Section of Odontology

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Experimental Investigation Into Factors Concerning the Growth of Cysts of the Jaws

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INTRACYSTIC PRESSURE

THERE is much evidence to suggest that certain cysts increase in size by reason of the fluid tension within them. This was recognized early by the French and German surgeons after the discovery that opening a cyst into the mouth checked further growth and subsequently led to a decrease in size of the tumour. Cysts occurring between the roots of teeth cause these roots to be displaced apart as if by pressure (cases quoted by Potts, 1927). Another observation concerns the migration of teeth associated with dentigerous cysts. Included teeth are frequently found lying at relatively great distances from their sites of development. These occurrences are strongly suggestive of a pressure effect, since if the growth of the cyst had simply been due to the proliferation of tumour cells then it would be expected that the tooth would remain static in relation to the bone and the tumour would grow around and pass it.

An interesting point to notice is that teeth included in dentigerous cysts appear to be moved by forces acting on the crown and its epithelial attachment. Collected cases and reports of cases show that cementum is not exposed in a cyst cavity even when cysts are in long-standing contact with tooth roots. Slow absorption of roots sometimes occurs. These facts tend to argue that simple pressure largely effects the expansion of a cyst.

Warwick James (1926) was the first worker to investigate whether a true positive pressure existed within cysts. He made a number of interesting observations on the various factors possibly concerned with the ætiology of cysts and maintained that pressure was a very important factor affecting the growth of a mature cyst. He performed a number of experiments to determine intracystic pressure and he found that all his results showed higher pressure values than the known value for capillary pressure. He suggested that cysts showing higher pressure may display a more flattened appearance of the cells of their epithelial linings.

James also showed that intracystic pressure fluctuated slightly in accordance with the cardiac pulse, and he considered that this was accounted for by the normal pulsations in the capillary bed surrounding a cyst wall. He stated, however, that the methods he had at his disposal at that time prevented an accurate measurement of fluid pressure being made.

Experimental

It was considered that an investigation into cyst growth might well begin by an attempt to obtain accurate experimental data on the hydrostatic pressure within cyst cavities *in vivo*.

The first procedure was to study the various types of apparatus for pressure recording and to design an apparatus most suited to the problem under consideration. The pressure ranges likely to be encountered were known to be between 10 cm. and 100 cm. of water (James). A water manometer was selected as a suitable type of apparatus since it would enable a sufficiently extended scale of measurement to be used, which in practice provides an error of about 0·1%.

The disadvantage of this apparatus is that a manometer tube of at least one meter in length is needed, which is manageable in a laboratory but not in the ward or operating theatre. Mercury manometer or simple aneroid types were not considered sufficiently accurate although both have occasionally been used for the sake of convenience.

The size of the exploring cannula had to be selected carefully for several reasons: (*a*) The semi-fluid contents of some cysts tend to choke a narrow cannula; (*b*) a wide cannula has a lacerating effect on the tissue as it is inserted and a minute escape of fluid might result. A wide cannula would also have a disturbing effect on the volume of a small cyst, especially if it had to be passed through bone; (*c*) a narrow bore tube results in increasing the inertia of a hydrostatic system, by reason of the "drag effect" varying as a function of the diameter of the bore.

In a study of intracranial pressure O'Connell (1943) demonstrated an experiment to show that variations in pressure were imperfectly transmitted through a system which incorporated a ventricular cannula of 2 mm. internal diameter when the rate of variation was about that of the cardiac rhythm. When a lumbar-puncture needle of small bore was used (0·8 mm. bore) the inaccuracy was very pronounced, though slow variations (four variations per minute) can be recorded accurately through a system of such narrow bore. This consideration is only of importance when measuring variations of intracystic pressure with the cardiac pulse.

