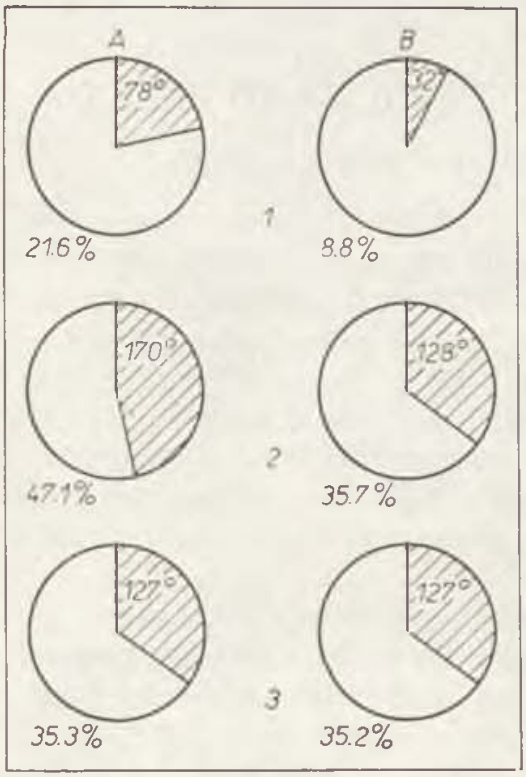

Fig. 1. A = group I, B = group II, 1 = familial incidence, 2 = stress, 3 = undernourishement.

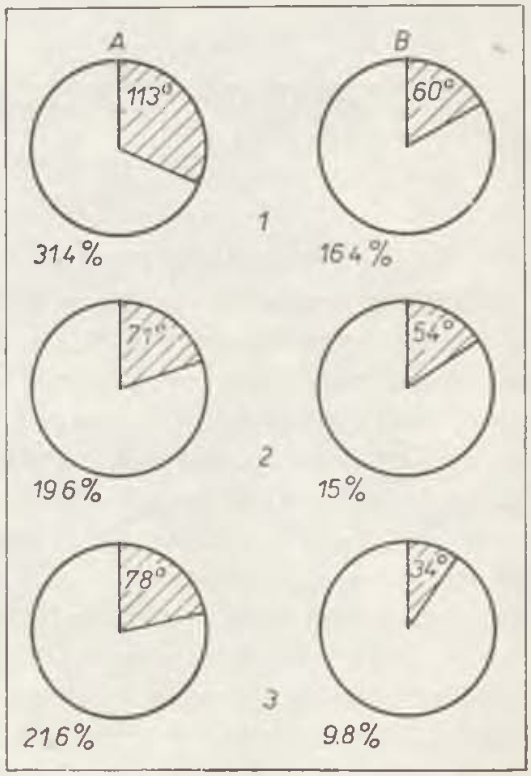

Fig. 2. A = group I, B = group II, 1 = acute diseases, 2 = chronic diseases, 3 = vaginal bleeding.

6. The summarized findings of various authors indicate that about 4 per cent of women have vaginal bleeding in early pregnancy. The average for our group I is 21.8 per cent, for the group II — 9.8 per cent. It should be noted that 5 women of group I gave a history of menstrual difficulties before the pregnancy.

Unfortunately, there is not yet sufficient material for a statistical evaluation of other factors.

In a few cases information was not satisfactory. Parents of the child were often reluctant to give a full account. There are also other cases in which one cannot hope to obtain all the data without metabolic and biochemical studies of the mother.

We have not found any consistent data on the part of the father. A few cases (congenital anomaly, radiation damage etc) do not exclude mere coincidence. Parental alcoholism has not so far been found teratogenic, it represents, however, an important social problem and contributes by making family life

miserable thus exerting indirectly an adverse influence upon the course of pregnancy.

We are presenting a brief account of ten cases of group I. All the events during the pregnancy, cited from mother's history, happened in the first trimester and are related to the child affected with bilateral cleft lip and palate. Mother's age refers in each case to the age when abnormal child was born.

Case 1. Age 23. First child was affected with the same type of cleft. Had kidney trouble and herpetic infection as well as severe vomiting. Premarital pregnancy, was severely disturbed.

Case 2. Age 23. First pregnancy produced normal child, second and third ended in spontaneous abortion, fourth — extrauterine. Adnexitis and pyelitis. Overworked, undernourished.

Case 3. Age 25. Three previous pregnancies ended in abortion (Rh incomptability). Had adnexitis. Threatened abortion resulted in severe nervous depression — the child much desired.

Case 4. Age 25. Two children normal, third died in neonatal period, fourth stillborn, fifth pregnancy ended in spontaneous abortion. Had vaginal bleeding, overworked, undernourished. Family conflicts, shock from being beaten by her husband's mother.

Case 5. Age 25. The child (our patient) was the product of the fourth pregnancy. First child normal, second, born prematurely, had unilateral cleft lip and palate and died in early infancy. Third pregnancy ended in miscarriage. The patient had haemangioma on the upper lip treated with radium when 7 years old. Suffered from liver trouble and gall-stones, was X-rayed, fainted several times. In second month had a large haemorrhage from the uterus. Depressed, very anxious to keep the pregnancy. Her mother died of cancer, brother had speech defect. Her husband was illegitimate, from hard living conditions, had gastric trouble, alcoholic. Worked in a chemical factory where he permanently inhaled poisonous material, worked in high temperatures.

Case 6. Age 26. Only child. She had the same type of cleft as her son. Menstrual troubles. Contracted influenza. Had acute liver insufficiency as sequel of infectious hepatitis. Her brother had hay fever. Husband had occupational contact with mercury vapour and radioactivity.

Case 7. Age 30. The child was product of sixth pregnancy. Two children normal, two died, the fourth, with the same type of cleft, died in early infancy. Contracted gonorrhoea from her husband. Undernourished, overworked. Had abscess on the upper lip and was given penicilin. Several times severely beaten by her husband, alcoholic.

Case 8. Age 30. One child normal, the second (boy) had symptoms of Fröhlich's syndrome. Menarche at 17, had menstrual troubles. Experienced sudden shock in the first weeks of pregnancy — her husband had an accident in the factory and was operated on in the hospital. She thought he would die. Severely disturbed, overworked. Husband had congenital ichthyosis, spontaneous loss of all his teeth at 16 year of age. Mother's family: her mother and one sister insane, father's sister and other sister's son epileptics.

Case 9. Age 32. Only child. Has lived in one room with a woman (a stranger) mentally ill, dangerous, ill-tempered. Was very depressed, frightened, cried all the time. Overworked. (When pregnant again, she made a decision for abortion by curettage in spite of desire for the second child.)

Case 10. Age 33. Four children normal, one died. Worked hard as a laundress, almost starved (during the war). Experienced severe shock in the sixth week of pregnancy when her husband was arrested. She was beaten and threatened by German policemen. Illiterate. Husband alcoholic, tuberculous, had the same type of cleft as his son.

SUMMARY

1. In conformity with the most probable hypothesis, clefts of the face seem to be determined by a dominant gene which is found less frequently and manifests itself to a varying degree in the phenotype (2, 4, 5). According to the generally accepted view, the degree to which the gene becomes manifest, depends to a certain extent on adverse exogenous influences which have proved to be more numerous in cases of bilateral hare-lip and cleft palate.

The authors came to the conclusion that it was necessary to continue detailed investigations of each patient in order to reveal the cases of hare-lip and cleft palate which belong to the group of hereditary deformities.

2. The authors have compared the subjects investigated not with normal children, but with other patients with clefts. The difference between these groups is very significant, with the exception of those connected with the state of the mother's nutrition.

3. The authors' ascertainments illustrate once more the generally accepted view that the majority of hereditary deformities is the result of the mutual effect of both genetic and non-genetic factors. The greater the hereditary sensitivity of the embryo to irregular influences of the internal environments of the mother, the greater the probability of extensive damage to its development. Often only the "predisposition" to cleft deformities has been inherited, but the deformity becomes manifest only if the embryo has been exposed to conditions particularly unfavourable to its development.

RÉSUMÉ

L'étiologie des bec-de-lièvre avec division palatine bilatérales

W. Poradowska, M. Jaworska

1. A croire l'hypothèse la plus vraisemblable, les fentes faciales font suite de l'apparition d'un gène domminant à la fréquence diminuée et instable dans le phénotype 2, 4, 5. En général, on s'imagine que l'affectivité du gène dépend en quelque sorte des influences exogènes infavorables. Celles-ci doivent être extrêmement riches en présence vis-à-vis des fentes labiales billatéralles et de division palatine.

Les auteurs sont d'avis, qu'il faut à tout prix examiner précisément tous les malades ayant pour but d'éclairer ceux d'entre eux, concernant les fentes labiales et du palais comme partielles dans une série des autres déformations congénitales.

2. Dans le travail que voici, le matériel en question n'a pas été soumis en comparaison avec des enfants sains, mais avec ceux, qui sont doués avec d'autres fentes. La différence entre ces deux groupes a été remarquable sauf des cas ayant à faire avec la désalimentation de la mère.

3. Les résultats de ces études illustrent favorablement l'avis général, supposant pour la plupart que les déformations congénitales sont dues au recours des facteurs génétiques et non-génétiques. Plus grande qu'est la sensibilité congénitale de l'embryon contre les influences irrégulières du milieu intra-utérin, plus grande en est la possibilité d'entrer en scène des déformités du développement. Très souvent, il n'existe que la prédisposition à la formation de la fente, la déformation elle-même n'apparaît qu'au moment où l'embryon vient d'être exposé à des circonstances infavorables du développement.

ZUSAMMENFASSUNG

Zur Aetiologie beiderseitiger Lippen- und Gaumenspalten

W. Poradowska, M. Jaworska

1. Der glaubwürdigsten Hypothese zufolge gehen Spaltenbildungen im Bereich des Gesichts aller Wahrscheinlichkeit nach auf ein dominantes Gen mit verminderter Frequenz und nichtkonstantem Auftreten im Phänotyp zurück (2, 4, 5). Allgemein wird angenommen, dass die Affektivität des Gens in einem gewissen Grade von ungünstigen äusseren Einflüssen abhängt, wobei diese Einflüsse besonders zahlreich in Fällen sein dürften, in denen beiderseitige Lippen- und Gaumenspalten auftreten.

Die Verfasser kommen zu dem Schluss, dass alle Befallenen weiterhin eingehend zu untersuchen sind mit dem Ziel, jene Falle aufzuklären, in denen die Lippen- und Gaumenspalte nur eine Teilerscheinung einer ganzen Reihe vorliegender kongenitaler Deformationen darstellt.

2. In der vorliegenden Arbeit wurde das Untersuchungsmaterial nicht mit normalen Kindern verglichen, sondern mit solchen, die mit anderen Spaltenbildungen behaftet waren. Die Unterschiede zwischen diesen beiden Gruppen waren bedeutend mit Ausnahme der Angaben, die sich auf den Ernährungszustand der Mutter bezogen.

3. Die Resultate dieser Studie sind eine weitere Illustration für die allgemein vorherrschende Ansicht, dass die Mehrzahl der angeborenen Störungen durch das Zusammenwirken genetischer und nichtgenetischer Faktoren zustande kommt. Je grösser die vererbte Empfindlichkeit des Embryos gegenüber nichtsystematischen Einflüssen des intrauterinen Milieus ist, desto grösser ist die Wahrscheinlichkeit, dass tiefgehende Entwicklungsstörungen auftreten. Häufig wird bloss die „Prädisposition" zu Spaltenbildung vererbt, die Deformation selbst tritt jedoch nur in jenen Fällen auf, wo der Embryo ausserordentlich ungünstige Entwicklungsbedingungen vorfindet.

RESUMEN

Algunas notas sobre la etiología del labio leporino y la fisura palatina bilaterales

W. Poradowska, M. Jaworska

1. Según la hipótesis más probable parece que las fisuras faciales estén transmitidas por el geno dominante con penetrabilidad reducida y expresividad baja (2, 4, 5). Está aceptado en general que la expresividad del geno depende parcialmente de las circunstancias adversas del ambiente que ocurren con más frecuencia en los casos con las fisuras de labio y paladar bilaterales.

Hay que concluir que el árbol genealógico de las familias en cada caso, en tanto que posible, debe excluir las condiciones bajo las cuales el labio leporino y la fisura palatina forman parte de un síndrome heredado.

2. En lugar de hacer una comparación de nuestro material con él de los niños normales, una comparación con los tipos restantes de las fisuras ha sido hecha. Las diferencias entre los grupos son muy notables con la excepción de los datos referentes al estado de nutrición de la madre.

3. Nuestros hallazgos muestran una vez más que las malformaciones más congénitas son resultado de la acción recíproca entre los factores genéticos y no genéticos. Cuanto más el embrión está susceptible genéticamente a la influencia prenatal anormal tanto más grande es probabilidad de la existencia de los defectos más extensos en el desarrollo. Muchas veces solamente una „tendencia" hacia las fisuras faciales está transmitida genéticamente y el defecto aparecerá sólo cuando el embrión encuentra ciertas condiciones de ambiente.

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CLEFT LIP AND CLEFT PALATE: A SUMMARIZED STATISTICAL SURVEY

M. JAWORSKA, W. PORADOWSKA

450 children with cleft lip and/or cleft palate were operated on in the Children's Surgical Department during a period of eight years (1953—1961). The data were recorded at an interview with the parents of all children though the full information was not given in every instance.

An attempt has been made to evaluate the genetic as well as some environmental factors influencing the development of this malformation.

RESULTS

Table 1 indicates a higher incidence of the malformation in males. A higher percentage of males than females had cleft lip or cleft lip and cleft palate, whereas a higher percentage of females had cleft palate only. Combined cases occurred more frequently than either cleft lip or cleft palate alone. Unilateral cleft lips were more common than bilateral and the left side was more frequently involved.

In these respects the results are similar to those of other reports.

GENETIC FACTORS

In our material only 10.7 percent of cases had a positive family history of similar deformities going back as far as grandparents in the maternal and paternal line. In other words, 40 affected relatives of three or four generations were encountered in the families of 36 children. The children with isolated cleft lip or cleft palate are not likely to have the relatives affected with a type of cleft other than theirs.

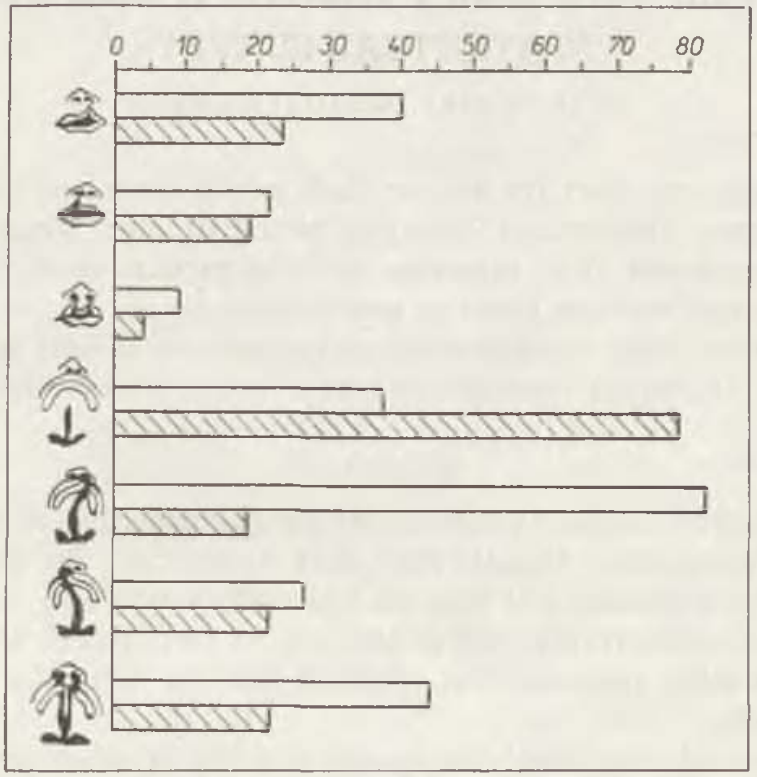
It should be emphasized that no consanguinity was encountered amongst the parents and that the inheritance was through one side of the family. Both findings are suggestive of dominant inheritance.

In a relatively small number of cases the cleft lip and/or palate is accompanied by other developmental defects. In our material 44 cases — 9.8 percent. This is to be expected since infants with multiple severe malformations are unlikely to survive the perinatal period. In many cases there are multiple facial

and skull defects as well as imbecility. The associated anomalies are significantly more numerous in group 2 of isolated cleft palate.

The 16 percent incidence of congenital malformations among cleft palate families appears to be higher than that of the average population. Speech defects and mental retardation were detected in 32 cases among the relatives of 54 children. The incidence of epilepsy is found to be relatively high and should be mentioned. These findings may be another example of the theory of genic transmission with regard to neural or anatomical deficiences.

Tab. 1. Incidence of cleft lip and/or cleft palate. [ ] = males, [////] = females



CONCLUSION

We may conclude from the analysis of our material that only autosomal dominant inheritance of clefts cannot be entirely eliminated as a possibility, but would involve the assumption that the penetrance of the gene concerned is very low and variable.

Tab. 2. Percentage distribution by maternal age in three age groups

Age groups in years	Birth of affected children	Control births	Difference
15—19	6.2	6.7	—0.5
20—34	76.1	81.0	—4.9
35—49	17.5	12.3	+5.2
Total	100.0	100.0	

Our findings have confirmed the possibility of different etiology in some cases of isolated cleft palate, postulated by several investigators. The pattern of sex incidence, association with other malformations with particular frequency of face and skull defects, the same type of cleft in the family of children with isolated cleft palate — all these findings are very conclusive.

Tab. 3. Maternal nutritional status

	Number of cases	Per cent
In the first trimester of pregnancy		
1. Diet not supplemented with vitamins	306	90.8
2. Insufficient diet	47	13.9
3. Persistent vomiting	28	8.3
4. Insufficient diet associated with persistent vomiting	77	22.8
In the period of growth and puberty		
5. Insufficient diet	86	25.5
In the whole maternal environment		
6. Inadequate, deficient diet	97	28.8

ENVIRONMENTAL FACTORS

There are many noxious factors which may directly produce clefts or may provide abnormal conditions interfering with the development of the embryo. Prenatal maternal factors have been the subject of many studies. Our observations confirm the previous results and provide still more evidence as to these factors in the etiology of clefts.

While 12.3 percent of the mothers for all births were over 35 years of age, 17.5 percent of the mothers of cleft cases were over 35. The difference is statistically significant. The reason why advanced maternal age increases the risk of certain malformations is unknown. The poor quality of the ova of the ageing ovary, delayed fertilisation, faulty implantation, spontaneous mutations, hormonal and metabolic disorders are all theoretically possible.

Fig. 1 shows the time of conception of 450 children in particular months of the year. The winter season shows a relatively higher incidence of cases. This might be thought to be related to the seasonal incidence of infectious diseases. On the other hand, it may result from the inadequate diet deficient in fresh fruit and vegetables during the cold months of the year.

The results of animal experiments prove conclusively that certain vitamin deficiencies are able to cause embryonic maldevelopment. It has been suggested that there is a significant relationship between nutritional deficiencies in the mother during pregnancy and the production of structural malformations in the child.

In 306 out of 337 pregnancies in our material no vitamins were taken or were taken late and irregularly. It is important to note that even a good intake of nutrients can result in deficiency if there is persistent vomiting or poor absorption. Many mothers may be at the borderline between deficiency and adequacy but during the critical stage of rapid development of the embryo the borderline condition might easily change to one of definite deficiency.

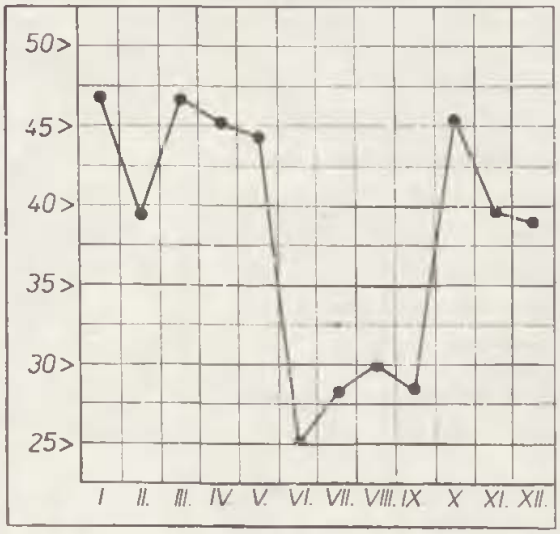


Fig. 1.

Tab. 4. Incidence and kind of stress

Mental stress	Number of cases
Familial conflicts	29
Death or disease of close relatives	22
Depressive states, anxieties (e.g. imprisonement of husband — 5 cases, war experiences — 6 cases)	29
Sudden fear, nervous shock (e.g. burning of the house — 2 cases)	21
Very poor living conditions	12
Physical stress	
Fall	19
Injury	12
Intoxication	5
Surgery under general anaesthesia	4

Maternal infection can change the chemical environment of the human embryo. The risk increases greatly when influenza is experienced early in pregnancy — it was in 10.2 percent whereas the average morbidity in Polish population for the years 1953—1959 was found to be 3.2 percent.

While these data are not alarming compared with the risk claimed for rubella, it deserves serious notice because of the absence of a lasting immunity, and, consequently, the high adult morbidity during an epidemic. It strongly suggests the advisability of affording protection by vaccination to pregnant women when an epidemic is in progress or expected.

The stress theory in humans assumes that emotional upset or other forms of stress in pregnant women induce the production of ACTH in the pituitary gland which stimulates the adrenal gland to secrete large amounts of cortisone. This excess cortisone during the early months of pregnancy, which are critical for the development of the palate, may inhibit fusion of the palate shelves. Critics of the theory point out that inhibitory substances slow down production of ACTH by the pituitary gland when cortisone is present in excessive amounts but it is possible that this balance may be defective in some pregnant women.

In our study, almost half the women were exposed to one (or more) category of stressful situation. Although the emotional and physical components of stress could not be separated distinctly, the majority of the troubles reported were primarily mental.

SUMMARY

In general, our findings conform to the surveys carried out by other investigators.

It is impossible to tell from the end result what particular combination of factors was responsible for the defect in any one case. However, it is possible to establish some statistical correlations that may at least be guides as to where one might look for specific factors.

Further documentation of cases of all types of cleft will provide the clue which may lead to a better understanding of the etiology of the anomaly under question.

RÉSUMÉ

Bec-de-lièvre et division palatine: résumé statistique

M. Jaworska, W. Poradowska

Nos données sont en général d'accord avec celles obtenues par d'autres investigateurs.

Dans aucun cas, il ne semble possible de tirer des conclusions en ce qui concerne les combinaisons ou les facteurs responsables de la déformation en se basant exclusivement sur le résultat final. Mais on est quand même en mésure d'établir certaines corrélations statistiques qui peuvent nous servir de guide dans la recherche des facteurs spéciaux.

A l'avenir, une documentation soigneuse, concernant tous les types des fissures, devrait être mise à point pour nous aider à mieux comprendre l'étiologie de l'anomalie en question.

ZUSAMMENFASSUNG

Lippen- und Gaumenspalte: eine Uebersicht statistischer Erhebungen

M. Jaworska, W. Poradowska

Die Ergebnisse unserer statistischen Studien stimmen im grossen ganzen mit denen anderer Verfasser überein.

Auf Grund des definitiven Resultates des teratogenen Prozesses ist es nicht möglich zu ermitteln, welche Faktoren in ihrem Zusammenwirken für das Auftreten der Spaltenbildung im konkreten Fall verantwortlich sind. Anderseits ist es jedoch möglich, einige statistische Korrelationen zu bestimmen, die die Richtung angeben könnten, in der spezifische teratogene Faktoren zu suchen sind.