Manometer.—A simple direct manometer was not considered sufficiently accurate to measure intracystic pressure, owing to the fact that fluid must flow out from the cyst cavity in order to cause the manometer to register. This egress of fluid slightly reduced the volume of the fluid in the cavity and consequently the pressure within the cavity diminishes, so the final reading is not strictly true. This error is most important when examining small cysts completely surrounded by bone.

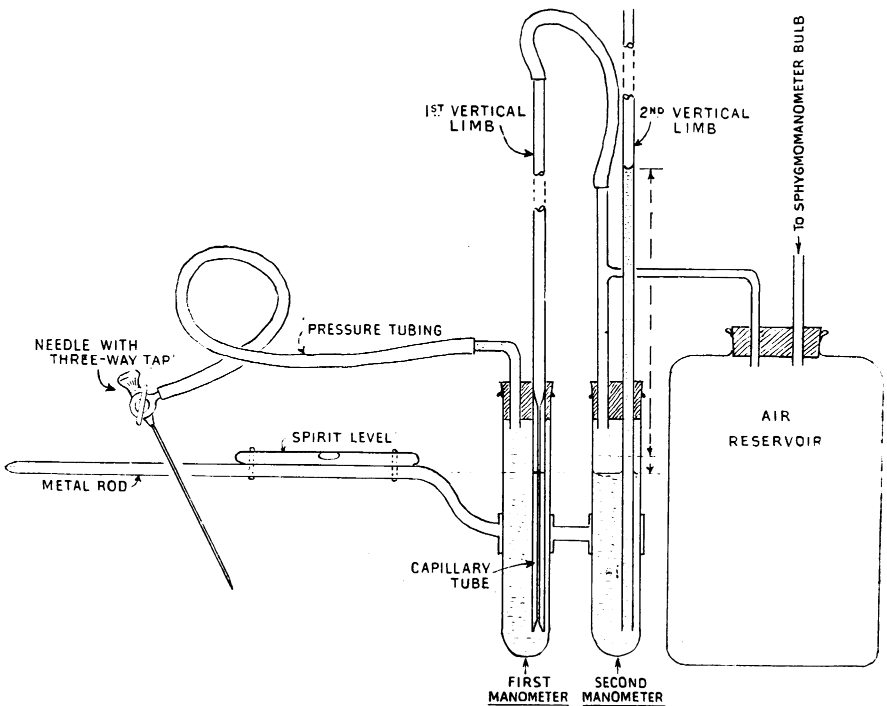

FIG. 1.—Manometer for measuring intracystic pressure.

A method was evolved in which the final reading was of that pressure required to prevent egress of fluid from the cyst. This method of applying counter-pressure effectively overcomes the tendency to inaccurate recording which might be due to blockage of the cannula by the semi-solid nature of the cyst fluid.

Description of apparatus.—A Greenfield's pattern spinal cannula is connected by 12 in. of narrow pressure tubing to the reservoir of the first manometer. The vertical limb of this manometer is made so that it is of very narrow bore in its lower part. This capillary portion is provided with a fixed mark. The level of this mark is made to correspond exactly to the vertical height of the tip of a horizontal rod which is fixed rigidly to the manometer. A spirit level is fixed to this rod. (Error would be introduced if there was a difference in vertical height between the manometer and the cyst cavity, owing to a siphon effect (fig. 1).)

The upper end of the vertical limb is connected by rubber tubing to an enclosed space above the reservoir of a second manometer. This space is also connected to a sphygmomanometer bulb, an air reservoir of at least 500 c.c. being included in the system in order that even pressure variations can be exerted by the rubber bulb.

Operation.—A sterile technique is adopted when using the apparatus, the cannula and pressure tubing being boiled and filled with sterile water.

The apparatus is held next to the patient at the level of the cyst, reference being made to the spirit level provided on the horizontal arm.

The cannula is first introduced into the cyst cavity with its tap in the closed position, and held to cause as little tension on the surrounding tissues as possible. The tap is then turned to connect the cyst cavity with the first manometer. Intracystic pressure will cause water to rise in the limb of the manometer. Air pressure is then applied to the surface of the water in this limb until the water is returned to, and maintained at, its original level. The air pressure needed to prevent egress of fluid from the cyst cavity is then noted by recording the water levels in the second manometer.