Weitere Untersuchungen über die Entstehung der verschiedenen Spaltentypen werden Resultate ergeben, die vielleicht ein besseres Verständnis der Aetiologie dieser Störungen ermöglichen.

RESUMEN

Labio leporino y fisura palatina: un resumen estadístico compendiado

M. Jaworska, W. Poradowska

En general, los resultados de nuestras investigaciones están en conformidad con los efectuados por otros investigadores.

Es imposible indicar a base del resultado último que combinación de factores fue responsable del defecto ni en uno de los casos. Pero es posible establecer algunas correlaciones estadísticas que, por lo menos, pueden servir como guías para poder determinar el lugar donde hay aquellos factores específicos.

Más documentación de los casos con todos los tipos con fisuras será un guía que pueda contribuir a una mejor comprensión de la etiología de dicha anomalía.

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HARELIP AND CLEFT PALATE — GENETIC CONTRIBUTION

J. ČERVENKA

The question of the heredity of harelip and cleft palate is becoming an increasingly important subject of research, in which a number of problems are encountered. The role of heredity was stressed by Fogh-Andersen (1942) on the basis of extensive material. He divided clefts into two categories, which he assumed to be genetically entirely independent of one another: I. harelip (and cleft palate) and II. isolated cleft palate. He showed the first type to be a "conditional" dominant, with a transition to recessivity and with sexual limitation to males. The second type, cleft palate, was an incomplete simple dominant, sexually limited to females. Similar views were expressed by Steiniger and other authors.

Other authors, however, expressed different views. Sanders: Complete clefts are determined by polymeric recessivity. Five different genes exist — two for the upper lip (left and right), two for the hard palate and one for the soft palate. Fortuyn: clefts are determined by digenic recessive inheritance, i.e. the hereditary factors behave like recessive, sex-bound factors and like autosomal recessive factors. Mengele and Simon: A general, universal, atypical common defective gene exists for abortions, still births, clefts, twins, etc... Other such views are to be found in the literature, but they seem to be no more than indefinite hypotheses for which no factual support has yet been found.

Most authors are agreed that clefts involve complicated transmission with very low penetrance and that they are not bound completely to the sex chromosome. "Low penetrance" is capable of different interpretations. It may involve the integration of two genes occupying different loci, or it may be due to the infrequent and irregular manifestation of a single gene. Information in this respect would be much more accurate if some non-cleft manifestation of a defective gene were found, which could always be determined if the gene was present, even if it did not produce a cleft. This manifestation could be either a morphological abnormality or an observable metabolic anomaly.

The participation of genetic mechanisms in the formation of a defect is also confirmed by clear limitation to sex. Isolated cleft palate is more frequent in females and harelip (and cleft palate) is commoner in males. The sex

hormones of the foetus cannot be assumed to influence the formation of clefts, which develop in about the seventh week pregnancy, i.e. relatively early.

Preliminary classification of the author's series of twins with clefts and a few findings on a common incidence of both types (I and II) in a single genealogical record may help to contribute to these questions.

Tab. 1.

		Monozygotic	Dizygotic
Harelip (and cleft palate)	Concordance	8	1
	Discordance	9	4
Cleft palate	Concordance	1	0
	Discordance	4	3

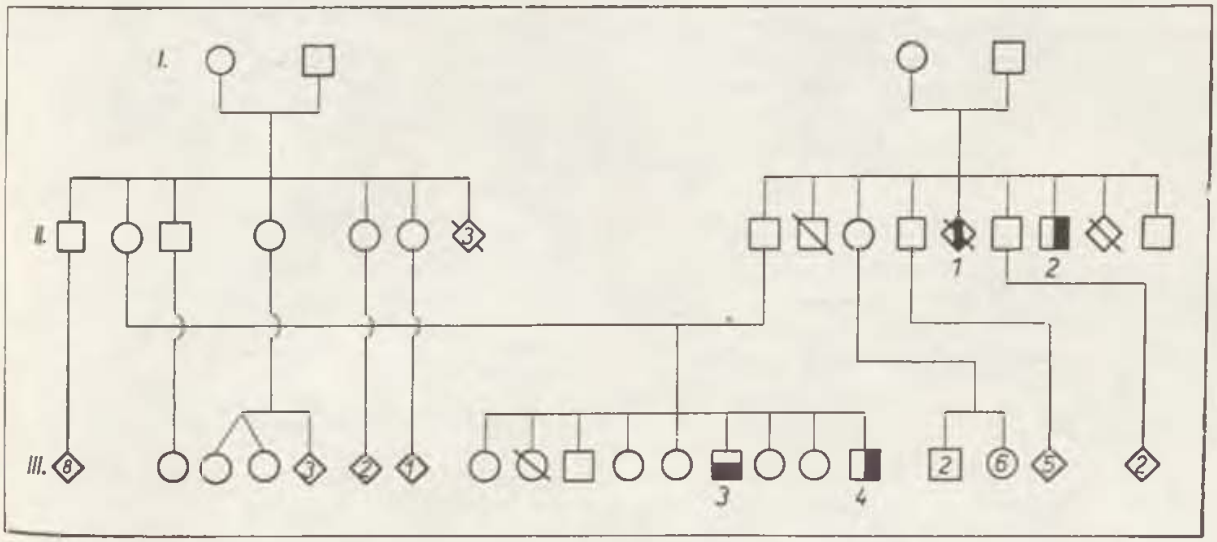
In genetics, the study of twins is one of the most important methods, since it helps, among other things, to determine the proportion of the part played by heredity and environment on the formation of a defect. Thirty pairs of twins with different types of harelip or cleft palate were observed at the Charles University Clinic of Plastic Surgery in Prague. Their distribution according to zygosity, concordance and discordance is shown in Tab. 1. The table shows marked predominance of concordance in monozygotic twins, which is more marked in harelip (and cleft palate) than in isolated cleft palate (47% and 20% respectively). Concordance in type II in monozygotic twins is thus less than half as frequent as concordance in type I. Fogh-Andersen gives hereditary disposition as 36.7% for type I and 19% for type II. The author's findings in twins do not therefore differ significantly from Fogh-Andersen's findings. They also support the view that genetic systems participate about twice as frequently in the formation of harelip (and cleft palate) as in the formation of cleft palate only.

No significant signs of pleiotropism were found in this series. In one pair of twins, concordant syndactyly of the second and third toe was present, in another pair the twin without cleft had syndactyly and in a third pair the twin without cleft had talipes equinovarus. In three pairs one twin was stillborn or died at birth. According to the parents, none had clefts.

Attention must also be drawn to the determination of zygosity in this series. In six pairs of twins of the same sex, monozygosity was determined by comparing blood groups and by polysymptomatic tests. In three pairs reciprocal grafts were exchanged. Other twins of the same sex, with the exception of one pair, were also classified as monozygotes on the basis of identical pigmentation, build, dental structure and appearance. The series is thus loaded with error, which it is hoped to correct in the near future by an exchange of grafts, since only reciprocal homografts, supplemented by a comparison of blood groups and other signs (the dermal papillary lines, the colour of the iris, the texture and colour of the hair, the shape and structure of the teeth and jaws,

weight, height, etc.) permit reliable determination of zygosity. Genetic chimaeras and cases of agammaglobulinaemia cannot affect the material because of their rarity.

It can be said that the author's findings on the incidence of harelip and cleft palate in twins does not differ significantly from those in most of the series published by other authors.



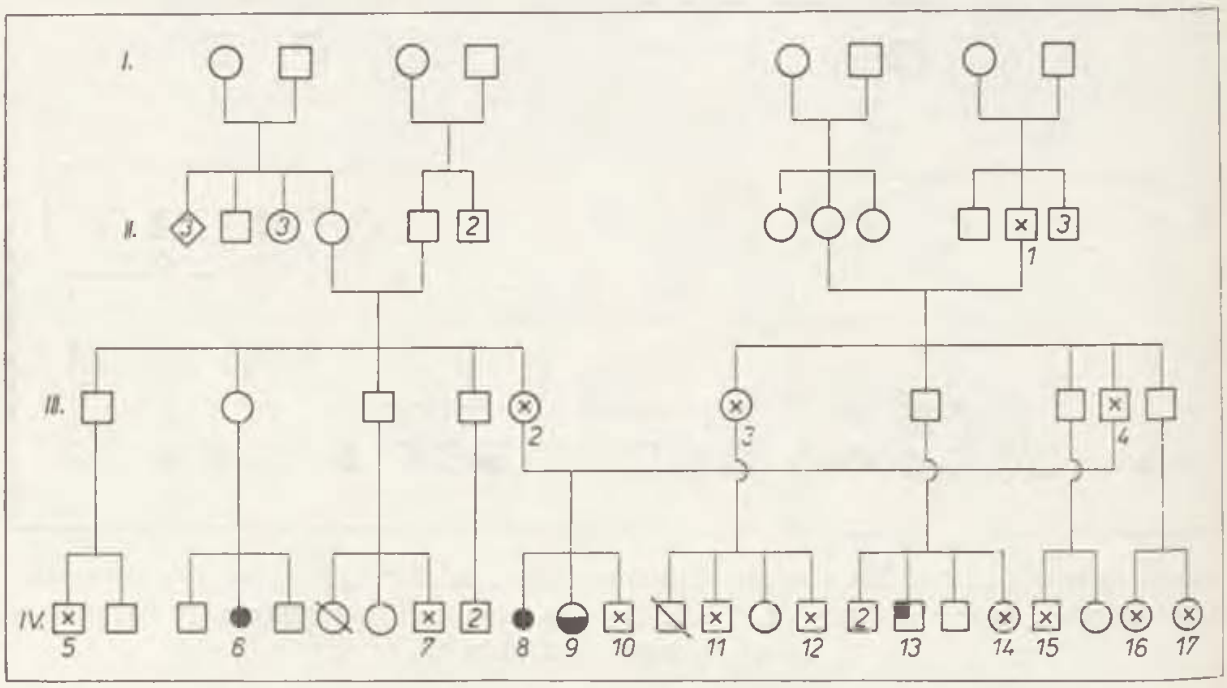
Genealogical chart No. 1.: 3 Isolated cleft palate, 2 and 4 right-sided complete cleft, both operated on at the Clinic of Plastic Surgery, Prague, 1 complete cleft, not known on which side; died at birth.

When drawing up genealogical charts, a simultaneous incidence of type I and type II clefts was found in several families. In 703 families of patients with clefts, Fogh-Andersen found seven cases of isolated cleft palate and four of harelip and cleft palate in the families of probands with the opposite type of cleft. Both the seven and the four cases occurred in the siblings of the proband's parents or in the children of the parents' siblings. The author estimated that this incidence could be accidental and he therefore regarded the division of clefts into the groups I — harelip (and cleft palate) — and II isolated cleft palate — as correct and claimed that they were genetically independent of one another.

In the series of the Clinic of Plastic Surgery (the histories of 405 families have so far been studied), eight cases of cleft palate only were found in the families of probands with the first type of cleft; six of these were among the parents' siblings, one in the mother's father and one in one of the proband's own siblings. Among the families of patients with isolated cleft palate, three clefts of the first type were found — one in the son of the father's brother, one in the daughter of the mother's father's brother and one in the proband's own brother. Fogh-Andersen found no cases in relatives closer than the parents' siblings. It was found by calculation that in the present author's material, five type I clefts could be anticipated in the families of probands with isolated cleft palate (4,250×1.5‰×75% — the number of the members of the families

of probands with isolated cleft palate × the incidence of clefts in the population × the percentage of harelip (and cleft palate) among all types of clefts. In actual fact, fewer, i.e. three, were found.

In the families of patients with harelip (and cleft palate), the mean value of the accidental incidence of isolated cleft palate was four (10,380×1.5‰× ×25%). Double this number, i.e. eight, was actually found.



Genealogical chart No. 2.: 9. Isolated cleft palate and congenital dislocation of the hips, 13. left-sided harelip, 1. congenital cardiac defect, 2. small upper lip, rotation and atypical shape of left incisor, 3. night blindness, 5. congenital inguinal hernia, 6. spontaneous abortion, 7. strabismus, 8. artificial abortion 10. congenital cardiac defect, 11. mentally backward, attending special school, 12. congenital cardiac defect, 14, 15, 16, 17. congenital dislocation of the hips, 4. experiences bitter taste after diphenylthiourea (twenty to one million) 9. no sense of taste for diphenylthiourea.

The findings are not unequivocal, but the fact that both forms of cleft were found in two pairs of siblings and that they are found together in general, drew the author's attention to the work of the Australian authors Rank and Thomson. These authors — a plastic surgeon and a geneticist — studied 221 cases of cleft lip and palate in Tasmania and made a detailed genetic evaluation of the results.

Among the 47 families of probands with harelip (and cleft palate), they found an incidence of isolated cleft palate in 16, i.e. 33%. In this respect their series differs from other series published.

The above authors concluded that two genetic systems participate in the formation of type I and II clefts, but that some cases of isolated cleft palate may be produced by the complex of genes for harelip (and cleft palate). In their opinion the two types are not genetically strictly separable.

It should be added that fistulae of the lower lip were found in one of the probands in the author's series, in whose genealogical chart both types of clefts appeared. These symmetrical fistulae also appeared in relatives with clefts. Fogh-Andersen regards this combination (cleft and fistulae of the lower lip) as an exception to the rule of the genetic independence of types I and II.

SUMMARY

In a preliminary series of 30 twins with clefts, greater predominance of concordance was found in monozygotic twins than in dizygotic twins, which was more marked in type I clefts than in type II.

Four hundred and five genealogical charts of patients' families were drawn up. In this material, 11 cases of a different type of cleft from that of the proband were found among the latter's relatives. In two cases one of the proband's siblings had the opposite type of cleft. This finding ought to stimulate deeper study of the question of the genetic difference between harelip (and cleft palate) and isolated cleft palate.

RÉSUMÉ

Bec-de-lièvre et division palatine. Contribution génétique

J. Červenka

A l'occasion de l'examen d'un ensemble de 30 couples jumeaux, on a constaté qu'il y a prédominance de la concordance chez les couples monozygotiques, par rapport aux couples dizygotiques, ce qui se manifeste d'une manière plus prononcée pour le type I. que pour le type II.

On a établi 405 arbres généalogiques des malades atteints de chéiloschisis ou de palatoschizis. Dans ce matériel, on a constaté parmi les parents des probands l'existence de 11 cas d'un autre type de fissure que celui dont était atteint le proband. En 2 cas, les frères et soeurs des probands étaient atteints de l'autre type que ce n'étaient les probands. Ces données pourraient encourager des études plus approfondies de la question de la différenciation génétique de la chéiloschisis (et palatoschizis) et de la palatoschizis isolée.

ZUSAMMENFASSUNG

Lippen- und Gaumenspalte. Genetische Bemerkungen

J. Červenka

In einer früheren Serie von 30 Zwillingen mit Spaltenbildung wurde ein Überwiegen der Konkordanz bei monozygoten gegenüber dizygoten Paaren festgestellt, was bei Typus I deutlicher als bei Typus II in Erscheinung trat.

Es wurden 405 Stammbäume von Patienten mit Spaltenbildung aufgestellt. In diesem Material wurden bei den Verwandten der Probanden 11 Fälle von Spaltenbildung anderen Typs, als der Proband selbst aufwies, gefunden. In 2 Fällen wurde sogar bei den Geschwistern der Probanden der entgegengesetzte Typus festgestellt. Diese Tatsache sollte Anlass zu einem tieferen Studium der genetischen Unterschiedlichkeit von Lippen- (und Gaumen-) Spalte und der isolierten Gaumenspalt bieten.

RESUMEN

Fisura de labio y paladar. Notas genésicas

J. Červenka

En un grupo preliminar de 30 casos de la fisura de labio y paladar fue averiguada la preponderancia de la concordancia de los pares monocigomáticos en comparación con los dicimáticos, más aparente en el primer tipo que en el segundo.

Fueron elaboradas 405 genealogías de los pacientes con la fisura de labio y paladar. En este material fue averiguada la apariencia de 11 casos de un otro tipo de la fisura entre los parientes de los pacientes a diferencia de la fisura que tuvo el enfermo. En dos casos se trató directamente de los hermanos del paciente que fueron afligidos por el tipo opuesto. El resultado de esta investigación podría presentar un motivo para un estudio más profundo del problema de la diferenciación genésica de la fisura de labio (y paladar) y de la fisura aislada de paladar.

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ANALYSIS OF 147 FATAL THERMIC INJURIES*

S. HÁJEK, Z. GREGORA, J. ŠTEFAN, Z. KRÁL, J. CHYBA, L. RŮŽIČKA
M. DOBRKOVSKÝ, J. DOLEŽALOVÁ

Although damage to the organism caused by high temperatures is not the most frequent type of injury, it still remains an important problem on a world-wide scale with regard to both its sociological and biological aspects. According to the estimate of Baxter (2), several hundred thousand people with burns are taken to hospital each year; about 60,000 of whom die.

In Czechoslovakia the mortality rate from burns and scalds shows a slight decline but 200 persons still die from this cause each year (7). The age representation of these victims is given in Fig. 1.

From Fig. 1 it becomes evident that the largest number of deaths occurs up to the age of three and from 60 years upwards. Up to the age of 60, men die more frequently from burns, over 60 more often women.

A similar conclusion has been reached by the evaluation of a group of 147 cases treated at the Burns Unit of the Clinic of Plastic Surgery and autopsied at the Department of Pathology and Forensic Medicine both of the Medical Faculty of Hygiene, Charles University, Prague, Czechoslovakia, in the years 1954 to 1961.

Fig. 2 again shows a higher number of deaths up to the age of four and an increase of the death rate in the older age groups. As in the graph comprising the total number of deaths for Czechoslovakia, also in this graph the number of men is larger in the middle-age group, that of women in the old-age group.

This series of 147 cases of burns sickness which terminated fatally, constituted the material for our further analysis. It comprises 135 adults and 12 children up to the age of 14.

*) Read at the tenth Czechoslovak Congress of Forensic Medicine held in Prague in Nov., 1962.

The accidents in adults were grouped into those which had occurred at home ("domestic"), at work ("occupational") — according to the Czechoslovak ÚRO*) Public Notice No 7/62 — and "others" (the latter comprising road accidents, suicides, etc.). Tab. 1 shows the division of the series of cases according to the groups mentioned above and the mechanism of accident.

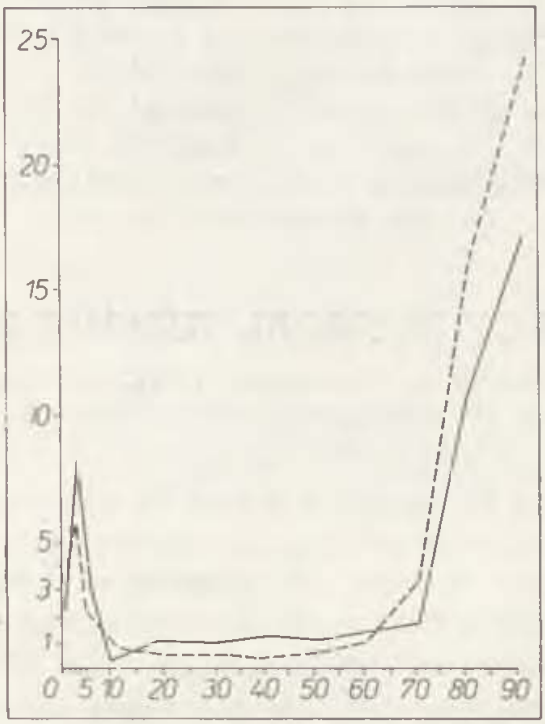

Fig. 1. Death rate from burns and scalds in Czechoslovakia-average for period 1956—1959. (x — age of patient at death, y — number of deaths per 100,000 population of a given age group. Men are marked with full, women with dashed line.)

In domestic accidents the large proportion caused by stoves, burning alcohol and kerosine, stands out. Burns caused by stoves were sustained mostly by elderly people. Most frequently this was due to their clothes catching fire when lighting or stoking the stove or when warming themselves standing or sitting too near the red-hot stove. Not infrequently these accidents happened by people falling onto red-hot stoves, mostly on sudden indisposition or loss of consciousness. Explosion of alcohol or kerosine usually took place by using these combustibles for lighting the stove or refilling a burning cooker. This type of accident was the cause of fatal burns mostly in women. Of the other combustibles used for domestic purposes, petrol, acetone, butane, floor polish, etc. also caused accidents with fatal consequences. Apparently surprising is the fact that the second most frequent cause of domestic burns in men is smoking, mainly by a blanket or quilt catching fire from a cigarette smoked in bed.

In the statistics of Winterscheid (20) getting burned while smoking in bed was one of the most frequent causes of burns in men. It was registered in one-fifth of cases, two-thirds of which occurred while under the influence of alcohol.

*) Czechoslovak TUC — note of translator

The group of "various sources of accident", for instance, includes burns from hot water bottles, fire breaking out at home, etc., apart from not quite clear causes and sources of thermic injuries. Scalds sustained at home were found mostly in women, e.g. by pouring hot fluid over themselves when slipping while carrying it from one place to another or by falling into the hot fluid itself. Scalds while taking a bath occurred exclusively in men.

The most frequent source of burns in occupational accidents were the various combustibles and explosives. Although we are fully aware of the fact that the main cause of these accidents was, as a rule, careless and incorrect handling of these substances, we nevertheless, should like to draw attention to one circumstance which reappeared several times in our series: the working clothes catching fire from having been soaked with grease or even a first class combustible. The group of "various sources of accident" e.g. include burns from red-hot slag or those sustained while burning down the dead stalks of grass, etc. Occupational injuries causing scalds were sustained from explosions of central heating boilers during repair or by the bursting of hot water or steam pipes.

The various sources of accident in children of the series studied are given in Tab. 2.

Tab. 2 shows that the causes of thermic injuries in the children of our series are much less manifold than those in adults. Of our cases, 50% were scalds. The most frequent mechanism of accident was the child falling into a receptacle filled with hot water which had been prepared for washing the laundry or for a bath.

Tab. 1. Grouping of our series of adults according to mechanism of accident

Mechanism of accident	Total		Number of cases					
			Domesting accident		Occupational accident		Other accidents	
	Men	Women	Men	Women	Men	Women	Men	Women
Stove	11	21	11	21				
Denaturated alcohol	1	17	1	16				
Kerosine	1	5	1	5				
Other combustibles and explosives	14	10	1	6	11	4	2	
Electrical and gas appliances	4	4	3	4	1			
Smoking	6	—	5				1	
Electric current	6				5		1	
Various	9	9	3	5	4	2	2	2
Scalds	12	5	1	5	9		2	
Total	64	71	26	62	30	6	8	3

The conclusions and the possibilities of prevention following from this analysis of the mechanism of accident in our series of cases, are given at the end of this report.

On preliminary evaluation of our series from a biological point of view we assumed that the prognosis of burns is basically decided by three factors: the

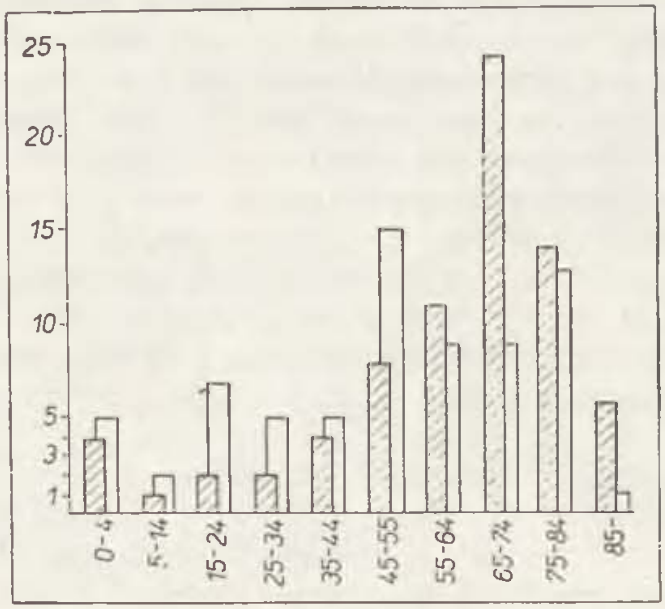

Fig. 2. Death rate from burns and scalds in our series of cases. (x — age of patient at death, y — number of deaths in absolute values. Men are marked by white, women by shaded columns.)

Tab. 2. Grouping of our series of children according to mechanism of accident

Mechanism of accident	Number
Stove	2
Denaturated alcohol	2
Film	1
Electrical appliance	1
Scalds	6
Total	12

age of the patient and his state of health prior to the accident, the severity of the injury determined by the extent and depth of the burns and the time and method of treatment. Of these factors, the state of health of our patients prior to the accident occupied our interest in the first place. We, therefore, divided the series of cases into two groups; one comprising patients who died from burns but did not suffer from any serious disease prior to injury (we called it the group of "healthy" patients) and the other comprising patients who, prior to the injury, had suffered from some kind of serious, usually chronic

Tab. 3. Grouping of entire series of cases according to area of burned skin

Percentage of burns	−10	−20	−30	−40	−50	−60	−70	−80	−90	−100	Total
"Healthy"	—	3	1	5	7	15	11	6	8	9	65
"Sick"	24	16	10	7	6	8	1	4	4	2	82
Total	24	19	11	12	13	23	12	10	12	11	147

disease (we called it the group of "sick" patients). The reason why we decided upon this division was quite simple. We assumed that a healthy organism suffering thermic injury struggles only against the consequences of this noxa and if the patient dies, death occurs in direct causal dependence on the thermic injury. Defence in a sick organism looks quite different. A patient suffering from a cardiovascular disorder, a lesion of the liver or a disorder of the nervous systems shows a much worse reaction to the thermic noxa, and his life is, therefore, threatened by a smaller percentage of the area burned. In such cases death is frequently in no direct causal dependence on the thermic injury. This division of the series into groups of "healthy" and "sick" can clearly be seen, if we note the percentage of the area burned (see Tab. 3).

Tab. 3 shows that the most striking difference between the two groups becomes evident in the cases with a low percentage of area burned; the mortality rate of the "sick" is much higher than that of the "healthy". With 30% burned body surface, for instance, the "sick" had 50 deaths, whilst the "healthy" only four. The mortality rate of the "healthy" rises up to 60% of body surface damaged and then drops. This drop may be explained by the more severely burned patients often dying before they reach hospital and that is why they are not included in our series. The continuous decrease in the number of deaths registered in the group of the "sick" in parallel with the increase in the area of body surface burned, can be explained in a similar way.

Division of our series into the above two groups resulted in 65 "healthy" (44%) and 82 "sick" (56%). We then proceeded to divide these groups according to the cause of death into four subgroups: death from 1. shock or toxaemia, 2. infection (sepsis and bronchopneumonia), 3. heart failure and 4. other complications (see Tab. 4).

Tab. 4 shows that shock and toxaemia constitute about two thirds of all causes of death in the group of the "healthy", whereas in the group of the "sick" half of this number is substituted by heart failure. This increase in the number of deaths from heart failure substituting that from shock and toxaemia can be explained by the comparatively small area of body surface burned (as can be seen in Tab. 3 in the group of the "sick") which is too small to cause shock severe enough to lead to death. In addition to this, the group of the "sick" also comprises the cardiacs in whom even a small area of body surface burned may cause decompensation and death. Finally, one of the factors increasing the death rate from heart failure in the group of the "sick", was myocardial infarction.

Infection as a complication reaches, on the whole, the same percentage in both groups. Sepsis developed in the group of the "healthy" with large burns. Most frequently the haemolytic staphylococcus was cultivated from the blood or the spleen, less often beta-haemolytic streptococcus, pyocyaneus and proteus. The patients usually died between the second and fifth week after injury, on an average on the 23rd day.

Tab. 4. Grouping of entire series of cases according to causes of death

Cause of death	"Healthy"	"Sick"	Total
Shock and toxaemia	41	25	66
Infectious complications	14	18	32
Cardiac complications	0	29	29
Other complications	10	10	20
Total	65	82	147

Among the cardiac complications, we most frequently diagnosed coronary sclerosis apart from degenerative and fibrotic changes in the myocardium. The two cases in which we found an abscess of the myocardium, we registered with the group of infectious complications. Myocardial infarction as the cause of death in burns was found in nine cases which were registered with the total of 29 deaths from cardiac complications. These were subjects of a higher age group with small burns, at the most 30% of body surface. These infarctions occurred on the basis of a more or less marked coronary sclerosis roughly between the second day and second month after the accident.

Among the complications in the group of "other causes of death" we found thrombosis of cerebral vessels, cerebral haemorrhage, pulmonary embolism, uraemia, ileus, hepatic coma in concomitant infectious hepatitis, etc. Perforated or bleeding gastric or duodenal ulcer which is sometimes referred to as a cause of death in burns was not observed in our series of cases.

After having evaluated the morphological findings and the causes of death, we attempted to analyse our series from a dynamic point of view. We looked for a dependence of the period of survival on the size of the area burned and tried to elucidate the relationship between the vegetative system and death.

Let us first note whether and how, in our series of cases, the time of survival depended on the area burned. In order not to have to include any other factor, such as the depth to which the skin was damaged, which may interfere with our assumption, we selected only cases with IInd and IIIrd degree burns. These cases also constituted the majority of the whole series. We, however, excluded those whose death did not occur in direct causal connection with the thermic injury and those who died from one of the complications in burns. Basically, therefore, the selection consisted only of subjects who died from shock or toxaemia as a direct consequence of the thermic trauma. There was a total of 56 cases; their time of survival is given in Fig. 3.

Fig. 3 shows that the selected set of cases splits up into two groups.

The values of the first group lie close to the y axis and slightly recede from it with the decreasing percentage of the area burned. The dashed line which passes through the concentrations of dots of our registrations, has not been calculated from our set but from the data referred to by Hofmann et Haberda

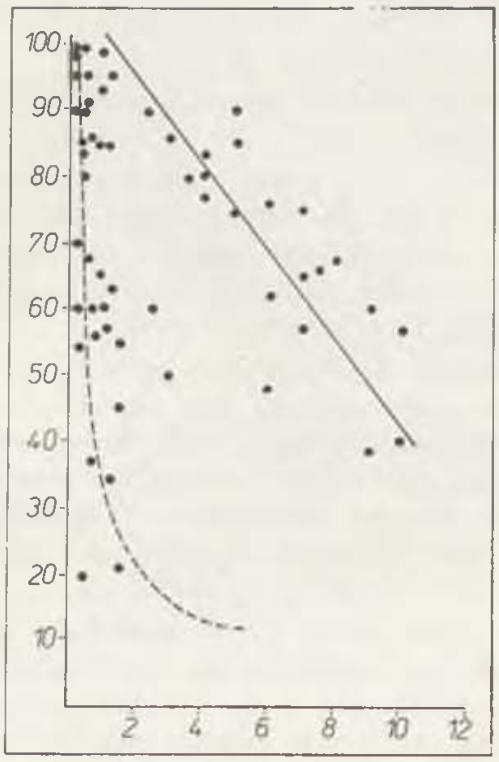

Fig. 3. Relationship between time of survival and area burned. (x — time of survival in days, y — area burned in percent. For details see text.)

(12) in their textbook of Forensic Medicine, 1919, i.e. long before modern anti-shock therapy had been introduced. It can be seen that this line (with the exception of a slight deviation around 60%) fully fits into the distribution of our values. This, next to the morphological findings, confirms that in the first group of the selected set of cases of our series death was caused by shock.

The values of the second group recede relatively quickly from the y axis in proportion with the area burned. On trying to find the mathematical relationship of these values, we discovered that a straight line given by the equation of $x = 16.35 - 15.12\ y$ will fit in best (the values for y, i.e. the percentage of burns had to be multiplied by 10^{-2}, i.e. had to be lowered by two orders, before being inserted into the equation). The result is demonstrated in Fig. 3 by a full line.

This linear dependence, as found in the above group, is, to our contention, of great significance; it proves the linear dependence of the time of survival on the area burned. It also supports the correctness of the conception of the relationship between the immunological processes and death in burns sickness. We should only like to recall the older and nowadays omitted papers (4, 6, 8, 9, 10, 11, 13, 17, 18) proving that death in burns sickness was due to anaphylactic shock.

In this connection it may be worth while to refer to yet another observation. We have mentioned above that patients whose conditions were complicated by sepsis, died on an average on the 23rd day after the accident. This finding is in accord with those in the literature (3, 16). We have further pointed out that sepsis occurred more frequently in patients with burns of greater extent. Now, here we should like to put the following questions: Why did the patients who died from sepsis on about the 23rd day not die already during the toxaemic period, i.e. a few days after the accident, in the same area of burned skin?

If we regard this question from an immunological point of view, two explanations may be considered:

1. The patients suffering from sepsis possessed enough of their own defensive forces to overcome the toxic period; the defence of the organism, however, did not suffice to combat sepsis which developed later and thus became the cause of death. This explanation provides for a primary resistance to an otherwise fatal course of immunological reactions during the critical toxaemic period.

2. The patients suffering from sepsis were primarily not more resistant to a fatal deterioration during the toxaemic period. They gained this resistance through sepsis which had started to develop already during the toxaemic period and thus helped them to survive this period. In the light of this explanation the whole picture looks as though the infectious agent influenced and broke up the immunological reactions developing between the burned skin and the organism, reactions which otherwise cause death at the toxaemic stage of burns sickness.

Theoretically one may also reflect on the influence of therapy, i.e. that patients developing sepsis had been more effectively treated during toxaemia. The patients with sepsis were, unlike the other patients, given transfusions of whole blood in addition to the other treatment, but the blood was administered only when sepsis had started to become manifest and thus been diagnosed. This, as a rule, took place at a time when the patients had already overcome the critical toxaemic period. We may, therefore, conclude that more effective treatment was not a factor decisive for survival of the toxaemic period.

On evaluation of our series of cases, we have also tried to find a relationship between the condition of the vegetative system and the death rate. We were well aware of the fact that this question was particularly difficult and that we did not possess sufficient data for its full appraisal. In our series the patients' temperature appeared to be a suitable indicator of the function of the vegetative system; it was registered every hour, day and night, starting with the day of accident. It was taken with a clinical thermometer of a scale ranging between 34.8 and 42.0° C. For evaluation we used the last registered temperature. For simplicity, we are going to call it the "last" temperature, although we are fully aware of the fact that it was not exactly the last temperature in the true sense of the word; between this registration and the moment of death a period elapsed which, theoretically, could amount to a maximum of 60 minutes. However, in practice this period was, as a rule, shorter.

When evaluating the series from this point of view, we excluded the cases whose death was caused by infectious complications and those whose death had no causal connection with the thermic injury. Roughly, therefore, this group consisted of subjects who died from shock or toxaemia.

With regard to the "last" temperature the patients were divided into three groups: 1. patients with a "last" temperature lower than 35.8° C, 2. with a "last" temperature ranging between 35.8 and 37.5° C and 3. with a "last" temperature higher than 37.5° C. Tab. 5 shows that about 25% of patients died in hypothermia, another 25% in normothermia and about 50% in hyperthermia. In the latter group some temperatures were so extreme that the thermometer did not suffice to register them.

Tab. 5. Grouping of our series of cases according to time of survival and last measured temperature

Last measured temperature	Death after			Total
	2 days	3—5 days	5 days	
<35.8°C	11	2	0	13
35.8°—37.5°C	9	1	2	12
>37.5°C	4	8	12	24
Total	24	11	14	49

On further analysis of this phenomenon it became evident that the patients' temperature reacted differently at the different periods after the accident. We, therefore, made a new division of this set of cases into three groups according to the period of survival. The first group consisted of subjects who died within two days, the second of those who died up to the fifth day and the third of those who died later than the fifth day after injury (see Tab. 5).

Tab. 5 shows that 11 patients, i.e. almost half the number died in hypothermia up to second day after the accident; between the second and fifth day there were only two deaths, i.e. not quite one fifth the number, and at a later period death in hypothermia was not observed at all. In contradistinction, only four patients, i.e. one sixth the number died in hyperthermia up to two days, eight, i.e. almost three quarters the number between the second and fifth day, and twelve, i.e. five sixths the number at a later date after injury.

As can be seen, death in hypothermia prevails in the first days after injury; in the later periods, death occurs mostly in hyperthermia. The question as to whether hypothermia registered at the beginning of burns sickness had not been due to hibernation, can be answered in the negative, because our patients did not receive such treatment.

CONCLUSION

From a biological point of view it will now be necessary to concentrate on the following:

1. on the study of the enzymo-immunological reactions already developing in the early stages of burns sickness. The necessity for this study emerges from the knowledge that the time of survival, during the toxaemic period, is in linear dependence on the percentage of the area burned. We need to know the

spectrum, both as to quality and quantity, of the sensitizing substances which are freed from the burned skin and the defensive processes constituting the reaction of the organism to them. After elucidating these problems, we shall know whether and to what extent anaphylactic processes play a part in the toxaemic phase.

2. on the study of the fluctuations in the vegetative system during burns sickness. Hypothermia and hyperthermia accompanying the various stages of the disease point to serious disorders of the thermoregulative system and lead us to anticipate disorder of the rest of vegetative functions.

3. on paying increased attention to burns sickness in elderly patients. We have to bear in mind that these are mostly sick people in whom burns even of small extent may lead to death. Apart from surgical treatment, therefore, thorough medical care must not be neglected in these cases.

From a sociological point of view it will be necessary to concentrate on prevention in the broadest sense of the word, in particular of domestic and occupational accidents. Preventive measures referred to above are based on the analysis of fatal accidents. It is, however, quite clear that this must be enlarged by the findings resulting from an analysis of non-fatal accidents which this paper does not deal with.

From our analysis it becomes evident that mainly children, women, old and sick people meet with domestic accidents.

The responsibility for these accidents in children lies mainly with the parents who carelessly handle hot fluids, leave the child near the stove without proper supervision or hand the child over to the care of its older brothers and sisters or some other person. This goes to show that most accidents in children could be prevented by the parents taking proper care of them. Education not only of children but also of parents is, therefore, of great importance. In the prevention of domestic accidents in women, stress is to be laid on combating negligence and carelessness in handling combustibles, their improper usage, e.g. for lighting the fire in stoves. It is also important to suppress haste in the domestic work of women. In elderly or sick people additional factors, such as slow reaction, lowered sensory perception, limitation of movements, psychic disorders, etc., have to be accounted for. Elderly people sometimes carry out domestic work which they have become physically unfit for and which they perform without help or supervision, particularly when living by themselves.

Analysing occupational accidents we have pointed out the incidents where burns were caused by the working clothes, soaked with grease or a first class combustible, catching fire. From this it becomes evident that the demand for wearing clean clothes at work is fully justified. White or light-colour working clothes immediately showing any soiling and manufactured from non-inflammable material, should not remain only a theoretical presupposition of accident prevention, but must actually be produced and made available for usage. We must, naturally, also deal with all other factors, such as lack of discipline, carelessness, negligence, etc., although it may appear to us that there is no end to the roads of prevention. The building and organization of accident pre-

vention on the basis of the new law on safety and the protection of health during work, and of the notice of ÚRO*) as well as the activity of the work safety squads make improvement possible even in this direction.

SUMMARY

An analysis of a group of 147 patients (135 adults and 12 children) who died from burns sickness at the Burns Unit of the Clinic of Plastic Surgery, and autopsied at the Department of Pathology and Forensic Medicine, Medical Faculty of Hygiene, Charles University, Prague, Czechoslovakia, was carried out both from a sociological and biological point of view. Apart from the most frequent causes of death and their stratification, the relationship between the extent of the burned area of skin and the time of survival as well as that between the time of survival and the "last" temperature, were studied. The most frequent causes of domestic and occupational accidents were analyzed from a sociological point of view and the criteria of prevention determined.

RÉSUMÉ

Analyse de 147 accidents thermiques mortels

S. Hájek, Z. Gregora, J. Štefan, Z. Král, J. Chyba, L. Růžička, M. Dobrkovský, J. Doležalová

Présentation d'une analyse sociologique et biologique d'un groupe de 147 brûlés (135 adultes et 12 enfants), soignés dans le service des brûlures de la clinique de chirurgie plastique de la Faculté de Médecine et d'Hygiène de l'université Charles et autopsiés dans les services de la chaire d'anatomie pathologique et de médecine légale de cette Faculté à Prague. A côté de la distribution des causes de la mort les plus fréquentes, on a étudié également les rapports entre l'étendue de la surface cutanée brûlée et la durée de la survie des sujets atteints, ainsi que le rapport entre la durée de la survie et la „dernière" température des victimes. Du point de vue sociologique, on a analysé la genèse la plus fréquente des accidents dans le ménage ou pendant l'exercice professionelle et établi des critères préventifs.

ZUSAMMENFASSUNG

Analyse von 147 tödlichen Verbrennungen

S. Hájek, Z. Gregora, J. Štefan, Z. Král, J. Chyba, L. Růžička, M. Dobrkovský, J. Doležalová

In der vorliegenden Arbeit wird vom soziologischen und biologischen Gesichtspunkt eine Gruppe von 147 Patienten mit Verbrennungen (135 Erwachsene und 12 Kinder) analysiert, die an der Station für Verbrennungen bei der Klinik für plastische Chirurgie der Hygienisch-medizinischen Fakultät der Karlsuniversität in Prag behandelt worden waren und im Institut für pathologische Anatomie und gerichtliche Medizin derselben Fakultät seziert wurden. Ausser den häufigsten Todesursachen wurde die Abhängigkeit der Überlebenszeit

*) Czechoslovak TUC — note of translator

der Patienten vom Ausmass der verbrannten Hautfläche untersucht sowie die Beziehung zwischen der Überlebenszeit und der „letzten" Temperatur der Verunglückten studiert.

Vom soziologischen Gesichtspunkt wurden die häufigsten Ursachen der Unfälle im Haushalt und am Arbeitsplatz geprüft und Kriterien einer Prophylaxe aufgestellt.

RESUMEN

Análisis de 147 accidentes térmicos que resultaron en la muerte

S. Hájek, Z. Gregora, J. Štefan, Z. Král, J. Chyba, L. Růžička, M. Dobrkovský, J. Doležalová

Desde el punto de vista social y biológico fue analizado el grupo de 147 quemados (135 adultos y 12 niños) que fueron tratados en el Instituto de Quemaduras de la Clínica de Cirugía Plástica y disecados en la cátedra de la anatomía patológica y de la medicina legal en Praga. Aparte de las causas más frecuentes de la muerte fue observada la dependencia de la extensión del área quemada de la piel del tiempo de la supervivencia de los quemados y la relación entre el tiempo de la supervivencia y la temperatura „última" de los quemados. Desde el punto de vista social fueron analizadas las génesis más frecuentes de los accidentes que ocurren en casa y en los lugares de trabajo y fueron fijados los criterios para la prevención.

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NOTES ON THE QUESTION OF CEREBRAL OEDEMA AFTER BURNS*)

J. ŠTEFAN

Cerebral oedema is a nonspecific and common reaction of the central nervous system in a wide range of pathological conditions. It is also encountered at different stages after burns. It is known from the clinical course of burns that the signs can include signs of injury to the central nervous system, such as acute vomiting, delirium, hyperkinesia, clonic spasms (sometimes leading to opisthotonos) or focal cerebral signs (2, 4, 13, 18). Children are particularly liable to oedema (8, 18, 19). After burns, the brain is usually enlarged at autopsy and the meninges and brain tissue are hyperaemic. Histological examination shows dystrophic changes of varying degrees in the ganglion and glia cells, affecting different parts of the central nervous system (2—5, 19, 20). The vascular system is most involved (2, 4). A focally varying picture is observed in the blood vessels. These are usually dilated and filled with blood and in some places with hyaline thrombi, while the walls are swollen and oedematous, with more or less marked loss of structure and with fibrinoid necrosis of the elastica and the media. The endothelial and adventitial cells are swollen and show an increase in numbers. The perivascular spaces are dilated, with accumulation of homogenous or granular matter.

Many authors have studied cerebral oedema in different conditions, but some of the basic questions of its origin have still not been explained (6, 7, 10, 16). The evaluation of the clinical picture and of the morphological picture presents certain difficulties. From the morphological aspect, two pictures of diffuse increase in the volume and weight of the brain are observed, with actual oedema and with swelling. In oedema the brain tissue is moist and shiny; on section a large amount of fluid runs out and the blood drops readily spread out and merge with one another. In swelling, the tissue is dry and firm and adheres to the knife (7, 10). The macroscopic and microscopic diagnosis of both processes is very difficult and apart from autolytic changes it is rendered even more difficult by the fact that they can appear together in different stages of

*) Presented at the Tenth National Congress of Forensic Medicine in Prague, November 1962.

development. In recent years electron microscopy has provided new information in this direction, e.g. on the question of the perivascular spaces (15). Because of the difficulty of morphological diagnosis, physical-chemical methods can also be used (1, 11, 12, 14, 17, 22). In swelling of the brain, an increase in the amount of dry matter is usually found, owing to an increase in the amount of protein

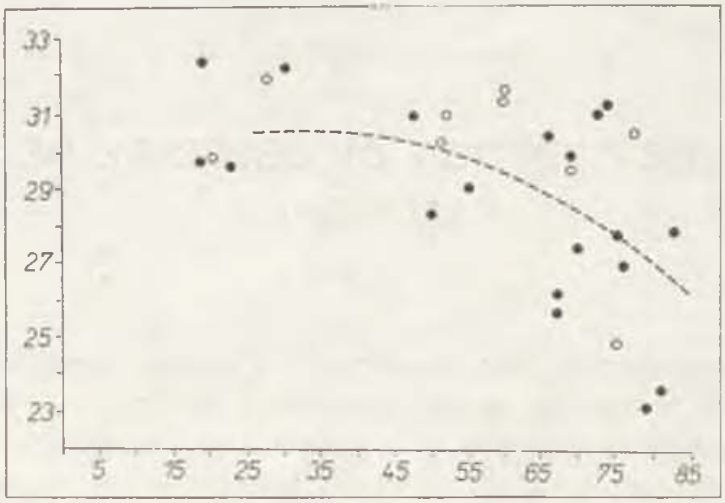

Fig. 1. Dry weight values of brain tissue after burns in relation to age. — y = dry weight, as a percentage, x = age, ○ = died from shock, ● = from other causes

and other substances. In true oedema of the brain, which usually involves the accumulation of fluids poor in protein, the amount of dry matter is small.

With reference to the frequent finding of enlargement of the brain after burns, the author attempted to determine the degree of cerebral oedema on the basis of determination of dry weight. The possibility of differentiation between oedema and swelling of the brain also depends on the determination of dry weight. If this question were resolved, it would further help to explain the pathogenesis of cerebral changes in burns.