This reading represents the hydrostatic pressure within the cyst. Correction can be made for the volume of the portion of cannula which is inserted within the cyst cavity.

SUMMARY OF INTRACYSTIC PRESSURES FOUND IN A SERIES

Dental cysts

Highest recorded pressure	95·0 cm. water
Lowest recorded pressure	56·6 cm. water
Average pressure in 51 cases (to nearest whole number)	70 cm. water

Dentigerous cysts

Highest recorded pressure	94·7 cm. water
Lowest recorded pressure	22·5 cm. water
Average pressure in 9 cases (to nearest whole number)	65 cm. water

Adamantinoma

3 cases (1) 10·0 cm. water
(2) 12·0 cm. water
(3) 8·5 cm. water

Developmental cyst—premaxilla

One case—Recorded pressure—87·5 cm. water

This series of cases is too small to draw any significant conclusions, but the following points were noted:

(1) The intracystic pressures fall within similar limits, whether the cyst, either dental or dentigerous, was large or small, or whether the patient was young or old.

(2) Similar pressures were recorded in dental and dentigerous cysts.

(3) The pressures in the three adamantinomata were much lower than those found in other types of cyst.

Variation of Cyst Pressure with Cardiac Pulse

It was noticed in several cases that the water level in the first manometer varied slightly with the cardiac pulse. Using a cannula and capillary tube of much larger diameter than usual in order to reduce the fluid inertia of the system, an attempt was made to assess the intracystic pressure differences due to the cardiac pulse.

Fluctuations in the first manometer limb were observed and readings were taken of the counter-pressure required to return the fluid level: (1) To the original level at maximum displacement of the fluid column; (2) to the level at minimum displacement.

In the three cases tested, the average pressure difference between the displacement levels was 4·5 cm. water. This figure will be inaccurate, erring on the low side of the true figure, owing to the inherently high fluid inertia of the system when recording such relatively rapid changes of pressure.

DISCUSSION

The foregoing experiments serve to confirm that positive fluid pressure exists within cystic cavities. The pressures recorded are all above capillary blood-pressure which Hill gives as about 3·5 cm. of water. (Starling states that capillary pressure can often be as high as 10 cm. water.)

It is obvious that if this full intracystic pressure was exerted upon the surrounding capillary bed, the walls of the capillaries would collapse resulting in cessation of the local circulation of blood. There may in fact be a slight compression of the surrounding capillaries, producing a slight ischæmia. This may be a factor in the pressure atrophy of the surrounding bone.

In some cysts it is possible to find degenerating cells close to a capillary. Such cases are not easy to explain on the grounds that the degeneration is caused by the cells being too far removed from a blood supply unless that blood supply itself is inadequate. Local ischæmia due to abnormal pressure of the cyst may hasten the degeneration of the cells of a cyst lining.

It is likely, however, that the main bulk of the cystic pressure is borne by its own epithelial and fibrous walls, in a similar manner to the way in which blood-vessels carry a positive pressure.

Those studying pathology in relation to the orthodontic traction state that the pressures used in orthodontic appliances must not cause a tooth to apply a pressure on its surrounding structures more than capillary pressure, otherwise necrosis of bone may result instead of physiological absorption. Necrosis of bone is not observed in relation to cyst growth. It would seem that the actual expansive pressure that the cyst exerts on the surrounding tissues is likely to be very small, i.e. below 3·5 cm. water.

Intracystic pressures which have been recorded can be considered as high in comparison with capillary blood-pressure; they are comparable to pressures found in arterioles. The only arteries of any large size that are found in relation to cysts of the jaws are the inferior dental vessels and sometimes a fairly large vessel is encountered on the deep posterior aspect of maxillary cysts.