METHOD OF DETERMINING DRY WEIGHT

When determining the dry weight of brain tissue, the grey matter must be completely separated from the white. Because of the big difference in the amount of dry matter, traces of grey or white matter could seriously affect the results. The best and most accurate method is to determine the dry weight of the white matter. Tissue of the white matter of the frontal lobe, near to the pole, was therefore used in this study — as far as possible always from the same site. The tissue was removed at autopsy in amounts of 100—150 mg., was weighed on a balance as quickly as possible and was then dried to constant weight in a desiccator at 105° C. Constant weight was obtained after about 24 hours. Since little information was found in the literature on the determination of the dry weight of human brain tissue and relatively few systematic

Tab. 1. Amount of dry brain substance in individual cases of burns

Case No.	Sex	Age in years	Extent of burns %	Time of survival	Cause of death	Dry weight in %	Dry weight as comp. with age curve
68/61	F	73	5	18 days	heart failure	31	raised
51/62	M	75	8	65 days	coronary thrombosis	27.7	0
226/62	M	67	10	12 days	heart failure + bronchopneumonia	26.1	lowered
61/61	F	79	15	60 days	heart failure	20.8	lowered
138/62	M	76	20	10 days	sepsis + bronchopneumonia	26.9	lowered
16/62	F	63	20	28 days	sepsis + bronchopneumonia	30.4	raised
49/61	F	83	25	19 days	heart failure	27.8	raised
207/62	F	81	30	5 days	heart failure	23.5	lowered
217/62	F	19	30	54 days	heart failure	29.8	lowered
133/61	F	74	32	49 days	heart failure	31.2	raised
17/61	F	70	35	10 days	heart failure + bronchopneumonia	27.4	lowered
37/61	F	67	38	9 days	toxaemia	25.6	lowered
41/62	F	69	40	16 days	heart failure	29.8	raised
140/62	F	55	58	7 days	toxaemia	29	lowered
182/61	M	52	60	19 hrs.	shock	30	0
112/61	M	20	60	12 hrs.	shock	29.8	lowered
119/61	M	19	60	16 days	sepsis	32.4	raised
109/61	M	31	65	6 days	cerebral haem. + bronchopneumonia	32.1	raised
121/62	M	23	66	32 days	sepsis	29.6	lowered
140/61	M	60	80	12 hrs.	shock	31.4	raised
120/61	M	50	80	4 days	toxaemia	28.3	lowered
123/61	F	48	85	5 days	toxaemia	30.9	raised
220/61	M	68	85	4 hrs.	shock	29.5	raised
245/62	F	60	90	16 hrs.	shock	31.6	raised
52/61	F	78	90	2 days	shock	30.4	raised
148/62	F	75	95	9 hrs.	shock	24.8	lowered
135/62	M	28	100	3 hrs.	shock	31.9	raised
118/61	F	52	100	6 hrs.	shock	31	raised

measurements have been published (17), preliminary tests had to be carried out to determine the influence of the postmortem interval, age and possibly sex on the amount of dry matter. Preliminary tests in over 100 cases covering a wide range of causes of death, showed that a difference of a few dozen hours between the time of death and removal of the material did not basically affect the amount of dry matter, which was likewise not found to be influenced by sex. There was a marked relationship, however, between age and dry weight, which is illustrated in the figure by the broken line of the equation $Y = 28.617 + 1.139 \times 10^{-1} \times X - 1.679 \times 10^{-3} \times X^2$. In children and in the lowest age groups the course of the curve is not shown, because of the small number of cases. On the basis of the results of measurement of the specific gravity of the brain (1), it can be assumed, however, that from the ages of 20 to 50 the amount of dry matter is stable. In the higher age groups the values show a marked decrease. Dry weight values are particularly low in cases of marked arteriosclerosis and atrophic changes in the brain.

RESULTS

The actual tests were carried out with brain tissue from 28 patients who died from second and third degree burns. Nine died from shock, the others in the later phases of the disease as a result of toxic injury to the organs and complications. Dry weight values were compared with the curve illustrating the relationship of dry weight to age (Fig. 1). These values were also studied in relation to the extent to the burns, the time of survival and the direct cause of death (Tab. 1). Both the figure and the table show that in patients who died as a results of burns, increases in dry brain matter (corresponding to swelling of the brain) and decreases (corresponding to cerebral oedema) were found. Raised values were found chiefly in cases of severe, extensive burns. Burkhardt (1), who measured the specific gravity of the brain in different pathological conditions, likewise found high values after burns. The results also show that raised dry weight values were more frequent in patients who died from shock. The author cannot therefore confirm the view of Zinck (21) that oedema occurs in early cases of death and swelling in the later phases.

No other relationships or associations were demonstrated by these measurements. It will therefore be necessary to study the question of oedema after burns on a broader basis and to use other methods and examine other parts of the central nervous system. In particular the possibility of the formation of local oedema in the diencephalon and brain stem, with resultant temporal conus (9), will have to be considered. Temporal conus causes further deterioration of the circulation in the region of the posterior cerebral artery and injury to the hypothalamus and the adjacent parts. Evidence of this is to be found in some of the signs in patients with burns, e.g. disturbances of thermoregulation, opisthotonos, etc. Study of changes in these very important parts of the central nervous system ought to furnish further findings.

SUMMARY

The dry weight of the brain tissue after burns was determined and its relationship to the extent of the burns, the time of survival and the cause of death was studied. Elevated dry weight values, corresponding to swelling of the brain, and low values, corresponding to cerebral oedema, were found. In patients who died from shock, raised dry weight values were much more frequent.

RÉSUMÉ

Contribution à la question de l'oedème cérébral chez les brûlés

J. Štefan

On a évalué, sur des brûlés, la matière sèche des tissus cérébraux et étudié les rapports entre cette dernière et l'importance des brûlures, la durée de la survie et la cause de mort. On a pu constater aussi bien l'augmentation de la matière sèche qui correspond à une enflure cérébrale que des valeurs basses, correspondant à l'oedème cérébral. Chez les sujets décédés en état de choc, l'augmentation quantitative de la matière sèche a été constatée baucoup plus fréquemment.

ZUSAMMENFASSUNG

Beitrag zum Problem des Hirnoedems bei Patienten mit Verbrennungen

J. Štefan

Bei Patienten die an Verbrennungen starben, wurde die Trockensubstanz des Hirngewebes bestimmt und die Beziehung zum Ausmass der Verbrennung, zur Überlebenszeit und zur Todesursache untersucht. Es wurden sowohl erhöhte Trockensubstanzwerte, die einer Schwellung des Gehirns entprechen, als auch verminderte Werte, die Hirnoedem anzeigen, gefunden. Bei Patienten, die im Schock starben, wurden weitaus häufiger erhöhte Trockensubstanzwerte festgestellt.

RESUMEN

Contribución al problema del edema cerebral en quemados

J. Štefan

En los enfermos quemados se determinaba la parte seca del tejido cerebral y se observaba la relación con la extensión de la quemadura, con el tiempo de la supervivencia y la causa de la muerte. Se han confirmado los valores elevados de la parte seca correspondientes a la tumefacción del cerebro tanto como los valores bajos correspondientes al edema del cerebro. En los pacientes que fallecieron durante el choque aparecieron con más frecuencia los valores elevados de la parte seca del cerebro.

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LIVER DAMAGE IN BURNS*)

Z. GREGORA

Less attention has been paid to liver injury after burns than to other organs, e.g. the skin and kidneys. The importance of the role of the liver in the organism prompted the author to study this question in some detail, however.

From the history of research on morphological changes in the liver tissue, mention should be made of the most important contributions. Details are given in the monographs by Sevitt (1) and Allgöwer (2). In 1897, Bardeen (3) observed parenchymatous swelling of the liver cells and vacuolation of their cytoplasm. More attention was paid to the liver during the era of treatment of burns with tannin, when necrosis of the liver (not previously mentioned) was described; in the pre-tannin period it was actually often stressed that no changes occurred in the liver. Treatment with tannin undoubtedly caused varying degrees of necrosis of the liver parenchyma, but tannin alone is not responsible for necrosis of the liver cells. Many authors found it in cases in which tannin was not used. Ellenberg (4) considered that central necrosis was due to prolonged vasospasm, anoxia or acute circulatory failure. Shock of less than 24 hours' duration seldom results in central necrosis. James (5), in five fatal cases, did not find constant morphological changes. He found fatty degeneration, cloudy swelling, pigment in the reticuloendothelial system, focal necrosis and congestion. Gillman (6) describes vacuolation of the cells, loss of staining capacity, fatty degeneration and atrophy of the cells in the centre. Zinck (7) made a detailed study of the pathologic anatomy of burns. The latest detailed experimental publication is by Arturson (8).

In order to obtain a picture of changes in liver tissue after burns treated by modern methods, ten patients who died at different intervals after injury were selected (from 2½ hours to eight weeks). Young patients aged from three to 31 years were chosen. Only one (a female patient aged 52) was older. Before injury all were healthy and autopsy likewise showed no pathological changes of older origin. All suffered from burns or scalds (mainly third degree), involving 30—100% of the body surface.

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Autopsy was carried out within three to 15 hours after death. Liver tissue specimens were fixed for 24 hours in buffer formalin and were imbedded in paraffin in the usual manner. Sections for staining fats were prepared in a freezing microtome, for PAS and ninhydrin staining they were fixed with water and in other cases with glycerin and egg-white. The sections were stained with haematoxylin and eosin and Heidenhain's haematoxylin. Histochemical reactions included the PAS reaction, using Hotchkiss's method (in positive cases also after digestion by diastase), Feulgen's reaction for deoxyribonucleic acids, staining with methyl green and pyronin by Brachet's technique for ribonucleic acids and Perls' reaction for iron, using Lison and Bunting's technique. The methods were taken from Pearse's book on histochemistry (9). The reaction for amino acids was done by the method of Yasuma and Ichikawa (10), with ninhydrin and Schiff's reagent. It was blocked by deamination. Fats were stained with Sudan orange by Romeis's technique (11) and neutral fats with Nile blue sulphate by Lorrain Smith's technique (11). The size of the nuclei was measured by an ocular micrometer in two directions perpendicular to one another and their area was calculated by the formula for the surface of an ellipse, taking the average for 100 nuclei.

The results in the individual cases were as follows:

1. Patient A. A., autopsy record No. 135/62, aged 28 years, male. Burns, 100%, third and fourth degree. Shock. Death 2½ hours after injury. Autopsy four hours p.m.

Structure of liver trabeculae intact. Interlobular veins dilated and containing eosinophils, sinusoids dilated, mainly in centre, central veins indistinct, eosinophils and erythrocytes in collecting veins. Hepatic arteries empty. Kupffer cells hypertrophic, with local necrobiotic changes. Liver cells swollen and vacuolated (mainly in centre). Changes in nuclei relatively slight; vacuoles present in some (Fig. 1a).

PAS: positive granules in Kupffer cells. Feulgen: nuclei rich in deoxyribonucleic acid. Ribonucleic acids: fairly marked, generally even reaction. Fe: weak diffuse reaction in some places in sinusoids. Ninhydrin-Schiff: amino acids adequate. Fats: central fatty degeneration (Fig. 2); part of the fats composed of neutral fats. Area of nuclei: 118 μ^2.

2. Patient B. J., autopsy record No. 118/61, aged 52 years, female. Burns, 100%, second to fourth degree. Shock. Death 5½ hours after injury. Autopsy 15 hours p.m.

Structure of liver trabeculae intact. Most blood vessels empty; a little plasma and leucocytes in the central veins. Hepatic arteries contracted, with proliferation of the endothelium. Sinusoids not dilated, with leucocytes and necrobiotic changes; local activation only of Kupffer cells. Marked accumulation of mononuclear cells in portobiliary spaces. Structure of cells somewhat obliterated, large numbers of vacuoles in cytoplasm (mainly in central zone) and in nuclei; accumulation of basophilic granules at nuclear membrane.

PAS: weak reaction in some Kupffer cells. Feulgen: positive reaction by basophilic granules in nuclei. Ribonucleic acids: weak reaction, disappearance

of purple-staining matter in vicinity of nuclei. Fe: small positive granules at cell periphery. Ninhydrin-Schiff: fairly marked positive reaction in some cells, very weak in most. Fats: large numbers of fat droplets, mainly in central zone; fair amount of neutral fats. Area of nuclei: 103 μ^2.

3. Patient K. P., autopsy record No. 112/61; aged 20 years, male. Burns, 60%, third degree. Shock. Death 11 hours after injury. Autopsy 12 hours. p. m.

Tissue structure intact. Liver cells showing regressive changes among blood cells in interlobular veins (Fig. 3). Sinusoids contracted, with erythrocytes and leucocytes in some places, but usually empty. Central veins distinct, with swelling of intima (Fig. 4); erythrocytes and leucocytes in collecting veins. Hepatic arteries contracted, with rugose intima and narrowing of lumen; pronounced hyperaemia of vasa vasorum. Marked oedema of blood vessel walls. Activation of Kupffer cells. Poor staining of cytoplasm, especially in binuclear cells. Nuclei pyknotic, with peripheral vacuoles; only nucleolus distinguishable in some (Fig. 1b).

PAS: slightly positive matter in sinusoids. Feulgen: chromatin pressed against the nuclear membrane in a fairly large number of nuclei; some nuclei negative. Ribonucleic acids: disappearance of purple-staining matter round nuclei; reaction generally weak. Fe: negative. Ninhydrin-Schiff: very weak reaction: Fats: isolated droplets in central zone, neutral fats negative. Area of nuclei: 100 μ^2.

4. Patient B. V., autopsy record No. 255/61; aged 6 years, female. Scalds, 40%, second degree. Shock. Death 18 hours after injury. Autopsy three hours after death.

Structure of liver trabeculae somewhat obliterated. Irregular hyperaemia. Liver cells swollen, with moderate numbers of vacuoles. Disintegrated chromatin pressed against the nuclear membrane in many nuclei; occasional empty nuclei with only a nucleolus near the membrane. Marked activation of Kupffer cells. Activation of histiomonocytes in portobiliary spaces.

PAS: pronounced reaction by PAS-positive substances in Kupffer cells. Feulgen: weak reaction in many cells, particularly at periphery. Ribonucleic acids: uniformly weak reaction; disappearance of purple-staining matter round nuclei. Fe: negative. Ninhydrin-Schiff: reaction generally weak, somewhat more pronounced in centre of lobules. Fats: centroacinous fatty degeneration; neutral fats negative. (Area of nuclei: 102 μ^2.)

5. Patient Č. A., autopsy record No. 267/60; aged 29 years, male. Burns, 90%, third degree. Shock. Death 30 hours after injury. Autopsy eight hours. p. m.

Tissue structure somewhat obliterated. Erythrocytes in interlobular veins, sinusoids narrow and compressed, containing lymphocytes or empty. Central veins fairly dilated, collecting veins filled with erythrocytes. Little activation of Kupffer cells. Liver cells swollen, nuclei often optically empty, others containing basophilic matter near the nuclear membrane (Fig. 1c). Changes in nuclei most marked at periphery. Some cells with necrobiotic changes; very large amounts of lipofuscin in cells in centre of lobules.

PAS: markedly positive in Kupffer cells. Feulgen: negative reaction in some nuclei, basophilic granules giving positive reaction in others. Ribonucleic

acids: very weak reaction disappearing in vicinity of nuclei (Fig. 5). Fe: fair quantity of positive granules in peripheral cells. Fats: isolated fat droplets in centre. Area of nuclei: 113 μ^2.

6. Patient Š. A., autopsy record No. 109/61; aged 31 years, male. Scalds, 65%, second and third degree. Cerebral haemorrhage, bronchopneumonia. Death six days after injury. Autopsy 12 hours p. m.

Structure of liver trabeculae destroyed in centre by release of necrotic liver cells. Marked hyperaemia, with haemorrhage in centre, central veins indistinct, peripheral sinusoids congested with erythrocytes. Decrease in number of Kupffer cells, remaining cells atrophied. Decrease in size of liver cells, large amounts of lipofuscin in cytoplasm; some nuclei with marked changes and large dimensions. Groups of cells with hyperchromatic nuclei, showing signs of regeneration, at periphery. Some proliferation of mononuclear cells in portobiliary spaces.

PAS: PAS-positive granules in isolated liver cells. Feulgen: coarse granular chromatin in many nuclei, loose chromatin network in others. Ribonucleic acids: marked reaction in some cells, especially at the periphery; general reaction weak. Fe: occasional positive granules in peripheral cells and Kupffer cells. Ninhydrin-Schiff: marked reaction in some cells. Fats: mild central fatty degeneration, very occasionally with neutral fats. Area of nuclei: 160 μ^2.

7. Patient K. I., autopsy record No. 281/60; aged four years, female. Burns, 65%, third degree. Bronchopneumonia, cerebral oedema. Death seven days after injury. Autopsy 14 hours p. m.

Extensive inflammatory disintegration of central part of lobules (Fig. 6), involving up to half the acini. Oedema and proliferation of Kupffer cells in peripheral zone. Very marked activation in Kupffer cells, with phagocytosis and histiocytic transformation. Endothelium of central veins swollen, polynuclear cells in sinusoids and in area of foci of necrosis. Increased granulation of cytoplasm discernible in intact liver cells. Liver cells not yet dissociated because of the strongly marked reticuloendothelial network.

Feulgen: dense chromatin network in nuclei at periphery. Ribonucleic acids: fairly pronounced reaction in peripheral cells. Fe: occasional diffuse, weakly positive reaction in sinusoids and Kupffer cells. Ninhydrin-Schiff: reaction generally weak. (Area of nuclei: 95 μ^2.)

8. Patient K. L., autopsy record No: 119/61; aged 19 years, male. Burns, 60%, third degree. Staphylococcal sepsis. Suppurative myocarditis. Death 16 days after injury. Autopsy eight hours p.m.

Regressive changes in liver tissue, most marked in centre of lobules, where the liver cells were necrotic and loose. Vacuolation of cells in central zone, local atrophy of trabeculae elsewhere. Nuclei of liver cells often hyperchromatic, with large nucleoli. Only slight activation of Kupffer cells.

PAS: Small amount of PAS-positive substance in some parts of sinusoids. Feulgen: dense chromatin network with marked reaction usually found in nuclei. Ribonucleic acids: reaction generally weak. Fairly marked reaction in nuclei of some peripheral cells. Fe: positive reaction in some Kupffer cells in

form of granules and also diffuse. Ninhydrin-Schiff: uniformly weak reaction. Fats: slight fatty degeneration in central zone. Area of nuclei: 84 μ^2.

9. Patient Z. V., autopsy record No. 282/60; aged 3 years, male. Scalds, 45%, second and third degree. Bronchopneumonia. Death four weeks after injury. Autopsy 12 hours p. m.

Atrophy of liver trabeculae, slight hyperaemia. Marked activation of Kupffer cells, with histiomonocytic transformation and in some places formation of multinuclear elements. These elements were irregular in form, with a small amount of acidophilic cytoplasm and small, round, numerous, varyingly groups and markedly basophilic nuclei. The individual nuclei were usually difficult to distinguish and the contours of the cells were indistinct (Fig. 6). The liver cells contained numerous vacuoles. The nuclei were larged and often empty; in some the chromatin had disintegrated. No regeneration discernible. No infiltration into the portobiliary spaces.

PAS: occasional PAS-positive matter in Kupffer cells. Feulgen: negative in a number of nuclei; the basophilic granules have a positive reaction. Ribonucleic acids: reaction generally weak. Fe: negative. Ninhydrin-Schiff: very weak reaction. Fats: diffuse, extensive fatty degeneration, with neutral fats.

10. Patient V. J., autopsy record No. 217/62; age 19 years, female. Burns, 30%, third degree. Sepsis (Proteus). Death eight weeks after injury. Autopsy nine hours p. m.

Liver cells in centre of lobules necrotic, regeneration visible at periphery. Regenerating cells of different sizes. In some places complete dissociation of liver cells, with destruction of reticulin. Regenerating cells hyperchromatic. Nuclei in some places pyknotic, numerous vacuoles in cytoplasm. Central veins indistinct. Irregular activation of Kupffer cells, local compression of sinusoids. Hypertrophy of Kupffer cells, with histiocytic transformation, in area of foci of necrosis; lymphocytes and polynuclear cells in sinusoids (Fig. 7).

Fe: quite strongly positive in Kupffer cells (diffuse and in small granules). Ninhydrin-Schiff: weak diffuse reaction. Fats: severe fatty degeneration, mainly in intermediate and peripheral zone, with large amount of neutral fats. Area of nuclei 113 μ^2.

In patients who died from shock at different intervals after burns, differences were observed in the filling of the various parts of the vascular system of the liver. In patients who died soon after injury, filling of the interlobular veins was slight, the sinusoids were dilated, the central veins were indistinct and the collecting veins were full. Later, the picture changed. The afferent branches were contracted, the central veins were dilated and the sinusoids were narrow, compressed by swollen cells. The interlobular veins (patient K. P.) contained blood cells and liver cells with regressive changes. The collecting veins usually contained erythrocytes. This seems to indicate that the dissociated liver cells got into the interlobular veins through a reverse movement of the blood column — which would be quite feasible (as in anaphylactic shock) (12). Marked eosinophilia was found in the patient A. A., who died 2½ hours after injury. This generally appears for only a short time after injury, as

pointed out by Sevitt et al. (1). Changes in the endothelium are usually marked in patients dying from shock, with swelling of the Kupffer cells (especially in protracted shock), which become detached from the endothelium or undergo phagocytosis. Changes in the behaviour of the Kupffer cells and endothelium are not always the same. Apart from activation, the complete reverse, i.e. inactivity, may be found, followed in later stages by atrophy and a decrease in their numbers. The multinuclear elements which evidently developed from Kupffer cells are interesting. In a paper by Lindlar (13), dealing with the chemical analysis of the liver of a 6-year-old girl who died four months after burns, the histological findings mention the unusual occurrence of elements apparently similar to those observed in the patient Z. V. Neoral (14) also observed these elements in a child who died from burns. Another finding worth mentioning is that marked activation of the Kupffer cells was found in all three children in the present series. The above multinuclear elements originating from Kupffer cells were not observed in adults. It is possible that histamine and substances causing inflammation participate in the activation of Kupffer cells (15, 16). Töro (16) isolated a substance, termed resactor, which is secreted by liver cells and activated Kupffer cells. Antihistaminics cause inactivity of Kupffer cells (15). None of the patients in the present series received antihistaminics, however.

In protracted shock swelling of the liver cells and changes in the liver are more pronounced. The area of the nuclei in patients who died on the first day after injury was diminished; from the second day it increased. It was largest in patients who died at the end of the first week. These changes are probably related to changes in osmotic pressure. Various observations indicate that liver cells have a considerably higher osmotic pressure than erythrocytes. Normal liver cells must produce energy in order to regulate their water content. If cell metabolism or the function of the membrane is disturbed by physical or chemical factors (which can easily occur in burns), fluid is absorbed. It has even been demonstrated that macromolecules can enter the liver cell without first being broken down. There is also sufficient evidence that at least some of the serum proteins are synthesized by the liver cells and that they can pass out of the cell. It must therefore be presumed that the liver cells are influenced directly by the composition of the plasma proteins (17).

In some patients, markedly large lipofuscin deposits were found in the centre of the lobules. Zinck (7) drew attention to this finding of lipofuscin, together with atrophy of the liver cells, after burns and described it as lipofuscin atrophy. Although it is known (18) that the amount of lipofuscin is not strictly related to age, the author is nevertheless of the opinion that the large increase in the amount of lipofuscin in relatively young patients must be attributed to the burns. This is borne out by the present view that this pigment is closely associated with cell metabolism and that it can both appear and disappear quite suddenly.

In patients who died after a long interval, hepatodystrophic necrotic changes were found in the centre of the lobules, together with inflammatory changes.