No opportunity has yet presented itself for the study of pressure in enclosed hæmatomata. No "bone cysts" have been investigated, although this type of fluid collection will be studied if the opportunity arises, since it may lead to a better knowledge of the pressures that may be expected in passive fluid collections in the tissues. Such study would provide a clearer idea of the part played by simple hydrostatic effects (i.e. the pressures due to blood-pressure, muscle-tone, posture) or cyst pressure.

The positive pressure remains much the same whether the cyst is small or large, in fact this pressure is maintained even when the cyst wall is just beneath the surface of the oral or nasal mucous membrane. An investigation was therefore carried out to determine whether there were other than purely hydrostatic factors maintaining the positive pressure.

The Osmotic Factor

It has seemed most likely that the factor causing the pressure within a cyst to be raised above the pressure of the surrounding tissues would be a difference in osmotic tension. This was suggested by James (1926) and has been mentioned from time to time since he published his experiments in connexion with cysts. Thoma mentions that it is possible that osmosis maintains intracystic pressure, and in 1939 Tratman wrote a paper suggesting that diffusion of fluids influenced cyst growth. In fact, he appears to have performed the only experimental work in the dental field to verify this theory. His experiments consisted of aspirating the contents of four cysts and observing that at the end of twenty-four hours the cyst cavities had again become distended with fluid. This interesting observation, which he recorded with care, suggests that the refilling of the cysts occurred by osmosis. However, any fluid remaining in the cavity after the original aspiration would need to have a fairly high osmotic tension, above that of the surrounding tissues, otherwise the incoming fluid from the tissues would bring about an osmotic balance before the cavity had completely refilled. It may therefore be a simple transudation of fluid from the surrounding tissues.

In other fields it is well to note that Schalyt (1930) suggested that the development of ovarian cysts was dependent on secretory activity and disturbance in osmotic equilibrium of the ovarian tissues. Gardner (1932) showed that the contents of old subdural cysts were of higher osmotic tensions than the surrounding cerebrospinal fluid and he suggested that the increase in size of these cysts was due to osmosis.

Osmotic pressure of a solution depends upon the number of submicroscopic particles in solution or colloid suspension. Animal tissues are pervious to water and dissolved crystalloids but are impervious to colloids except under certain circumstances. It will be seen that if a large molecule should break down into two simpler molecules, the number of particles dispersed in solution will be increased and the osmotic tension will rise, independent of the chemical nature of the molecule. If substances such as cytoplasm, nucleoprotein and other complexes associated with vital cells should be broken down to simpler molecules, as would be expected in a degenerative process in the tissues, then the osmotic tension of the resulting product would rise. If the products were surrounded by a membrane permeable to the solvent and impermeable to the solute then the pressure within that membrane would rise. This phenomenon may account, at least in part, for the presence and maintenance of positive intracystic pressure.

With this in view, an investigation was proposed: (*a*) To examine the epithelial linings of cysts and to determine whether they act as semipermeable membranes; (*b*) to examine some chemical and physical properties of cyst fluid.

Experimental

An apparatus has been devised to examine the permeability of freshly dissected cyst membrane.

The apparatus was also designed to study the osmotic tension of cyst fluid, blood and tissue fluids, and to compare the osmotic tensions of fluids directly through actual cyst membranes and through artificially prepared membranes.

Description of osmometer.—Two brass cylinders are provided with flanges which are ground together to have a perfectly flush fit. The cylinders are held on a hinged clamp so that they may be swung apart or brought tightly together. The chamber in each cylinder is slightly sloping upward away from the face of the flange and is accurately machined to be of equal volume with the other chamber. At the base of each cylinder is a narrow inlet tube leading to a small tap provided with an attachment for a record syringe (figs. 2 and 3).