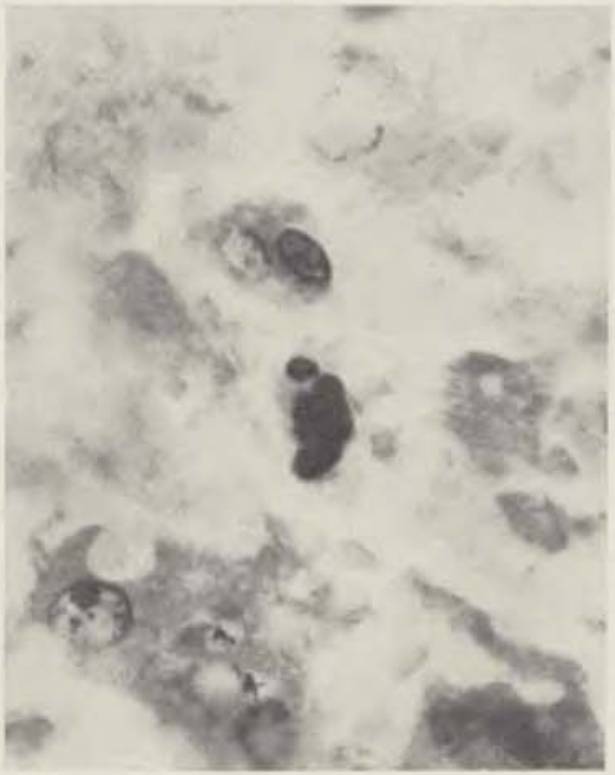

Fig. 7. Patient Z. V., 4 weeks after injury. Multinuclear elements from Kupffer cells. Haematoxylin and eosin.

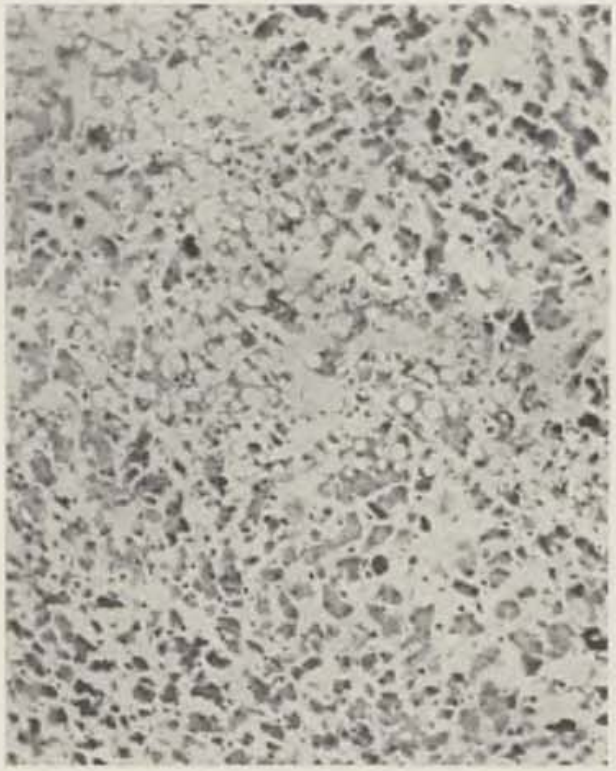

Fig. 8. Patient V. J., 8 weeks after injury. Necrosis and inflammatory dissociation of liver tissue. Haematoxylin and eosin.

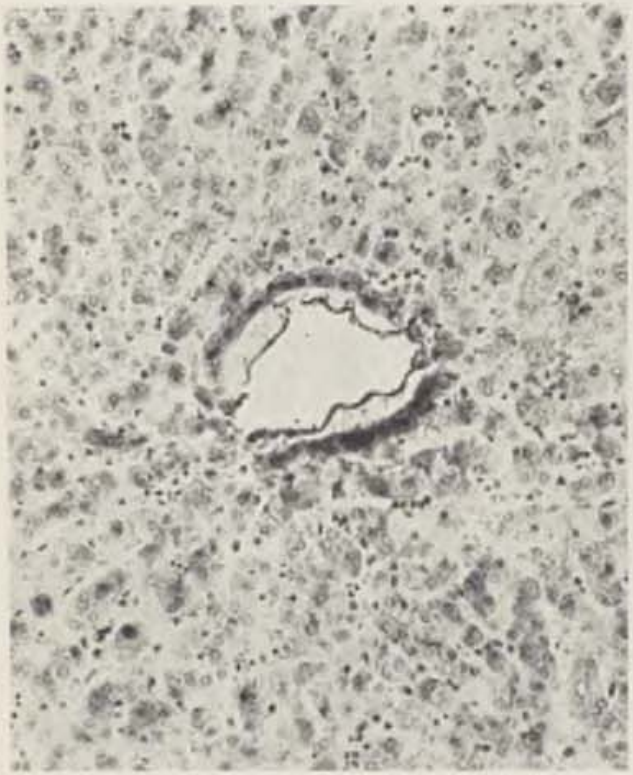

Fig. 4. Patient K. P., 11 hours after injury. Swelling of intima and oedema of wall of central vein. Haematoxylin and eosin.

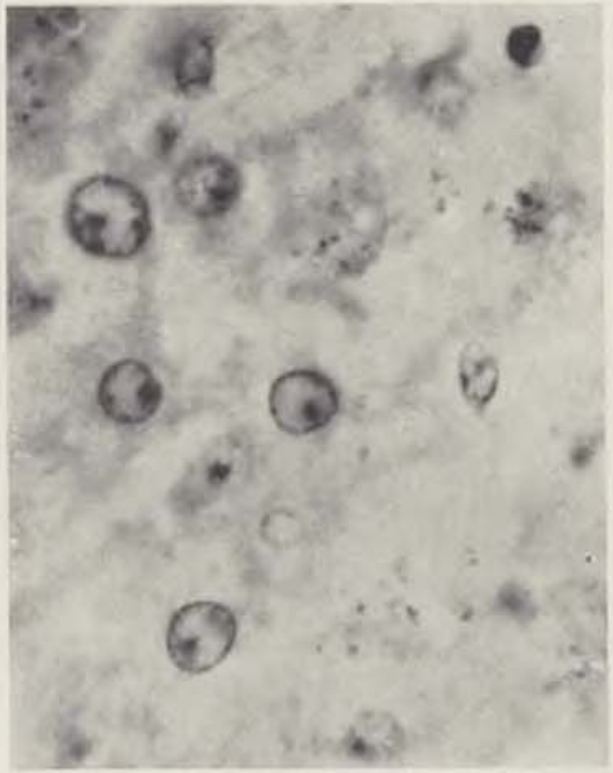

Fig. 5. Patient Č. A., 30 hours after injury. Disappearance of ribonucleic acids round nuclei. Methyl green pyronin.

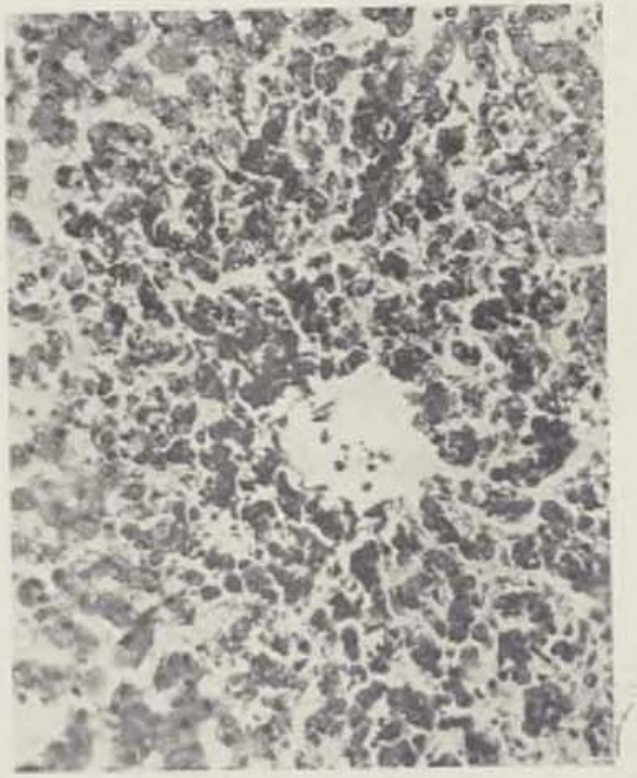

Fig. 6. Patient K. I., 7 days after injury. Central necrosis. Haematoxylin and eosin.

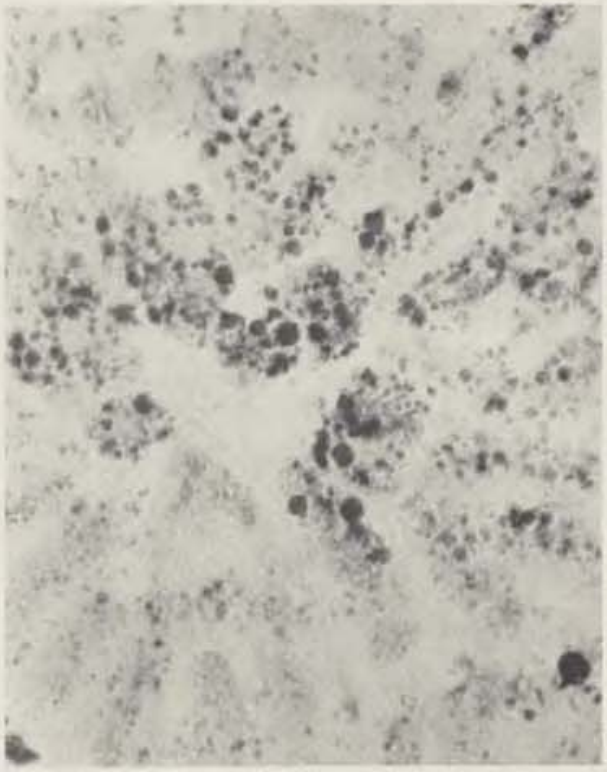

Fig. 2. Patient A. A., 2½ hours after injury. Central fatty degeneration. Sudan orange, haematoxylin.

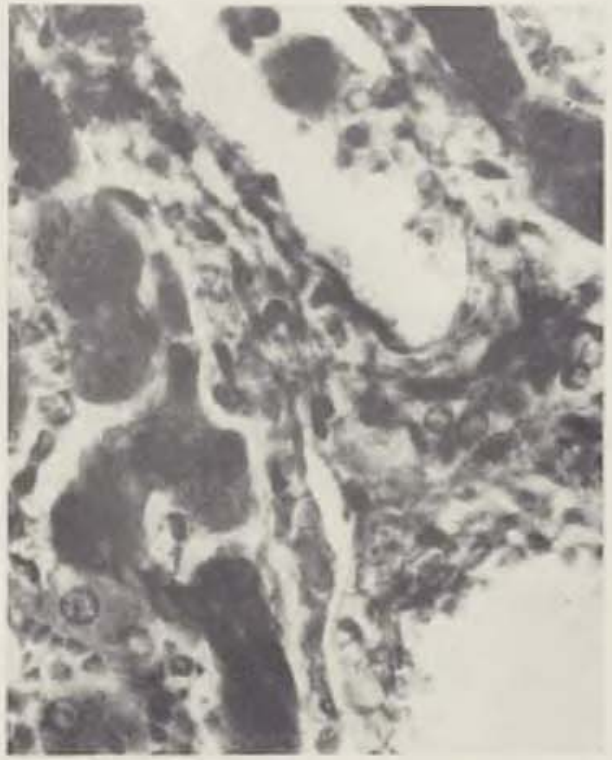

Fig. 3. Patient K. P., 11 hours after injury. Liver cells in interlobular vein. Haematoxylin and eosin.

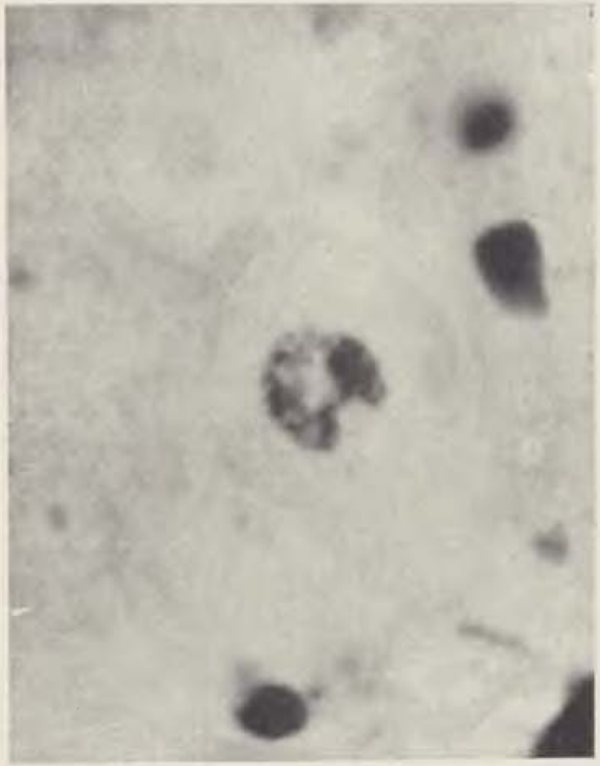

Fig. 1a. Patient A. A., 2½ hours after injury. Vacuoles in nucleus. Heidenhain's haematoxylin.

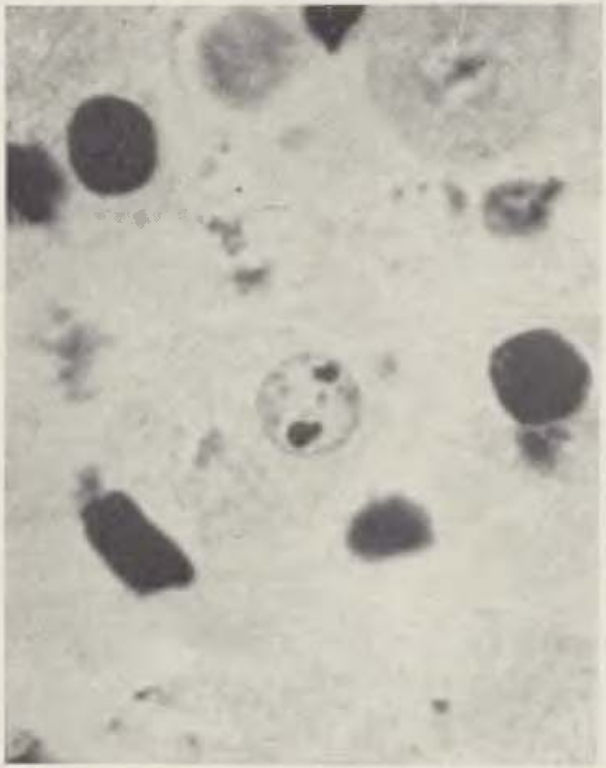

Fig. 1b. Patient K. P., 11 hours after injury. Empty nucleus with nucleoli. Heidenhain's haematoxylin.

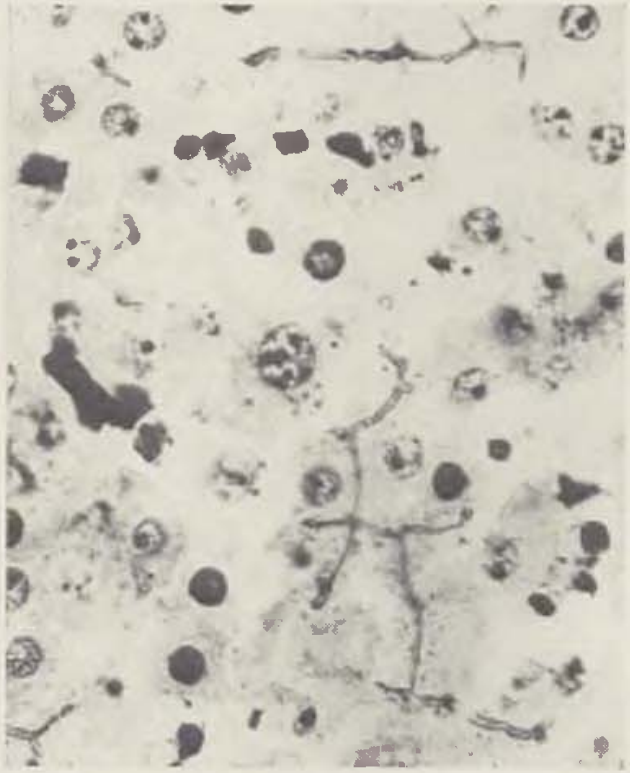

Fig. 1c. Patient Č. A., 30 hours after injury. Disintegrated chromatin in nuclei. Heidenhain's haematoxylin.

Complications due to infection in the later phases further affected the already much weakened liver cells, resulting in the severe liver changes described above. No Councilman's bodies (often described in the era of tannin treatment) were observed. Marked accumulation of PAS-positive substances of a non-glycogenic nature in the liver cells, described in various pathological conditions of liver tissue (19) was likewise not observed. In some patients with shock, an increase in the amount of these substances was found mainly in the Kupffer cells.

The weak ninhydrin-Schiff reaction for free amino acids indicates a general decrease in the amount of protein; this is also in agreement with animal experiments by Arturson (8), although the author realizes that formalin fixation is not ideal because of the formation of methylene bridges. The phenomenon described by Lindlar (13), who found an unusually high free amino acid concentration in the liver of a small girl with burns, was not observed. The question of ribonucleic and deoxyribonucleic acids is closely associated with the question of the decrease in protein. Ribonucleic acids are thought to be present as the outcome of protein formation (20). This is in agreement with the rapid disappearance of ribonucleic acids during starvation. The state of nutrition cannot be the only cause, however. It is known from experiments that changes found after six days' starvation are similar to these found one day after burns. The author himself found a marked decrease in ribonucleic acids (to be more precise, in substances staining purple with methyl green pyronin) in shock, with a somewhat higher level, though still generally below normal, in the later phases, together with hypertrophy of the nucleolus, which is regarded as the indicator of protein synthesis by liver cells (21). The amount of deoxyribonucleic acid tends to be higher in the presence of a decrease in proteins (8); this is also confirmed by the findings in patients who survived for longer periods. The frequent finding of siderosis, due to disintegration of the erythrocytes (which is usual after burns) and possibly to transfusions, is not altogether surprising. What is more remarkable is that in some cases iron was demonstrated in the liver cells only, evidently as a result of insufficiency of the Kupffer cells.

The genesis of fatty degeneration is not absolutely clear. Fatty degeneration was found in most cases, though not in all. Anoxic, toxic and nervous factors all participate; transport has also been described as a factor (22). The latter hypothesis is confirmed by the finding of fatty degeneration in patients who died only a short time after injury. In other types of shock, in which severe anoxic and nervous changes, etc. also occur — e.g. anaphylactic shock (12) — fatty degeneration is not usually found. Differences in localization (fatty degeneration was also found at the periphery of the lobules in patients who died after a longer interval) and the presence of neutral fats in most patients who died soon after injury and a long time after injury also indicate that fatty degeneration is mediated by different mechanism.

In conclusion it can be stated that the above changes are indicative of severe disturbances of liver tissue metabolism. Detailed chemical and histochemical studies will no doubt influence the treatment of severe injuries such

as thermic injuries. It is hoped that this study will make some small contribution to these questions, since as far as the author is aware, no biopsy studies have been carried out and present knowledge is based mainly on animal experiments.

SUMMARY

A study of changes in the liver tissue of ten young patients who died from burns or scalds after a varyingly long period, i.e. 2½ hours until 8 weeks after injury, was carried out by histological and some histochemical methods. The changes in the liver tissue in patients who died from shock, are described and discussed. In later periods of burns sickness, significant changes of a hepatodystrophic and inflammatory character, were found. In later periods, steatosis was frequently found even in the peripheral lobuli with a large amount of neutral fats. The amount of ribonucleinic acids was decreased, particularly in patients who died from shock. The author concludes on a shortage of proteins in the tissues. He also points to the appearance of multinuclear elements (altered Kupffer cells) in a child aged four.

RÉSUMÉ

La lésion hépatique des brûlés

Z. Gregora

On a étudié, à l'aide des méthodes histologiques et certaines méthodes histochimiques, les altérations du tissu hépatique chez 10 jeunes gens, décédés à une période plus ou moins longue après s'être brûlés ou ébullitionés (de deux heures et demi jusqu'à 8 semaines après l'accident). On décrit et discute les altérations du tissu hépatique des malades décédés en état de choc. A une époque plus tardive, on a pu constater des altérations importantes hépato-distrophiques et inflammatoires. Souvent, on a rencontré des stéatoses, situées souvent également à la périphérie des lobules à un stade plus tardif et contenant beaucoup de graisses neutres. On a trouvé une diminution des acides ribonucléiques, surtout chez les malades morts en état de choc; on considère qu'il y a carence protéinique dans les tissus. On attire l'attention sur la présence d'éléments polynucléaires (cellules de Kupffer transformées) chez un enfant de 4 ans.

ZUSAMMENFASSUNG

Leberschädigung bei Patienten mit Verbrennungen

Z. Gregora

Mit Hilfe histologischer und einiger histochemischer Methoden wurden die Veränderungen des Lebergewebes bei 10 jungen Personen untersucht, die in verschiedenen Zeitabständen nach einer Verbrennnung oder Verbrühung (2½ Stunden bis 8 Wochen nach dem Unfall) verstarben. Beschrieben und diskutiert wurden die Veränderungen des Lebergewebes bei Patienten die im Shock starben. In späteren Zeitabschnitten wurden markante hepatodystrophische und entzündliche Veränderungen festgestellt. In späteren Stadien wurde oftmals Steatose auch an der Peripherie der Leberläppchen mit bedeutendem Gehalt an Neutralfetten gefunden. Der Gehalt an Ribonukleinsäuren war vermindert, besonders bei Patienten, die im Shock starben; der Verfasser schliesst auf Eiweissmangel des Gewebes. Es wird auf den Befund vielkerniger Elemente (veränderter Kupfferscher Zellen) bei einem vierjährigen Kind hingewiesen.

RESUMEN

Lesión de los hígados en los quemados

Z. Gregora

Por medio de los métodos histológicos y algunos métodos histoquímicos fueron estudiados algunos cambios del tejido de los hígados en 10 hombres jóvenes que fallecieron dentro del período de varia duración después del accidente (quemadura o escaldadura), es decir, desde 2½ horas hasta 8 semanas después del accidente. Luego se describieron y discutieron los cambios del tejido de los hígados en los pacientes que fallecieron en el choque. En el período más avanzado se observaron cambios hepatodistróficos e inflamatorios importantes. Muy a menudo se hallaba esteatosis en aquel período también en la periferia de los lóbulos con una gran cantidad de las grasas neutrales. Fue halladà una cantidad reducida de los ácidos ribonúcleicos, especialmente en los enfermos que murieron en el choque, y fue juzgado en la carencia de las proteínas en el tejido. Se llamó atención a un hallazgo de los elementos multi-nucleares (las células de Kupffer alteradas) en un niño de 4 años.

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PERSONALITY OF PATIENTS WITH INADEQUATELY DEVELOPED MALE GENITALS, IN PARTICULAR, WITH HYPOSPADIAS

J. HYNIE, I. ŠÍPOVÁ

At the Naples Congress on Fertility and Sterility, Hynie read a paper on the incidence of hypospadias and other disorders of male sexual differentiation and on the sexuological aspects of their surgical treatment. Prof. Burian reported on these cases from the point of view of surgery.

Since then we have paid more attention to the development of the personality of patients with various types of deficient sexual development.

MATERIAL

We have carried out a detailed examination of 198 male patients. Apart from cases with hypospadias of various degrees and pseudohermaphroditism, there were those with other deficiencies of the penis (epispadias, phimosis, conditions after injury and other deformities), the testicles (undescended, migrant or small) and general pubertal development (pubertal dystrophy, pubertas praecox, tarda or disharmonica). The age of the patients ranged between one and 22 years.

In order to be able to calculate the significance of the individual factors, we excluded all cases with diagnoses only sporadically represented in the series, unless we could include them into other larger groups, and we also excluded the cases of sporadically represented age groups, particularly those remote from the average. Thus, the series of cases studied became more homogenous and easier to survey. The final series included 168 boys aged 2 to 15 years. The cases were arranged in the following groups:

A. Very slight hypospadias and migrant testicles

These patients are usually quite unaware of their deficiency. We did not find any particular aberration in the development of their personality. Lacking other possibilities we took this group as the control. It consisted of 33 subjects.