A vertical glass capillary tube leads out from the uppermost point in each chamber and a horizontal mark is provided at the same level in each tube. The design is such that liquids introduced through the inlets at the base of each chamber fill the chamber and rise into the capillary tubes without the inclusion of air bubbles. The inlet tubes are also directed so that the incoming fluid tends to flush over the face of the flanges, so bringing it into immediate intimate contact with any membrane that is placed over the face of the flange.

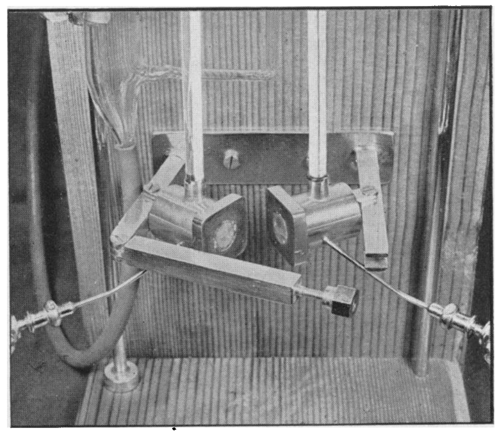

FIG. 3.—Osmometer with cylinders apart ready for reception of semipermeable membrane.

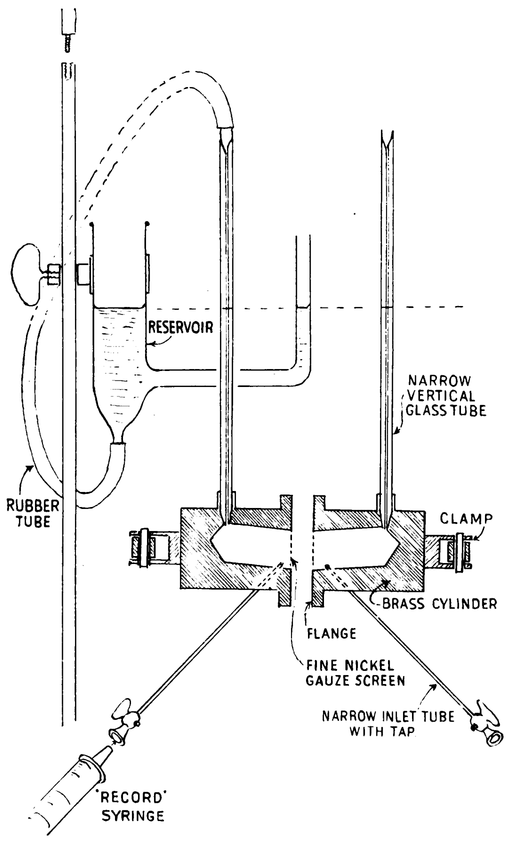

FIG. 2.—Diagram of osmometer used in the experiments.

A fine nickel gauze screen is let into the mouth of each chamber. This ensures that any membrane clamped between the cylinders will be supported firmly and atraumatically and it will prevent bulging or bursting of the membrane if an excessive pressure is applied to one side of it.

An extra manometer reservoir, provided at the side of the apparatus, is connected to the top of one of the vertical capillary tubes by rubber tubing. By raising or lowering this reservoir (usually filled with oil of known specific gravity) a counter-pressure can be applied to the surface of the fluid in the capillary tube. The reservoir can be moved up or down a vertical rod, this rod being supplied with an extension piece to enable the reservoir to be held at a greater height if necessary.

Operation of apparatus.—A membrane of unknown permeable qualities may be clamped between the two cylinders, and fluids of known character introduced simultaneously into the chambers on either side of it by injection with Record syringes. The two liquids are levelled to the marks on the capillary tubes and the taps closed.

The system then consists of two equal volumes of fluids separated by the membrane under examination.

The behaviour of the membrane can be assessed by observation of the fluid levels in the capillary tubes. A rise of level in one tube would be accompanied by a depression in the other if an osmotic transference takes place through the membrane.

The difference of osmotic tension between the two fluids, if the membrane is known semipermeable membrane, can be measured by applying a counter-pressure so that the levels in the two capillary tubes are kept the same so that equal volumes and the original concentrations of solutions are maintained. An oil manometer is used, oil not being miscible with the fluids under investigation, and, being of a small specific gravity, oil gives a good range of measurement for small differences in osmotic pressure.

First experiment.—Experiments were performed using freshly dissected cyst wall from 12 cases of dental cysts and 6 cases of dentigerous cysts. The wall was placed between the manometer cylinders and Ringer's solution introduced on one side. Ringer's solution to which had been added 5% egg albumin was introduced on the other side.

In all cases fluid passed through the membrane to the side containing the dissolved albumin. Transference of fluid continued until the capillary tube overflowed on one side and the fluid level disappeared in the other tube.

Second experiment.—A group of tests was made using direct comparisons of whole blood and cyst fluid taken simultaneously from the same patient. A known semipermeable membrane of cellophane was used.

In 11 cases of uninfected dental and dentigerous cysts: 4 cases showed no registrable osmotic difference, 7 cases showed cyst fluid to be of slightly higher colloid osmotic pressure than whole blood.

In these last 7 cases an average osmotic pressure difference of 3·7 cm. of oil (sp. gr. 0·8) was recorded, which represents an average pressure difference of 2·96 cm. of water.

Third experiment.—In 5 cases, the freshly dissected cyst membrane was placed in the osmometer and the aspirated cyst fluid from the same patient introduced on the epithelial side of it while the patient's blood was introduced on the other side.

In one case only (from a small dental cyst) was there a rise on the side of the cyst fluid (0·8 cm). The other 4 cases showed no change in level.

Summary of Experiments

A. I. A manometer has been described for accurate measurement of hydrostatic pressure within closed fluid-filled cavities within the body.

II. Intracystic fluid pressures have been measured in a series of cases of uninfected cysts before surgical interference.

III. Pressures ranging between 8·5 cm. of water and 95·0 cm. of water have been recorded.

IV. Lower pressures were noted in adamantinomata.

V. Blood-pressure has a direct effect on intracystic pressure.

B. I. An osmometer suitable for examination of the permeability of cyst wall and for comparing osmotic pressures of cyst fluid and blood has been described.

II. It has been shown that freshly dissected cyst wall behaves as a membrane impermeable to a colloid (albumin) and permeable to crystalloids and water.

III. Osmotic tensions of cyst fluid and blood from the same patient have been measured and compared directly. In some cases the osmotic tension of cyst fluid was found to be greater than that of the blood. In other cases no measurable difference in tension was noted. In no case has the cyst fluid shown a lower osmotic tension than that of blood.

Discussion

The results of the foregoing experiments support the theory that positive hydrostatic pressure within cysts is a factor influencing their growth. The fact that the exteriorization of a cyst cavity effectively checks further growth is strong clinical evidence in favour of the theory, although this does not rule out the possibility of the effect of accumulated products of degeneration of the tissues stimulating epithelial cells to proliferate.

The experiments indicate that the cause and maintenance of positive cyst pressure in dental and dentigerous cysts are likely to be related to the osmotic tension of the cyst fluid.

The positive pressure within a cyst is liable to be the result of several forces. First, there is the effect of pressure of the surrounding vascular network within the walls of the cyst. This will exert a pressure dependent upon the hydrostatic pressure within the surrounding vessels and its effect may be likened to that of a sphygmomanometer cuff. Then there is the effect of "tissue pressure" mentioned by Starling, which is the result of the tone of the living tissues and amounts to only a few millimetres of water. There is also the effect of the osmotic differences between cyst fluid and blood and the intervening tissue fluid which is in common relationship to both.

It has been shown that the osmotic pressure of cyst fluid varies over relatively small limits, which variations would be insufficient to account for the wide variations of pressure actually found within cysts. It has also been demonstrated that variations in fluid pressure due to the cardiac pulse (approximately 5 cm. water) are greater than the difference in osmotic pressure between blood and cyst fluid, so that it would seem that the main factor influencing positive intracystic pressure is the hydrostatic factor due to the surrounding vascular network.