B. Aberrant sexual differentiation

This group comprised more significant hypospadias and pseudohermaphroditism and consisted of 22 subjects.

C. Small and undescended testicles

These were cases with inadequately developed testicles without deficient differentiation in the other parts of the genitals. — 65 subjects.

D. Prepubertal dystrophy

Here we grouped cases of obesity with underdeveloped genitals. The hypothalamic region probably plays an important part in this disorder. However, in young subjects it cannot be termed adiposogenital dystrophy (DAG). — 33 subjects.

E. Disharmonious puberty

This group consisted of patients in whom the somatic and psychic components did not develop in parallel. — 15 subjects.

METHODS

The development of personality in boys was investigated by the method of standard interview with the patient and his mother or the nearest relatives living in the same home.

Apart from personal data, the entire structure of the family was ascertained, including its hereditary, social and educational conditions, how much the parents yearned to have a child, his fate prior to and after birth, his play, hobbies, the kind of sport he cultivated, his behaviour at school and at activities outside the school, how he behaved at home, etc.

Interest in reading was registered from the period the child started to listen to tales and other narrations when — at times — he already showed tendencies towards neurotic reactions. We also investigated the development of ideas and aspirations for the future. It is important to obtain information about the child's social relationships starting from the earlies possible age, his age and sex preference, if there were any difficulties in making friends and their causes, about other features of his character and their changes, etc.

Particularly important for this study is, of course, the process of becoming aware of the difference of sexes and of the development of the sexual signs primary, secondary and of the psychic components of adolescence, the development of the attitude towards the opposite sex, the awakening of the interest in sexual matters and functions, his own appearance, etc. For the evaluation of adaptability and sensitivity of the patients the reaction to psychic trauma was considered particularly important.

The neurotic symptomatology of the patient completed the above studied cross sections of the individual features of personality.

TREATMENT OF MATERIAL

The detailed interview was intended to obtain the most complete picture of the subject's personality, although we were well aware of the fact that it would not be possible to evaluate statistically all registered factors and that not all data would be equally significant for the given study. The psychological investigation and the evaluation of the data ascertained were carried out in all subjects by one and the same person

This report only deals with the following factors: 1. self-confidence, 2. awareness of belonging to the male sex, 3. sensitivity, 4. adaptability, 5. interests, 6. assertiveness.

Boys with insufficient *self-confidence* take little part in collective activities; they rather keep aside or engage passively and lag behind.

In a more marked developmental disorder in the sense of pseudohermaphroditism or hypospadias, making micturition possible only in a squatting posture, as in girls, we often found the child doubting as to whether he *belonged to the male sex*. He sometimes furtively reflected whether he was not a girl. Such thoughts are not voiced in the presence of other people but they weigh the heavier on the child's mind. This, however, need not always lead to a breakdown of self-confidence. Children differ greatly in *sensitivity*. We even met boys who became the leaders of a group of boys inspite of their markedly inadequate genitals.

Social *adaptability* to the demands of work and under aggravated conditions of health or family life, may be different in patients with various disorders of sexual development.

The interests of the patients were investigated mainly in the direction as to whether they were purely boyish or somewhat aberrant. The surroundings in which the child grows up, certainly plays an important part, and sometimes it is difficult to find out what exactly goes to the credit of aberrant sexual development. However, play and toys usually bear important witness to the development of the child's personality, even if aberrant.

Usually still more characteristic is the behaviour, particularly the assertivenes of the subject investigated, because this is a typical virile feature.

RESULTS AND THEIR EVALUATION

The results of the evaluated factors were set out in the following table:

Tab. 1

	A		B		C		D		E	
	norm.	aberrant	norm.	aberrant	norm.	aberrant	norm.	aberrant	norm.	aberrant
Self-confidence	28	5	11	11	44	21	17	16	10	5
Awareness of belonging to male sex	32	1	14	8	63	2	32	1	15	0
Sensitivity	19	14	10	12	17	48	9	24	6	9
Adaptibility	24	9	12	10	33	32	14	19	2	13
Interests	31	2	14	8	52	13	27	6	12	3
Assertiveness	28	5	11	11	30	35	7	26	7	8
Total	33		22		65		33		15	

A = almost normal, B = severe hypospadias, C = simple hypogenitalism, D = hypogenitalism combined with obesity, E = disharmonious puberty.

The mathematician Malý has calculated the significance of the individual factors and their deviations both in relation to the group of subjects least affected (A) where the children were not usually even aware of the fact that their genitals were slightly aberrant, and in the relations between the groups C and D (hypogenitalism with and without obesity). The figures are given in Tab. 2 made up according to the tables of detailed calculations which we do not publish. Significance up to the 5% limit is marked +, up to the 1% ++, up to 0.1% +++.

Tab. 2

Relationship	A × B	A × C	A × D	A × E	C × D
Self-confidence	++	−	++	−	−
Awareness of belonging to male sex	+++	−	−	−	−
Sensitivity	−	++	+	−	−
Adaptibility	−	+	+	+++	−
Interests	++	−	−	−	−
Assertiveness	++	+++	+++	++	+

Significant deviation: +++ = 0.1%; ++ = 1%; + = 5%; A = almost normal, B = severe hypospadias, C = simple hypogenitalism, D = hypogenitalism combined with obesity, E = disharmonious puberty

From the survey of the results it is evident that particularly in more marked hypospadias and pseudohermaphroditism the awareness *of belonging to the male sex* is affected most severaly and thereby the self-confidence of the patient. In cases where the genitals, no having a typical puerile appearance, show a deep cleft, so that the urine escapes not from the tip of the penis, but elsewhere and micturition is possible only as in girls, it is not surprising to find the child having doubts as to his belonging to the male sex.

In connection with this, we may find a *shaken self-confidence* in boys with inadequate differentiation. Obese boys with hypogenitalism show equally affected self-confidence, but this is based on something else. They are always the target of allusions as to their corpulence, clumsiness and misshape. The genitals are of secondary importance; they are usually small, particularly if compared with the big body, but otherwise unaltered as to quality, and, therefore, the awareness of belonging to the male sex is not affected; the same as in the remaining groups studied.

Boyish or girlish *interests,* as a rule, develop already in early childhood, i.e. at a time when the puberty hormones have not yet taken effect. Not without justification is it said that the psychic differences between small boys and girls are more marked than their differences in structure and shape of the body. Boys play at soldiers and with little machines but mainly take everything apart, break it, destroy it. Girls, on the other hand, play with dolls and handle things as though they were alive. Some authors (Beach, Lorenz, etc.) maintain that

already antenatally certain cerebral structures are differentiated for masculine activities, probably due to the effect of foetal androgens. In boys showing a more severe aberration of sexual differentiation there could have been a disturbance in foetal androgens whose manifestation could be the aberrant interest and behaviour. Such boys are also not quite as *assertive* as normal boys.

However, much greater lack of assertivenes is met with in boys with inadequate testicles whether combined with obesity or not. This more hormonally conditioned inadequacy, probably affecting the hypophysis, suprarenal glands, gonads and the thyroid, manifests itself somewhat differently than does inadequate foetal differentiation. In hypogenitalism, lack of assertiveness is usually combined with an increased *sensitivity* and lability of affection, sometimes even with a decreased adaptability to the conditions of life.

Adaptability, i.e. the capacity to adapt oneself to the various conditions of life, however, is mainly affected in disharmonious sexual development during prepuberty and puberty where, as is well known, various break-downs and transitory changes of character (not frequently in the wrong direction), take place. Initiative, too, is usually limited.

SUMMARY

In inadequate sexual differentiation through a severe degree of hypospadias we particularly meet with an aberrant awareness of belonging to the male sex due not only to the appearance of the genitals but also to the female mode of micturition and to peculiarities of inborn interests and behaviour. We, therefore, insist on early *surgical repair* so that micturition can be performed in a boyish fashion, even if not quite perfect, from the very beginning, e.g. by simple lengthening of the urethra to the penoscrotal angle. Stress is also to be layed on increased educational care so that self-confidence should not suffer on mixing with boys of the same age, and on mental development.

In hypogenitalism the lack of assertiveness is most conspicuous particularly if combined with obesity which leads to a greatly shaken self-confidence due to the frequent allusions on the part of children of the same age.

In disharmonious puberty adaptability to the demands of work and society is affected most.

RÉSUMÉ

La personalité du malade à développement incomplet de l'appareil génital mâle, surtout s'il s'agit d'hypospadias

J. Hynie, I. Šípová

Lorsque la différenciation est insuffisante dans le sens d'une hypospadias prononcée, nous rencontrons surtout des aberrations du sentiment de l'appartenance sexuelle, provoquées non seulement par la formation des organes génitaux, mais aussi par le fait d'uriner à la façon des femmes, ainsi que des particularités dans les intérêts spontanés et le comportement. C'est pour cela que nous insistons surtout sur la *réparation de la miction* aussitôt que possible, afin que le malade puisse uriner à la façon des garçons, même si ce ne serait pas tout de suite de manière parfaite, p. ex. si l'urètre a été simple-

ment prolongé dans la pli entre le scrotum et la verge; puis sur une éducation très soignée pour ne pas endommager la conscience de soi-même, les bons rapports avec les camarades de son âge et le développement mental.

S'il y a hypogénitalisme, l'irrésolution du malade est encore plus frappante, surtout s'il est également obèse et sa conscience de soi-même se trouve souvent ébranlée, à cause des allusions fréquentes de ses camarades.

Lorsque la puberté est déséquilibrée, c'est surtout l'adaptabilité aux exigences professionnelles et sociales qui est le plus sensiblément touchée.

ZUSAMMENFASSUNG

Die Persönlichkeit von Patienten mit unvollkommener Geschlechtsentwicklung, insbesondere durch Hypospadien

J. Hynie, I. Šípová

Bei einer unvollkommenen Geschlechtsdifferenzierung im Sinne einer ausgeprägten Hypospadie, begegnen wir einem abweichenden Gefühl der geschlechtlichen Zugehörigkeit, die nicht nur durch Genitalbildung, sondern auch durch eine weibliche Art des Urinierens und Besonderheiten in den angegebenen Interessen und im Verhalten gegeben ist. Daher drängen wir besonders auf eine *frühzeitige Regelung des Urinierens* auf Knabenart auch wenn dies nicht sofort vollkommen durchgeführt werden kann, z. B. durch eine blosse Verlängerung der Urethras in den penoskrotalen Winkel. Wir legen Wert auf eine gesteigerte Pflege der Erziehung, damit das Selbstbewusstsein, ferner der Kontakt mit den Zeitgenossen und die geistige Entwicklung keinen Schaden erleidet.

Bei Hypogenitalismus ist die herabgesetzte Durchschlagskraftigkeit der Patienten noch auffaliger, besonders wenn dieser mit Obesitas einhergeht, wobei das Selbstbewusstsein durch Anspielungen wesentlich erschüttert wird.

Bei einer ungeregelten Reife leidet besonders die Adaptabilität gegenüber Arbeits- und gesellschaftlichen Anforderungen.

RESUMEN

La personalidad de los pacientes con el desarrollo sexual masculino imperfecto especialmente con hipoespadías

J. Hynie, I. Šípová

En la diferenciación sexual imperfecta en el caso de una hipoespadía expresiva podemos encontrarnos con una sensación especialmente diferente en cuanto a la pertenencia sexual, que está dada no solamente por la forma de los genitales sino también por el modo de la micción de manera femenina y los rasgos especiales de los intereses y de la conducta congénitos. Por este motivo es necesario *adaptar muy temprano el modo de la micción,* en nuestro caso al modo masculino, aunque no lo sea perfecto enseguida, por ejemplo, por un prolongamiento de la uretra en el ángulo penoescrotal. Luego es necesario poner el acento sobre el cuidado educativo para no hacer sufrir el el orgullo, el contacto con los grupos de los coetáneos y el desarrollo psíquico.

En caso del hipogenitalismo nos sorprende aún más la falta de iniciativa, especialmente en los pacientes con obesidad, durante la cual la confianza en sí mismo sufre un choque durante alusiones frecuentes de los coetáneos.

En caso de una adolescencia confusa y irregular sufre especialmente la adaptabilidad en cuanto a las exigencias sociales y las de trabajo.

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NEUROGENIC ETIOLOGY OF DUPUYTREN'S CONTRACTURE
Part I.

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The contracture of the palmar aponeurosis, the so-called Dupuytren's contracture (DC), has become well known to every medical practicioner since it was first described by Guillaume Dupuytren 130 years ago. Though clinical symptomatology, histology and therapeutic methods have been studied successfully the question of etiology has remained unsolved up to the present. This is not due to a lack of interest on the part of scientific workers; on the contrary, over 300 papers have been published, among these several monographs, some dealing only with the question of etiology. This is why today a whole paper can deal exclusively with this problem.

On studying the extensive literature, it becomes evident that perhaps there is no single factor which has not been charged with being somehow connected with the origin of DC. This is mainly due to the frequent incidence of DC; it is found in 10% of the older male population. Proving an etiological factor is mostly impeded by the fact that it is usually but an a c c i d e n t a l concurrence of two or more pathological conditions. It may by interesting to list the table of etiological factors according to G. Maurer:

1. Traumatic theory:
   - A. chronic occupational trauma
     - a) heavy loading
     - b) slight but repeated leading
   - B. single trauma
2. Congenital Theory:
   - A. theory of sesamoid bones
   - B. metaplasia of persistent short flexor muscles (Krogius)
   - C. hereditary disposition — familial incidence
3. Neurogenic etiology:
   - A. peripheral: irritation of peripheral nerve endings by certain manual work, lesion of ulnar nerve or brachial plexus
   - B. spinal: tabes dorsalis, syringomyelia, haematomyelia, myelitis

C. cerebral: disseminated sclerosis, cerebral haemorrhage, epilepsy
D. trophic: sympathicotonia (Nippert), lesion of centres C8-Th1, increased irritability of vascular nervous system, vasomotor disorders (Schulthess)

4. Endocrine etiology:
   A. hypothyroidism
   B. hypocalcaemia and hypoparathyroidism (Leriche, Jong)
   C. hypofunction of hypophysis — narrow sella turcica (Frund)
5. Infectio-toxic etiology:
   A. chronic intoxication:
      a) alcohol
      b) saturnism
   B. tuberculosis (Poncet)
   C. focal infection
   D. local pyogenic infection (Wyss)
6. Diabetic and constitutional theory:
   A. rheumatism, osteoarthritis, gout, diabetes
   B. tendency towards indurative processes: fibroplastic diathesis, plastic induration of the penis, torticollis, keloids, fibromata, adhesions
7. Other etiology:
   A. old age and aging: degenerative nutritional component, physico-chemical changes in tissues, diminishing cushion of palmar and digital pulp (Madelung)
   B. atherosclerosis
   C. pellagra (Parhon)
   D. use of barbiturates in epilepsy (Skoog)
   E. cirrhosis of liver (Weyer)

We have considered the extent to which neurogenic factors are involved in the etiology of DC.

We based our study on a group of 140 patients with DC operated on at the Clinic of Plastic Surgery in Prague; these, therefore, are not cases detected in out-patients or at the wards of a neurological or psychiatric department. We carried out the usual clinical examinations and then in different groups of patients, EEG, EMG, X-ray of cervical spine, examination of the automatic nervous system, chronaximetry, measurement of skin conductivity and skin temperature. The age of the patients ranged between 12 and 82 years, the average was 52.2 years. There were 107 men and 33 women.

In the following we intend — as far as our findings permit — to state our point of view with regard to the condition of the various parts of the central and peripheral nervous system and on the possibility of a lesion of the central nervous system or the nervous system as a whole having a causal relationship with the manifestations of DC.

CEREBRAL LESION

Cerebral etiology was suggested by Manclaire who found DC on the hemiparetic side after haemorrhage in the basal ganglia. Others, too, maintained that lesions of the basal ganglia may lead to the development of DC. Most

authors, however, deal with the relationship between DC and epilepsy. Lund found DC in 50% of men and 25% of women with epilepsy. At the same time he observed other disorders of connective tissue, such as plastic induration of the penis, knuckle pads, etc. more frequently in epileptics. From acrocyanosis, which is also more frequent in epileptics, and from the changes in skin temperature, he assumed that these were manifestations of a cortical lesion of the trophic centres. Skoog, too, found 42% DC among 207 epileptics, but he assumes that this is more probably associated with the chronic taking of barbiturates. He supports his view by pointing to the fact that DC is also found frequently with humero-scapular and other types of periathritis which, like epilepsy, are usually treated with barbiturates.

Other authors (Francillon, Kramer, Hilbers) did not observe such a high percentage of DC in epilepsy.

The cerebral changes found in our series of DC cases are given in tab. 1.

Tab. 1

Total number of patients with DC accompanied by:	140	100%
primary epilepsy	3	2
secondary epilepsy	1	0.7
disseminated sclerosis	1	0.7
neurosis	7	5
migraine	3	2
spasmophilia	4	3
cerebral atherosclerosis	8	5.7
conditions after cerebral haemorrhage	2	1.4
Parkinson syndrome	1	0.7
Thompsen myotonia	1	0.7
arachnoiditis of brain convexity	2	1.4

Cerebral lesions concurrent with DC

As can be seen from this table, the number of central lesions is not large enough to justify the assumption that there might be a connection with DC. The higher percentage of artherosclerosis in our patients is due to the high mean age in the series. The incidence of neurosis and migraine — by number and nature — corresponds to that in the general population. In the series there were four epileptics. One was a case of Jacksonian epilepsy following an operation for arachnoiditis of the convexity of the brain. The second manifested itself with attacks of unconsciousness which could not be distinguished with certainty from syncope: the EEG did not show signs of typical epileptic activity. Since there are stated to be 0.5—1.0% epileptics in the general population, there is no reason for seeking a connection between epilepsy and DC in

our series. However, prompted by the reports in the literature we carried out additional EEG examinations in 15 patients with DC, selected at random. We endeavoured to maintain proportional age representation. The investigations were carried out by assistant Roth of the Neurological Clinic in Prague. In ten cases normal rhythm was registered, in three there were signs of lowered vigilance or sleep rhythm and in two the tracing showed dysrhythmia. We made no further examinations, because our clinical material and the EEG excluded any higher incidence of epilepsy.

How, therefore, can the higher percentage found by Lund and Skoog be explained? Firstly, the former registered 11.6% of clinically manifest and definite DC, whereas the latter 23%. In their papers, however, both authors took into account even very minute changes in the palm, and thus the percentage approached 50%. Maybe if someone else who had not made such detailed examinations, would not have included these suspected cases of DC in his total. Anyway, the percentage even so is very high. This can probably be explained by the fact that all subjects investigated were in-patients with severe epilepsy who had a great number of paroxysms. We assume that the clinical picture resembling DC in these cases may partly be evoked by clonicotonic spasms of the muscles of the hand with subsequent trophic manifestations and repeated small injuries with subsequent minute tears in the skin and palmar aponeurosis, i.e. that there are peripheral, mechanical changes connected with the epileptic fit. There is no justification for assuming any connection between the central cause of epilepsy and DC.

SPINAL LESION

When considering a spinal lesion in the cervical region as pathogenetic for DC, one would first think of an irritation or lesion of the trophic centres in the area of the lateral horns. Only Abbé assumes reflex irritation of the spinal cord with secondary trophic changes in the medulla following injury to the hand. Alajaunine also assumed that the frequent affection of both hands was caused by reflex irritation of the spinal trophic centres. More frequently findings were described in patients with DC which — to a certain extent — justify assuming the presence of a spinal lesion. Horner's syndrome occurring together with pyramidal signs or tendon hyperreflexia in patients with DC, have been described. Other authors have associated DC with other spinal lesions. Oppenheim thus described a case of spinal gliosis with DC, Bieganski, Hadji Dimo and Testi syringomyelia with DC and Parhon spinal leptomeningitis with DC. Caspari et Dejerine take injury to the lower cervical medulla as the cause of DC. Many papers report about DC in tabes dorsalis, for instance Noica in a case of Charcot's disease and Dejerine in haematomyelia.

In our series of 140 patients we found spinal lesions three times. One was a case with clinical signs of disseminated sclerosis, another of tabes dorsalis. The third case was a seventy-year-old patient with a posterior tract syndrome whose etiology could not, however, be ascertained definitely. Trophic changes, particularly in the periphery such as acrocyanosis, Horner's syndrome, hyper-

hidrosis, exfoliation of the skin, etc. were found more frequently (see later), but the spinal etiology of these changes was disputable. We have studied the case papers of 35 patients with syringomyelia, but only in one was there a reference to palmar contracture. It is certainly possible that the initial stage of DC remained unnoticed, or was not registered. On the whole it may be said that the results of our investigation do not justify assuming any affection of the spinal cord in DC any more frequently then would correspond to accidental concurrence.

CHANGES OF CERVICAL SPINE

The development of DC is also frequently connected with pathological conditions of the cervical spine. As the only cause, or more often as an associated cause, were considered: intervertebral disc prolapse, anterior and posterior osteophytes, cervical rib, scalene syndrome or traumatic changes in the cervical vertebrae (Pomme, Scholtz, quoted according to Lund). It has been assumed that in these cases a lesion of the roots or nerves passing through the intervertebral foramina or an irritation of the rami communicantes (inferior cervical ganglia) had occurred. In order to prove the correctness of these theories, the incidence of osteochondritis and other vertebral changes in patients with DC has been compared with that of the same changes in subjects of the same age without any signs of DC. Particularly after the age of fifty — as is well known — changes in the intervertebral disc and other osteochondritic manifestations are extremely frequent and in no parallel with clinical symptoms.

We have carried out clinical examinations in our patients with special regard to the cervical spine. In the case history we searched for data on cervico-cranial and various cervico-brachial symptoms from which the patients had suffered in the past and which they frequently called "rheumatic pain"; we examined the cervical spine for limitation of movement in any direction, the brachial plexus for pain and tenderness, the spinous processes, the ganglia, skin folds, etc. In 18.2% of the patients no cervical spine symptoms were found; 15.6% of the patients gave a history of cervical complaints. *Apart from complaints in their case history the majority of patients (66.2%) showed objective clinical signs of cervical vertebral lesions.* Particularly often limited rotation or lateral bending of the head, tenderness of the spine to pressure, contractures of the paravertebral muscles and hyperalgesia of respective skin zones were found.

Tab. 2

Cervical spine without any pathological findings	18.2 %
Cervical spina disorder ascertained from case history	15.6 %
Pathological conditions of cervical spine also found clinically	66.2 %

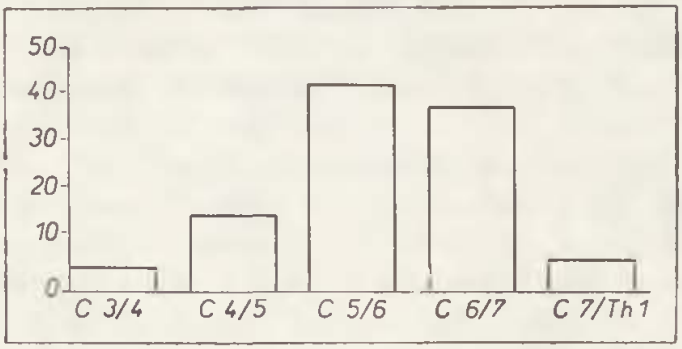
Incidence of cervical spine changes found together with DC

These findings led to our concentrating on X-ray examination of the cervical spine. We procured radiograms of the cervical spine in 92 patients. We evaluated only gross changes, i.e. locking of cervical vertebrae, narrowing of

intervertebral space, osteophytes, sliding of vertebrae against each other in a forward or backward direction and marked changes with regard to rotation (slight lateral shifts, particularly in the region of the first and second cervical vertebrae, were not counted). We did not take into consideration slight postural changes, e.g. inferior or superior C-1. The results showed: 10 patients with normal findings, 41 with changes in the segment C5—C6, 37 in the segment C6—C7, 12 in the segment C4—C5, 3 in the segment C3—C4, 2 with changes in all cervical vertebrae and 6 in the segment C7—Th1.