If, for instance, a small semipermeable sac is partly filled with a hypertonic solution and it is immersed a few inches beneath the surface of some water, then, so long as the sac is not completely filled by its contained fluid, the hydrostatic pressure within the sac will be the same as that of the surrounding water. Only when the sac becomes filled with fluid and the walls become taut does the pressure within the sac rise above that of the surrounding water. Then the pressure within it is the sum of the difference in osmotic pressure between the fluid and water, and the pressure due to the depth it is immersed in that water.

Hydrostatic pressure in the larger capillaries and arterioles varies between 10 cm. and 100 cm. of water (Starling).

If hydrostatic equilibrium is attained between the cyst and the surrounding vascular and tissue pressure, there is always the tendency to slightly greater pressure within the cyst due to the osmotic imbalance and it is likely that this slight but ever-present osmotic pressure is responsible for the increase in size of the cyst.

If the osmotic imbalance is always present in the cyst fluid, despite the fact that the cyst grows larger and that there is always a tendency to bring about isotonicity, then it follows that there must be a continual supply of substances maintaining the hypertonicity.

It has been previously mentioned that degeneration of tissues is likely to produce a liberation of substances of lower molecular weight than those which make up vital tissue. Analysis of the proteins involved in vital tissue is itself a vast study, and one about which knowledge is yet in its infancy. Suffice it to say that molecular weights as high as 300,000 have been calculated for certain tissue proteins. An analysis of cyst fluid shows that it is made up largely of simple proteins with molecular weights of about 30,000. Thus it is likely that the breakdown of complex tissue proteins into a larger number of molecules of simple proteins is responsible for the raised colloid osmotic pressure found in cyst fluid.

I wish to express my special thanks to Mr. Rainsford Mowlem, Mr. B. W. Fickling and Dr. A. B. MacGregor at the Plastic and Jaw Unit, Hill End Hospital, for their patience and assistance.

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Kostecka's Osteotomy for the Correction of the Prognathous Mandible[1]

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I SHOWED this patient (M. K.) before the Odontological Section in April 1946, nine weeks after operation, as an example of Kostecka's closed method of bilateral osteotomy of the rami for the correction of mandibular prognathism. I had followed Kostecka's technique precisely as to the surgery, but I had varied the form of fixation. Kostecka favours fixing the floating mandible by ligating the upper and lower teeth together with orthodontic wires applied after cutting through the rami. The operation is thus extended by a somewhat fiddling procedure which would also have manifold disadvantages in cases where several teeth were missing. It seemed to me, when considering this operation, that the duration of operation could be markedly reduced and a more positive result, according to pre-operative planning, would be obtained if cast metal splints with a simple rapid interlocking device were to be cemented on to the upper and lower teeth previous to operation. I modified Kostecka's technique accordingly.

This patient, therefore, when shown originally before the Section, was still splinted and the sites of puncture for the needle and saw were clearly visible. Immobility was maintained for six weeks after which progressive function was allowed and within the next fortnight he was masticating ordinary food. The splints were left in situ so as to discipline the mandible for a further period of ten weeks. After they were removed the final occlusion was established by slight grinding of the cusps. Mastication became normal and there was no limitation of opening.

In view of the novelty of the operation and certain adverse criticism when the case was shown, I offered to keep the Section informed as to progress. Accordingly, the patient was demonstrated again twelve months later (Clinical Meeting, Odontological Section, April 1947) as a clinically completed case, when the functional and æsthetic results were seen to be entirely satisfactory. This demonstration of the final skiagrams on April 26, 1948, concludes the case.

[1]The follow-up and final skiagrams of a case previously shown before the Odontological Section, 1946, *Proc. R. Soc. Med.*, **39**, 646.