Tab. 3

Pathological changes in X-ray of cervical spine in 92 patients with DC. The majority of changes in the region of C4—C7



		%
Cervical spine without pathological findings	10	11
Changes in the segment C 3/4	3	3.3
C 4/5	12	13.3
C 5/6	41	44.5
C 6/7	37	40.0
C 7/Th 1	6	6.6
In the entire servical spine	2	2.2

Diffuse bone atrophy was a very frequent finding. Occasionally we found a cervical rib or a similar anomaly. The majority of subjects in our series were old people (average age 52.2). It may seem simple to compare our findings with the incidence of changes in the cervical spine in healthy individuals of the same age. A number of papers are available which report on the incidence of pathological changes in the cervical spine found on mass miniature radiography. Unfortunately, however, the criteria are different from ours so that comparison becomes difficult and may easily lead to distortion. One may admit that the incidence of clinical manifestations of cervical complaints in the patients of our series is almost the same as that in subjects of the same age without DC (81.8%).

Our X-ray findings, however, prove that these changes are, after all, more frequent than those found on mass miniature radiography. Pathological changes

in the cervical spine were found in 89% of patients with DC; a number to a certain degree significant. Reischauer (quoted according to Scholtz), however, found osteochondritic changes in 16% of all 50-year-old, in 40% of all 60-year-old and in 48% of all 70-year-old persons mass X-rayed. As has been mentioned above the various authors evaluate these changes differently and thus it becomes difficult to compare our X-ray findings with those of Reischauer. We, for instance, have taken into account even locking which most radiologists do not include.

We have hitherto been unable to elucidate the relationship between the higher percentage of pathological findings in the cervical spine and the manifestations of DC.

Views have been raised that the changes in the cervical spine could be secondary, i.e. that DC, already developed, leads to atypical, asymmetrical and disharmonious movements and thus to pathological loading of the cervical spine with subsequent anatomical changes.

TROPHIC CHANGES

Many authors assume a trophic lesion to be the only or one of many causes of DC. The basis for this theory is the clinical experience of DC occurring simultaneously with other trophic disorders, e.g. with Horner's syndrome (Alajouanine) angioneurotic syndrome, Raynaud's disease (Powers), hyperhidrosis, sclerodermia, hypertrophic osteoarthropathy, myocardial infarction (Kehl), etc.

Frequently the hands of patients suffering from DC are cyanotic or puffy. We often find the trophic Froment-Babinski or the shoulder-hand syndrome. A few authors assume trophic etiology of DC from the findings in tests for trophic changes. Deviations in skin temperature were repeatedly found (Maire). Interesting measurements were carried out photoelectrically by Paletta who found the vasomotor reactions in the hand altered proportionally to the stage of DC. The values were also altered in the unaffected hand. After operation these changes disappeared.

There are many interesting speculative theories: Schaefer assumes that the tissue proliferation taking place in DC depends on the blood supply which itself is dependent on the innervation of vessels. Focal irritation evokes long-lasting hyperaemia and thereby tissue proliferation. The focus of irritation might be the trophic spinal ganglia (Kehl, Nippert, Powers). The cause of irritation may be spondylosis, osteochondritis and other pathological changes in the cervical spine. Domnick has elaborated a whole theory about diseases caused by liquor hypotonia leading to slight radical lesions and thereby to disorders in the bradytrophic tissues, such as joints, tendons and cartilage.

The possibility of a primary lesion of the higher trophic centres in the brain stem and the hypothalamus has also been suggested. Other authors speak about a general trophic inferiority of the individual and presume that any cause (e.g. trauma) may lead to the development of DC on the basis of a thus altered

terrain (Maire, Pavlák, Padovani, Powers). A clear proof of DC being caused by a lesion of some trophic centres, i.e. the discovery of specific morphological changes there, has not yet been provided. From the history of the search for the causes of Reynaud's disease (a disorder in a way similar to that of DC), we can imagine how difficult a problem this is. Gagel and Watts found degeneration of motor sympathetic cells in the spinal cord. Afterwards, however, nobody has ever found similar changes.

Among our 140 patients we have found gross trophic changes limited to the acral part of the hand in 63%. These were acrocyanosis, hyperhidrosis and oedema. Sometimes we met with impaired healing of small wounds, rhagades in hyperkeratotic skin and callosities, and with trophic ulcerations. We saw these changes mainly in patients after operation (a total of 86% showed trophic changes after operation). In six patients of our series we observed various degrees of the physiopathic Froment-Babinski syndrome. Another three patients gave a history of complaints which were of a similar character. The signs and symptoms in these nine patients were of various degree; in some there was only a slight degree of stiffness of the shoulder joint with atrophy of the deltoid muscle and acrohyperhidrosis; others showed severe tenderness, stiffness of the entire arm, oedema and cyanosis in the hand and fingers. These syndromes were first described in angina pectoris, later in connection with Raynaud's disease and sclerodermia. They probably have a marked trophic vegetative vulnerability in common with DC. Although on clinical examination we did not find a general trophic disorder very frequently in our series of patients, we, nevertheless, attempted in 20 subjects to test the tone and irritability of the trophic nervous system.

We investigated the potassio-calcium quotient and found excess of potassium ($K/Ca = 2.42 \pm 0.6$, the norm is given as 1.96—2.06). In the subjects investigated we, therefore, ascertained a slight relative tendency towards vagotony.

The atropine test was carried out by the method described by Servít. On comparison with Servít's norm we found normal tone of the vagus and sympathetic in 16 patients, pathological tone of the vagus in 3 and of the sympathetic in 2. The number of patients and the results obtained do not permit us to draw a final conclusion. On the whole, however, it seems that the atropine test does not show any gross deviations from the norm.

The orthostatic and clinostatic test was carried out in the following way: we registered the pulse rate per minute prior to standing-up, one minute during standing and one minute after lying-down. In contradistinction to Servít, we did not measure the individual values during standing at ten-second intervals throughout a whole minute. The increase in pulse rate on standing amounted to an average of 17.2/min. $\pm$ 3.2. This corresponds to the norms as referred to in the literature. The clinostatic reaction was compared with Servít's values (normally slowing-down by 0.885/10 sec. $\pm$ 0.7). Our 20 patients showed slowing-down by 5.8 $\pm$ 0.5/min. which, therefore, can be evaluated as a slightly increased vagus (histiotrophic) excitability.

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NEUROGENIC ETIOLOGY OF DUPUYTREN'S CONTRACTURE
Part II.

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In the further study of the condition of trophic innervation in the upper extremities, we tested the electrical conductivity, the "dermatophoria" according to Lesný (1953, 1957), in 26 patients with Dupuytren's contracture (DC). The test is carried out in the following way: the patient is connected to a circuit of direct current fed by a 12 V source and the course of the skin reaction is registered by means of a cathode oscillograph. In all cases pathological findings were registered on both hands, i.e. even on the hand not affected by DC. We, therefore, assume that it is neither a secondary change caused by the nerves being compressed within the thickened palmar aponeurosis, nor a change produced by the operation. Our findings bear witness to the presence of primary inadequate or abnormal trophic innervation in both hands, and that this change is not quite dependent on the stage of DC. In the initial stages of DC or in the absence of clinical signs, we found high and steep curves characteristic for trophic lesions. These were the findings in 16 patients. In the remaining ten, the curves were markedly low and shallow as in peripheral lesions. In these cases DC was always bilateral and the aponeurosis severely changed.

Since in addition to other facts, dermatophoria is also affected by the blood supply and perspiration of the skin, these findings indicate that the function of the trophic nerves is affected at a time when DC is clinicall, not yet manifest, e.g. in the unaffected hand of patients with unilateral DC. Later, when the contracting palmar aponeurosis causes mechanical compression of the branches of peripheral nerves, the picture is that of a typical peripheral lesion.

SKIN TEMPERATURE

Another accessible method of investigation by which it is possible to obtain a picture of the peripheral trophic innervation, is that of measuring the skin temperature. We took the skin temperature with the thermocouple apparatus MAB made by Elektrolaboriet, Copenhagen, in 25 patients with DC. We measured

eight points on both upper extremities and endeavoured to maintain standard conditions. We took the measurements after the patients had become adapted to room temperature which ranged between 17^0 and 21^0 C, and always at the same time of day. We compared the absolute values with those given by Talbot, White and Smithwick. From this it followed that six patients showed a considerable difference between the temperatures of the shoulder and the hand, i.e. of more than 12^0 C, which is charactristic for vasospasm in the hand. In nine patients this difference was small and in five the temperature in the periphery was higher than that of the shoulder. Ten patients showed temperatures which could be considered normal in a wide range of the norm. We were unable to find any connection between the clinical picture and the absolute values of skin temperature. Comparing the temperatures taken on the left and right upper extremities in 17 patients we found the difference less than 2^0 C. It has generally been admitted that a difference of only two degrees does not indicate a pathological condition. In eight patients this difference was greater and reached up to 8^0 C. In correlating these findings with the clinical picture we found that the temperature in hands operated on for DC was lower. In the late stages of the disease with considerable contractures, the more affected hand always showed a lower skin temperature. In one case with an initial stage of DC, however, the affected hand had a higher temperature. This difference in temperature between the two sides was only ascertained on the fingers, the palm and sometimes the dorsum of the hand; it was never found more proximally. The skin temperature depends on the blood supply to the periphery which is mainly governed by the sympathetic. Although the vascular reaction is very sensitive and there are many factors evoking it, the values of skin temperature as obtained in the majority of our patients are definitely pathological and bear witness to a lesion of peripheral trophic innervation in DC. The findings, however, do not permit differentiation between the various stages of the disease. Only the area of the hand was found to be affected by this asymmetry in skin temperature; the forearm and arm never showed any deviation. The changes in skin temperature do not exclude the possibility that they may be due to secondary changes in trophic innervation, just as it cannot be stated with certainly that a primary trophic disorder in itself could cause DC.

PERIPHERAL NERVE LESION

Based on clinical observations the origin of DC was repeatedly connected with a disorder of peripheral nerves. Some authors simply assumed a lesion of the ulnar nerve and explained the development of DC by an affection (or irritation) of its trophic fibres. The first to describe a bilateral lesion of the ulnar nerve with DC was Eulenburg; later, Laignel, Jahn and Coenen reported similar cases. It was frequently admitted that various pathological conditions affecting the anterior horns of the spinal cord also participate in the development of DC (Noica). Other authors (Jahn, Powers, quoted Skoog) described DC in patients with polyneuritis. Finally, there are authors to whom the explanation of DC as caused by a lesion of peripheral nerves, seems too simple. They assume

a more complicated pathological chain and to prove their point they refer to the following cases: Schaefer, for instance, saw DC developing after contusion of the shoulder joint and muscles and a lesion of the ulnar nerve. Ponzoni described DC developing in connection with humero-scapular periathritis. Hines referred to a patient with polyneuritis, Raynaud's syndrome and DC. Baliff described a case of polyneuritis with trophic changes and DC. On the whole, a combined sensory, motor and trophic lesion is considered probable. Interesting features were described by Reichel in a patient who after contusion of the ulnar nerve developed DC on the other hand. Skoog observed a patient with DC who complained of paraethesiae in the affected hand. These complaints ceased after removal of the aponeurosis and liberation of the peripheral nerve fibres.

In our series of cases we did not find any single case in which it would have been possible to prove a primary lesion of peripheral nerves in the hand. Neither could we detect any definite sensory lesion in the area of the forearm or arm. The innervation and function of the forearm was always normal. We observed, however, atrophy of the interosseal muscles and in 17 cases we found affected movements of the muscles of the antithenar together with a slight atrophy in the thenar and the interosseal muscles. In these cases it was not always possible to explain the muscle weakness only by the mechanical obstacle caused by the contracting aponeurosis. We observed sensory lesions on the little finger in 95% of patients after operation; in three (5%) we found it already prior to operation. Eight patients had clinical signs of humero-scapular periarthritis on the side affected by DC with limited shoulder movements, slight atrophy of the deltoid muscle and tenderness on pressure at its insertion. In these eight patients the signs and symptoms of periarthritis were more severe on the side less affected with DC. These eight cases were differentiated from those with trophic syndromes as described previously in trophic disorders. We have also studied anew the material of 60 glass-blowers with established isolated lesions of the ulnar nerve (Kvíčala) and searched for signs of contracture in the palmar aponeurosis. We only found an indication of thickening in four cases (6.6%) which represents a minimal concurrence.

CHRONAXIMETRY

Measurements of chronaxie were taken in 25 patients with DC. We tested the flexor digitorum sublimis et profundus, the extensor digitorum longus and brevis, the opponens pollicis and the abductor digiti quinti. The measurements were taken by the chronaximeter Flag, type 218, made by Leichti, Berne and carried out by assistants Stein and Jindrová. In four patients the findings were normal, in six the anodal rheobase was raised, in one the cathodal, in three both. In six cases chronaxie was lengthened. Six patients showed a compensated difference between antagonists. Slight to marked reaction of degeneration was found in five cases. 78% of all pathological findings were registered in the muscles of the hand, 12% also in the muscles of the forearm. In four patients the pathological findings were registered in the muscles of the hand which

did not show any signs of DC. From these chronaximetric measurements it may, therefore, be concluded that in the majority of cases there was a mixed lesion of the peripheral motor neuron and that also signs were found of a lesion in the muscles investigated and in the extrapyramidal system.

ELECTROMYOGRAPHY

The electromyography examinations were carried out with a bipolar needle electrode. The bioelectric activity of muscles was registered by photographing the oscillation directly from the screen of the oscilloscope after amplification with a four-degree symmetrical amplifier. We studied activity at rest during relaxation, the insertion activity, the reaction on passive stretching of the muscle and the electromyogram during gradation of voluntary contractions. Using the standard method we investigated the small muscles of the hand: abductor digiti quinti and opponens pollicis. A total of 20 patients with DC, 16 men and 4 women aged between 35 and 72 years and with the disorder lasting from 2 to 17 years, were tested. The electromyographic findings can be summed up as follows:

1. cases with a normal basic EMG (4 cases). In two of these we still found slight signs of disturbance in gradation of contraction (imperfect interference activity with a tendency towards forming groups of action potentials of motor units).

2. a group of six cases with EMG typical for a lesion of the peripheral motor neuron. This picture remained stable in three patients with DC not operated on as well as in the other three who investigated two to five years after operation. During gradation of contraction, we found single action potentials of motor units up to a maximally transitory stage of the action potential whose amplitude was lowered (around 800 micro V with a duration of 7—10 msec and a low frequency). Both in the early and late stages of the disease we observed manifestations which may be regarded as the reflexion of an increased excitability in the area of the motor nerve endings, the membranes and muscle fibres or the myelinized terminations of the peripheral motor neuron. In none of our patients did we meet with fasciculation, fibrillation or insertion action potentials.

3. a group of four cases with DC whose EMG specifically indicated a lesion of muscle fibres and another group of six cases with additional findings typical for a slight lesion of the innervating motor neuron. The EMG showed a lowered voltage of the action potentials down to 200 mV with a maximum up to 600 mV, polyphasic units 3—9 msec. and numerous very narrow, spiky and monophasic potentials. Action potentials of a 5—7 msec mean duration, biphasic and triphasic potentials were registered but occasionally; more often group potentials. All subjects in whom EMG was typical for lesions of the peripheral motor neuron, were cases of clinically simple DC of an ulnar type. On clinical examination, a fibrous band was found on the ulnar side of the little finger and the palm in addition to the typical picture of the contractures in the palm, as was described by Karfík. According to his anatomical analysis,

a fibrous band runs from the gap between the bellies of abductor digiti quinti and flexor digiti quinti brevis into the subcutaneous tissue and compresses the ulnar branch of the arterial palmar arch supplying the little finger and the ulnar branch of the nerve. At this site the palmar fascia approaching the ulnar border of the palm lies close to the fascia of both muscles thus forming a sort of septum which includes the above neurovascular bundle. It may, therefore, be admitted that proliferation of the fibrous system with contracture and thickening could directly lead to compression of the nerve bundle and thus first to a functional and later to an anatomical and irreversible disorder of the fibres of this nerve bundle. This explanation is also borne out by the fact that although changes were found in the entire palmar aponeurosis in our patients with this type of DC we did not find any changes of electrical activity in the opponens pollicis which is innervated by the median nerve.

EMG pictures typical for an affection of the muscle itself, though occasionally combined with the signs of a lesion of the peripheral neuron, were found in cases of complicated DC. These are cases with clinically more advanced and severe affection of the palmar aponeurosis and contractures of more or all fingers. In cases of this type in which the process has been developing for a considerable time, secondary ankylosing fibrous changes take place in the motor system of the palm with contracture a tightening of the hand muscles, the tendon sheaths and joint capsules which themselves have a secondary trophic influence on the small muscles and the supplying motor branches of both nerves of the palm. Here the EMG findings were similar in the abductor digiti quinti and the opponens pollicis. A lesion chiefly of the muscle itself or a combination of this with a lesion of the peripheral motor neuron may be explained by a varied degree of development of DC and the topography of the fibrous changes in each individual case which then lead to anatomico-functional disorders in the neuro-muscular structure of the palm. Group 1 of our series are patients with a palmar type of DC with minimal changes, i.e. without contractures of fingers, with the aponeurosis thickened in the flexion groove of the fourth finger and only occasionally with a slight indication of contracture of this digit. In one case with a so-called desmogenic contracture of the little finger, we found an absolutely normal EMG picture. This — although only a single case — is proof of the already generally accepted opinion that this disorder represents a different kind of affection of the collagenous system of the hand than that of ordinary clinical DC.

DISCUSSION

In our series of patients we met with numerous neurological signs on clinical examination and many auxilliary tests were positive. In order not to give way to forcible and distorting attempts at connecting these findings with the origin of DC and to be able to take a critical view with certain justification of previous papers dealing with the etiology of DC from this aspect, we must base our considerations on the following:

DC is a frequent (and becoming still more frequent) disorder mainly of the older age groups, and from this it follows that neurogenic disorders can be quite accidentally associated with it.

Progressive DC can lead to secondary neurogenic changes (locally nerve fibres can be compressed, the muscles can atrophy through lack of activity, the unnatural manner of using the hand can cause even remote changes).

Our findings do not indicate that a cerebral or spinal disorder by itself can cause DC. In particular, it should be said that *we were unable to prove any connection with epilepsy clinically or by electroencephalography.*

We did find *unusually often,* however, *disorders of the intervertebral disc and osteoarthritis in the cervical spine.* The opinion, though rather disputable, may therefore be expressed that these changes are primary and somehow associated with the origin of DC or that they are secondary, developing due to the patient's unusually loading the structures of the shoulder girdle on the side of the affected hand, his incoordinated movements and the thereby asymmetrical loading of the cervical vertebrae and intervertebral discs leading to degenerative processes.

In accordance with the stage of DC, we found a series of changes in the EMG and of chronaxie. Much depends on how the contracting aponeurosis affects the nerve fibres or the muscles of the hand. This, sometimes, also explains the manifold trophic symptomatology. We are, however, unable to explain *the frequent occurrence and the nature of some trophic changes* otherwise than *by their being present prior to DC becoming manifest.* We have in mind particularly the frequent finding of the trophic Froment-Babinski syndrome not only at the periphery but also in the arm and shoulder, and also the trophic tests showing changes remote from the affected hand and on the side of the unaffected hand. EMG and chronaxie, too sometimes gave pathological findings in the clinically unaffected extremity. It is, however, quite impossible to connect the origin of DC with a lesion of any known specific or non-specific tracts or centres, not to mention an etiological relationship of DC with any disease of the central or peripheral nervous system as was occasionally done in the literature. We are also aware of the fact that we have found other features apart from lesions of the nervous system or directly connected with it, such as hereditary factors or the more frequent incidence in men, and we therefore consider the search for the etiology of DC only in the region of the trophic nervous system as a harmful simplification of the whole problem.

The practical conclusion drawn from our findings is the cognizance that the hand and the entire upper extremity of patients with DC is *trophically vulnerable* and that every *mechanical trauma* may cause a severe vegetative reaction to pain and thus contribute its part to the causes of the chain of events leading to manifestation of DC.

Preoperative preparation of the hand, the operation itself and postoperative immobilization and particularly rehabilitation must be carried out very carefully indeed in order not to worsen the already pathologically altered trophic nervous system so as not to bring about a functional and later also anatomical impair-

ment of the condition of the operated hand and also to avoid recurrence of DC. In addition, our investigation showed that apart from local mechanical changes in the palmar aponeurosis a kaleidoscope of changes takes place in the adjacent muscles, bones and skin which may be the source of complaints on the part of the patient not only prior to but also after successful operation.

SUMMARY

The authors dealt with the question as to whether and to what degree a disorder of the nervous system plays a part in the development of Dupuytren's contracture (DC). For this purpose they investigated 140 patients with DC carrying out clinical examinations of all subjects, and in various groups of patients EEG, EMG, chronaximetry, skin conductivity tests, measurements of skin temperature, some trophic tests and radiography of the cervical spine. They did not disclose any connection with diseases of the brain and the spinal cord and particularly could not prove any association with epilepsy. A great many of their patients showed gross changes in the cervical spine. Frequently, too, changes in the EMG, chronaxie, dermatophoria and the skin temperature were registered. Sometimes these changes had a character of a lesion of the peripheral motor neuron, at other times they indicated a lesion of the muscles. Most frequently, however, these changes were of the nature of a trophic disorder which was also very often found clinically. Some peripheral changes can be explained as being the consequence of a muscle and nerve lesion taking place in the close vicinity of the contracting aponeurosis. Some patients, however, showed changes which were in no parallel with the degree of contracture. These were also found elsewhere on the upper extremity and even in the hand not affected by DC, which indicates that they precede the actual manifestation of DC. The trophic changes thus ascertained may have taken their origin more proximally, i.e. at sites where the trophic nervous system is still united in centres common to both upper extremities which may indicate that DC is etiologically associated with a lesion of the higher vegetative centres.

The discussion also refers to some therapeutic conclusions emerging from these findings.

RÉSUMÉ

L'étiologie neurogène de la maladie de Dupuytren

V. Kvícala, J. Odvárková, J. Sedláček, J. Vacek

Nous nous sommes posés la question si et en quelle mésure les troubles du système nerveux participent à l'éclosion de la maladie de Dupuytren. Dans ce but, nous avons examiné cliniquement 140 malades atteints de cette maladie; dans chaque groupe des malades, nous avons réalisé les examens de l'EEG, de l'EMG, de la chronaximétrie, de la conductibilité cutanée, de la température cutanée, quelques épreuves végétatives et des radiographies des vertèbres cervicales. Nous n'avons pu constater aucun rapport avec les maladies cérébrales et de la moelle épinière. Tout spécialement nous n'avons pas été en mésure de confirmer les rapports avec l'épilepsie. Une grande partie de nos malades présentaient des altérations considérables des vertèbres cervicales. Nous avons

également constaté très fréquemment des altérations de l'EMG et de la chronaxie, ainsi que lors de l'examen de la dermatophorie et de la thermométrie. Elles présentaient parfois le caractère de lésions des neurons motoriques, parfois elles accusaient une atteinte de la musculature, mais le plus souvent elles présentaient le caractère des altérations lors des troubles végétatifs que nous avons souvent constatées également cliniquement. Quelques unes des altérations périphériques peuvent s'expliquer en tant que conséquences de la lésion des muscles et des nerfs dans le voisinage immédiat de l'aponévrose crispée. Toutefois, chez certains malades, les altérations n'étaient pas en rapport avec le degré de la contracture; on les rencontrait également en d'autres endroits de l'extrémité supérieure et dans la main qui n'était pas touchée de contractures, ce qui témoigne du fait qu'elles précédaient le départ de la maladie. Les troubles végétatifs constatés pourraient avoir leurs origines dans une région plus proximale, dans les endroits où les nerfs végétatifs se trouvent encore concentrés en commun pour les deux extrémités supérieures et témoigner ainsi en faveur du fait que la maladie de Dupuytren représente des rapports étiologiques avec une lésion des centres végétatifs supérieurs.

On discute également quelques conclusions thérapeutiques qui résultent des faits observés.

ZUSAMMENFASSUNG

Die neurogene Aetiologie der Dupuytrenschen Kontraktur

V. Kvíčala, J. Odvárková, J. Sedláček, J. Vacek

Wir hatten uns die Frage gestellt, ob und in welchem Ausmass eine Störung des Nervensystem an der Entstehung der Dupuytrenschen Kontraktur beteiligt ist. Zu diesem Zwecke untersuchten wir 140 Patienten mit Dupuytrenscher Kontraktur klinisch; bei jeder Patientengruppe untersuchten wir das Elektroenzephalogramm, das Elektromyogramm, die Chronaximetrie, die Leitfähigheit der Haut, die Hauttemperatur, einige vegetative Tests und die Roentgenbilder der Halswirbelsäule. Ein Zusammenhang der Dupuytrenschen Kontraktur mit Erkrankungen des Gehirns oder des Rückenmarks konnte nicht festgestellt werden, insbesondere konnte auch ein Zusammenhang mit Epilepsie nicht bestätigt werden. Ein Grossteil unserer Patienten wies grobe Veränderungen der Halswirbelsäule auf. Ferner wurden sehr häufig Veränderungen des Elektromyogramms und der Chronaximetrie sowie Abweichungen bei der Untersuchung der Dermatoforie und der Thermometrie vorgefunden. Diese Veränderungen wiesen manchmal den Charakter einer Läsion des Motoneurons auf, deuteten in anderen Fällen auf eine Muskelschädigung hin, besonders häufig jedoch hatten sie den Charakter von Veränderungen, wie sie vegetative Störungen begleiten, die wir auch klinisch sehr oft feststellen konnten. Manche periphere Veränderungen können als Folge einer Muskel- und Nervenschädigung in unmittelbarer Nachbarschaft der sich retrahierenden Aponeurose angesehen werden. Bei manchen Patienten waren jedoch die Veränderungen unabhängig vom Grade der Kontraktur; sie konnten auch an anderen Stellen der oberen Extremität und ebenfalls an der von der Kontraktur nicht betroffenen Extremität vorgefunden werden, was darauf hinweist, dass sie der Entstehung der Krankheit vorangehen. Die festgestellten vegetativen Störungen könnten ihre Ursache weiter proximal haben, an den Stellen, wo das vegetative Nervensystem noch für beide obere Extremitäten gemeinsam verläuft, und können darauf hinweisen, dass die Dupuytrensche Kontraktur ätiologisch mit einer Störung höherer vegetativer Zentren zusammenhängt.

In der Diskussion werden auch einige therapeutische Schlussfolgerungen angeführt, die sich aus unseren Befunden ergeben.

RESUMEN

La etiología neurógena de la contractura de Dupuytren

V. Kvíčala, J. Odvárková, J. Sedláček, J. Vacek

En este papel los autores se ocupan del problema de la participación del desorden del sistema nérveo en el origen de la contractura de Dupuytren. Para este motivo han examinado 140 enfermos con esta enfermedad de manera clínica; en este grupo han llevado a cabo las examinaciones de EEG, EMG, conaximetría, la examinación de la conductibilidad cutánea, algunos testes vegetativos y las fotos radiográficas de la columna vertebral de cuello. Los autores dicen que no han hallado la conexión con las enfermedades del cerebro y de la médula espinal. Tampoco pudieron comprobar la conexión con la epilepsia en particular. En la mayoría de sus pacientes se aparecieron cambios importantes en la columna vertebral de cuello. Aparte de esto a menudo se hallaban cambios de EMG y en la cronaxia, durante la examinación de dermatoforia y en la termometría. Algunas veces tuvieron el carácter de una lesión de motoneurono, otras veces afectaron los músculos, pero especialmente a menudo aparecieron en los trastornos vegetativos los cuales los autores podían hallar fácilmente. No es posible explicar algunos cambios periféricos como consecuencia de la afección de los músculos y de los nervios en la cercanía inmédiata de la aponeurosis que se fruncia. En algunos pacientes los cambios fueron independientes del grado de la contractura; se hallaron también en otros lugares, en las extremidades superiores y también en la mano que no fue afectada por la contractura, lo que comprueba que los cambios preceden el origen de la enfermedad. Los trastornos vegetativos averiguados podrían tener la causa más proximal, en los lugares donde los nervios vegetativos están todavía concentrados juntamente para ambas extremidades superiores y así pueden comprobar el hecho que la contractura de Dupuytren tiene relación de manera etiológica con la lesión de los centros vegetativos superiores.

En la discusión los autores presentan también algunos resultados terapéuticos a base de sus hallazgos.

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COMPLICATIONS DURING ANAESTHESIA IN CHILDREN WITH HARE-LIP AND CLEFT PALATE

M. ŠTEINEROVÁ-HANUŠKOVÁ

General anaesthesia in operations for hare-lip and cleft palate is a routine procedure at all departments of plastic surgery. Ever since 1951, when the Clinic of Plastic Surgery in Bratislava was founded, endotracheal anaesthesia has been employed for these operations. The experience collected from this was published by Šteller already in 1955 (1). In this paper we wish to report our experiences with endotracheal anaesthesia in more than 700 operations on children with hare-lip and cleft palate and point out the changes we have introduced in our methods as well as the complications we have met with and which are particularly instructive.

Infants are premedicated with atropine. However, we do not give atropine to children suffering from cardiac disorders with tachycardia. In one patient, D. G., a one-year-old child (case paper 3073), in whom a systolic murmur had already been found after birth, we observed tachycardia after premedication with atropine; the pulse rate rose to above 200/min., and we had to postpone the operation.

Children older than one year are given atropine together with an appropriate dose of Dolsin or a phenothiazine derivative. We should like to point out that the danger of overdosing premedication drugs is usually overestimated for children in good general condition. One of our patients, three-year-old Š. A. (case paper 349) received a full adult dose of the lytic cocktail M_1 by mistake. Apart from tachycardia (about 160/min), lasting for three hours and several hours of sleep, no striking signs of respiratory or circulatory depression could be observed.

Since 1956 we have used a 10% solution of Thiopental per rectum for basal anaesthesia in infants and small children, instead of the toxic Avertin which we had used previously. In our series there were two cases with complications after Avertin. In the first case a marked allergic reaction developed with exanthema lasting for several hours; in the second, cardio-respiratory depression occurred due to a large overdosage (a dose for a child weighing 10 kg. more) given by mistake. We succeeded in overcoming this by intubation, controlled respiration and noradrenalin infusion.

With Thiopental basal anaesthesia no complications have been encountered, although it must be said that in some cases we were not entirely satisfied. These were chiefly patients who had been given an enema prior to operation or those with an irritable intestinal tract and a history of frequent diarrhoea.

Since 1960, we have induced small children only with Fluothane given in a semi-closed circuit with the Boyle apparatus (chloroform vaporizer) or by the modified N-42 set. A minimum of Fluothane is needed; 10 ml. suffice to induce anaesthesia in 20 children. The infant, inhibited by premedication and the basal anaesthetic, passes into the surgical stage of narcosis after 5—8 inspirations, without signs of excitation; afterwards intubation is quite easy.

For the induction of older children (over 5) we use Thiopental plus Procuran intravenously.

During anaesthesia proper we give oxygen, ether or nitrous oxide and Fluothane. We do not use ether in children with a history of repeated affections of the respiratory system (pneumonia) because in these patients we have observed a higher incidence of post-operative pulmonary complications after ether anaesthesia. We, therefore, give nitrous oxide or Fluothane.

As to the technique of anaesthesia in infants, we use the Ayre system; in older children the semi-closed, one-way system. All children are intubated.

Old, kinking tubes frequently caused trouble and had to be replaced by firmer ones during operation. Old and loose tubes, too, sometimes got disconnected from the Cobb joint and slipped deeper into the trachea. In one case, J. Č., a five-month old child (case paper 1624), this caused a serious situation when, soon after intubation, the disconnected tube slipped down and passed the glottis into the right bronchus. We did not succeed in removing it with a Magill's forceps; on the contrary, we pushed it deeper and the child started to become cyanotic. The proper manoeuvre proved to be lifting the child by its feet head downwards, when the tube slipped out by itself.

When inserting the speculum, breathing must be checked to make sure that the mouth gag does not compress the tube.

Laryngospasm was observed in three cases during induction when the ether or Fluothane vaporizer was opened too suddenly. It sufficed, however, to compress the thorax slightly and the vocal cords moved apart so that the intubation could be carried out easily.

Bronchospasm was met with once in a two-year-old child (L. B., case paper 2898) with congenital bronchial asthma. We succeeded in controlling the acute condition by the administration of succinylcholine and atropine and the application of artificial respiration through the tube at a pressure of a 10 cm. water column. Even during the post-operative period serious asthmatic paroxysms repeatedly developed leading to dyspnoea, cyanosis and even to respiratory arrest. The anaesthetic unit had to be kept on hand all the time. Today, in such a case, we would give high doses of corticoids (2).

Another child, L. B., aged three (case paper 4641), with congenital laryngeal stridor, surprisingly showed no post-operative respiratory complications.

In seven children difficult breathing with a slight stridor was observed one to two days after operation. Except for two cases, respiration soon returned to normal after intensive conservative treatment. The trigger provoking post-operative stridor is either the trauma during intubation (an unsuitable tube, the "heavy hand" of the anaesthetist) or an infection introduced into the air ways by an unsterile tube. We have to bear in mind that small children are particularly prone to develop oedema, even of the subglottis.

We had two cases of oedema of the subglottis, one with a lethal outcome.

The first patient, J. M., aged five (case paper 1095), had been operated on at our Clinic twice previously for hare-lip during infancy and did not develop any complications. At the age of five he was operated on for cleft palate. Eight hours after operation the tongue became oedematous, but the breathing remained unaffected. The next day, at 7 a. m., the child was restless and breathing with a marked stridor. The temperature was 38.2° C, the pharynx showed oedema, particularly on the left side, and the tongue was swollen. We administered Sandosten, vitamin C and antibiotics by inhalation, and placed the patient into a moist atmosphere. When at rest, the child breathed freely but when crying, a marked stridor developed. Despite repeated administration of Sandosten and inhalations, the tongue became more and more swollen. Because of the distinct inspiratory stridor and the barking cough, tracheotomy had to be performed at 2 p. m. After that the condition rapidly improved and the oedema of the tongue receded. The tracheal tube could be removed four days later. In this case narrowing of the air ways developed most probably, due to oedema of the lower part of the pharynx or the subglottis following intubation. In the forefront stood the trauma during intubation; less conspicuous in this case was the part played by infection.

The second patient, F. K., aged two (case paper 1544), was operated on at 8.30 a.m.; a four-flap plasty of the palate was performed. During the operation a transfusion of 180 ml. blood of the same group was given. In the evening, at 10 p.m., slight stridor was registered; the temperature went up to 38.5° C. As a prevention of oedema Sandosten and antibiotics were given and a special nurse assigned to the child for the night. The next day the stridor increased, the auxilliary muscles came into play during respiration and the jugular region was sucked in on inspiration. Auscultation of the lungs revealed sharp breathing with rales. The pulse rate was 180/min., the temperature 39.5° C. Streptomycin, Phenergan, Calcium gluc. and oxygen were given. Because the condition deteriorated, tracheotomy was performed at 11 a.m. The condition improved, respiration became normal, but the pulse rate remained 180/min. The child started to be restless, tossed about in his sleep and again became asthmatic and cyanotic. The pulse rate rose to 200/min. and the temperature to 40° C. The child was given a tepid sponge, M_2 lytic cocktail and oxygen. At 7 p. m., while the breathing remained laboured and the pulse rate high, the pulse became irregular and the heart sounds weaker. Application of suction to the trachea was followed by long periods of apnoea and cyanosis. At 10 p. m. respiration and heart beats stopped.

On post mortem massive bronchopneumonia was found on the right side.

Conclusion: It seems that in this case acute infection stood in the forefront of the clinical picture and tracheotomy did not suffice to control the severe condition. Even after tracheotomy the child was unable to ventilate his lungs effectively and the respiratory effort surpassed its strength. Bronchoscopic toilet of the air ways and application of an automatic respirator could, perhaps, have saved the child's life by diminishing the respiratory effort and thus bridging the most dangerous stage, i. e. up to the time when the antibiotics would have started to take effect.

Important also is the position of the patient. It is known that excessive Trendelenburg position impedes respiratory movements and predisposes to the development of post-operative atelectasis in the non-ventilated parts of the lungs. It also ought to be pointed out that in an anaesthetized child the cervical spine is easily hyperextended. In our patient, V. K., a girl of 10 (case paper . . .), with a "short palate", pharyngofixation was performed. During the post-operative period the child held her head markedly stiff and complained of pain in the cervical spine. X-ray and neurological examination confirmed the diagnosis of cervical spondylarthritis.

Two children died during the anaesthetic due to hypoxia.

First patient, Z. M., a girl of 2 (case paper 87), had been operated on previously in 1951. From the case history only slight anaemia was of interest. About one hour after the start of the operation respiration became shallow and weak and the pulse filiform. Artificial respiration with positive pressure, using pure oxygen was started instantly and a blood transfusion of the same group given, but in spite of this, cardiac arrest soon set in. Noradrenalin administered intracardially remained without effect. No post mortem was carried out.

Conclusion: It seems that in this case hypoxic anaesthesia (too little oxygen and too much ether) was combined with haemorrhagic shock. These two dangerous conditions, of coinciding during the anaesthetic, are the most frequent causes of sudden death in children.

Second patient, J. T., a boy 5 months old (case paper 3663), with a double cleft, had been first operated at the age of 3 months on one side without complications. He was now operated on on the other side. The course of the anaesthetic was uneventful. Only towards the end of the operation respiration became rattling, the colour cyanotic and the pulse arrythmic. Assuming that blood had entered the trachea, we started to apply vigorous suction to the tracheal tube, and while this was proceeding cardiac arrest set in. Instant controlled respiration with the anaesthetic unit, massage of the heart, noradrenalin given intracardially did not renew heart action. Post mortem revealed cerebral oedema.

Conclusion: We assume that suction applied to the tube for a considerable time increased hypoxia and thus provoked heart failure. During the operation care must be taken to prevent aspiration of blood by repeated application of suction. If, in spite of this, respiration should become rattling because blood has entered the tube, the latter must be immediately disconnected from the anaesthetic unit and suction applied through it, both with care and for short periods.

We wish to stress in particular the efficacy of methods of artificial respiration and heart massage carried out from outside for the resuscitation of small children (3, 4). In our patient, I. S., a girl aged 8 months (care paper 6577), with hare-lip, sudden respiratory and cardiac arrest occurred on accidental extraction of the tube from the trachea while the patient was being taken to the ward in the elevator. By immediate application of mouth-to-nose artificial respiration and rhythmic compression of the sternum, we succeeded — after ten maneouvres — in renewing audible heart sounds and soon afterwards also spontaneous breathing. The child recovered from this accident without after-effects.

It is imperative that not only doctors but also nurses at every hospital should master this life-saving "external" method of resuscitation.

In conclusion the importance of preoperative treatment in children with congenital heart defects should be pointed out. Congenital heart defects may be found together with cleft anomalies. These children tolerate any anaesthesia badly and large statistics show a mortality rate on operation as much as 70% in patients up to one year of age (5). If the haemodynamic conditions are greatly affected by this defect, most surgeons warn against operating at an early age; operation ought to be decided upon only for vital indications.

In our Clinic quite a number of children have been treated who had both cleft anomalies and congenital heart defects (6).

In our patient, M. D., a boy aged 3 months (case paper 1925), with congenital mitral stenosis, the anaesthetist noted from the case history that the child had sometimes turned blue, particularly after feeding, with indrawing of the intercostal spaces. At 2 months he had had pneumonia. The operation for hare-lip was performed after a two-week preparation with strophantine, and although the anaesthetic was uneventful, bronchitis developed in the postoperative period.

Another three of our patients with congenital heart defects developed an apnoic pause during the induction and turned blue very fast. In two of them bronchopneumonia developed in the postoperative period. These were infants aged 3—5 months.

One case with congenital heart defect terminated fatally. In the patient A. J., a child aged 4 months (case paper 5112), suture of the lip by the Tennison method and reconstruction of the nasal floor was performed. From the very beginning of the operation the pulse rate was about 200/min. and respiration 60/min. Nitrous oxide was, therefore, shut off and only pure oxygen was given, but the pulse rate, nevertheless, rose to 230/min. Bleeding during the operation was negligible. 45 minutes after the start of the operation extrasystoles were registered. On putting in the last sutures, one hour after the start, cardiac and respiratory arrest supervened. Artificial respiration under positive pressure through the intratracheal tube, heart massage from outside and intracardially injected noradrenalin proved ineffective; heart action could not be renewed. Post mortem revealed a patent foramen ovale and stenosis of the pulmonary artery.

Conclusion: It seems that tachycardia and particularly extrasystoles were the warning signal in this child with a congenital heart defect. Heart failure took place because of the pathologically altered haemodynamic conditions.

SUMMARY

General anaesthesia has become a routine measure in operations for hare-lip and cleft palate in children. The most frequent complications occurring during anaesthesia in children operated on for hare-lip and cleft palate are analyzed on the base of the author's own experience. Errors in premedication, maintenance of anaesthesia and postoperative care are pointed out. In the conclusion the special problems arising from the combination of cleft anomalies with congenital heart defects are discussed.

RÉSUMÉ

Complications au cours de l'anesthésie chez des enfants avec bec-de-lièvre et la division palatine

M. Šteinerová-Hanušková

L'anesthésie endotrachéale est aujourd'hui couremment employée si l'on effectue des chiloplasties et des uranoplasties sur des enfants.

A base des expériences faites par l'auteur, on discute la problématique des complications les plus fréquentes qui se manifestent au cours de l'anesthésie des enfants atteints de cheiloschisis et de palatoschizis. Les erreurs possibles au cours de la médication préparatoire, pendant l'anesthésie et pendant le traitement post-opératoire sont soulignées. En conclusion, les problèmes spéciaux qui se présentent au cas d'une cardiopathie congénitale concomittante sont discutés.

ZUSAMMENFASSUNG

Komplikationen bei der Anaesthesie von Kindern mit Lippen- und Gaumenspalte

M. Šteinerová-Hanušková

Bei Operationen von Kindern mit Lippen- und Gaumenspalte ist die endotracheale Anaesthesie ein Routine-Eingriff.

In der Publikation werden auf Grund von eigenen Erfahrungen die Problematik der häufigsten Komplikationen bei der Anaesthesie von Kindern mit Lippen- und Gaumenspalte analysiert. Auf Fehler in der Praemedikation, Erhaltung der Narkose und postoperativen Pflege wird hingewiesen. Abschliessend werden Probleme von vergesellschafteten Herzfehlern besprochen.

RESUMEN

Complicaciones durante la anestesia de los niños con la fisura de labio y paladar

M. Šteinerová-Hanušková

En las operaciones de los niños con la fisura de labio y paladar hoy día se usa de manera corriente la anestesia endotraqueal.

A base de propias experiencias en este papel se analizan los problemas de las complicaciones más frecuentes durante la anestesia de los niños con la fissura de labio a de

paladar. La autora llama atención a las faltas hechas en la pre-medicación, en el mantenimiento de la anestesia durante el tratamiento postoperatorio. En la conclusión se habla de los problemas especiales que aparecen en caso de la afección cardíaca congénita asociada.

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NEW BOOKS

Rudolf Kós: **A kéz sebészete** (Surgery of the Hand). Published by Medicína könyvkiadó, Budapest 1961. 2,100 copies.

From an extensive knowledge of the literature and from his own experiences during ten years in a surgery and traumatology department and in cooperation with a big metallurgical works in Budapest, the author discusses the principles of surgical treatment of injuries and infections of the hand. He himself treated or examined 3,000 patients with injuries or other conditions of the hands.

The book is based on concepts of modern science, which regards the hand as an important sensory organ whose function must be restored. The author emphasizes the need for treatment by specialists with adequate experience of the complex problems of surgery of the hand, especially in the case of severe injuries and deep-seated, complicated infections. The patient ought to be put under the care of a specialist from the time of injury and remain in his care throughout the period of functional treatment until he returns to work, since that is the only way to ensure the desired result.

The book has 411 pages, 460 illustrations black-and-white and coloured) and is divided into six chapters. The references are given separately for each chapter at the end of the book, together with an index of books on surgery of the hand.

Chapter I deals with the development of surgery of the hand. During the First World War, 30% of injured hands were still amputated. During the Second World War, Bunnell laid the foundations for specialized surgery of the hand. After the war, special associations for surgery of the hand were formed in various countries.

Chapter II discusses the diagnostics of methods of operation and treatment. In this chapter the general diagnostics are discussed, while the detailed diagnosis is dealt with in connection with the individual injuries and infections of the hand. Emphasis is placed on the need for accurate records, which are provided by a special filing system. For photographic records the author uses a modification of Boyes' method. The instruments and suture material required for operations on the hand are described and illustrated,

together with the apparatuses and splints needed for treatment and rehabilitation. The principles of atraumatic technique are discussed in detail.

Injuries of the hand are described in chapter III. Primary reconstruction of the injured hand is recommended, as far as this is possible. The need for active prevention of oedema of the hand is stressed. The author clearly explains the surgical treatment of the various tissues of the hand and also the diagnosis. In the diagnosis of nerve injuries he uses the objective method of ninhydrin fingerprints, which he simplified himself for routine use. A brief account is given of foreign bodies, burns and frostbite of the hands, of delayed oedema and Sudeck's syndrome and of prevention and safety measures at work.

Chapter IV deals with infections of the hand. For nonspecific pyogenic infections on the volar surface, confined to the connective tissue, the author uses the term panaritia. The author uses a small blunt probe to localize the focus of infection. He does not use local anaesthesia and a penicillin block, in order to avoid pain and hence not lose the patient's confidence. The correct incisions for each type of infection of the hand are illustrated very clearly. The focus of infection can be removed only in a blood-free environment. In infections, however, blood must not be expressed from the hand before applying a tourniquet. Strict asepsis must also be observed. The author is opposed to soaking the hand after operation until the infection has been eradicated. Specific antibiotics are administered both systematically and by local instillation.

Only very brief mention is made of specific infections of the hand in this chapter.

Chapter V describes functional treatment of the hand. Therapy and rehabilitation should form a single unit, as achieved in the system of comprehensive functional therapy used in the U.S.S.R. Active, voluntary movement is commenced even before the dressings are removed. For active resisted movement of the individual joints of the fingers, a modification of Mayo's splint is used, for a passive adjacent finger, two fingers of a glove are sewn together. The author also gives a brief description of the gradual stretching of contractures ("Quengeln") as opposed to forcible correction ("redressement forcé"), which he rejects completely, and describes occupational therapy.

Chapter VI comprises six pages, four of which are illustrated, on evaluation of the degree of disablement of the hand.

A. Töröková

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