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The overview

Don’t lose sight of the forest for the trees.

International adage

Writing an original research article can be very complicated. After having done so much research—reading so many papers and doing so many analyses on your data—it is easy to get caught up in the details and lose sight of the big picture. A good manuscript is more than the sum of its parts. Manuscripts should be built around a unifying message. The earlier you decide on this message, the easier it will be create a harmonious whole. This is not to say that you need to have a refined version of your message at your fingertips when you first sit down to write. On the contrary, your message will evolve as you write and rewrite. Working through successive drafts will bring new insights into your work and help you discover new relationships among your data and analyses. Once you know what you want to say, you can concentrate on how to say it clearly, correctly, concisely, and convincingly. This is why the title, abstract, and conclusion should be the last parts of the manuscripts to be put into their final form.

This section deals with the parts of the article that represent the whole: the title, summary statement, abstract, and conclusion.

Titles

Your title is arguably the most important part of your paper. Prospective readers search for key words in search engines that return lists of titles linked to abstracts. Based on your title, they will decide whether your paper is potentially interesting; if they decide it is not, they will not bother to read the abstract. A well-written title should attract readers who might be truly interested in your work, but it should also redirect those who would definitely not be interested in it. To accomplish this, a title should be honest: it should give prospective readers a realistic idea of what to expect.

Titles must convey as much specific information as possible while remaining brief and clear. The same precepts that guide writing in other parts of the manuscript apply to titles; in other words, consider your audience and be meticulous in your choice of words and in how you put them together. If you are writing for a general science journal, it would be unwise to abbreviate the term "magnetic resonance imaging" in the title; however, if you are writing for a neuroradiology journal, you can be assured that your potential audience would understand and appreciate the abbreviation.

Titles can be classified as indicative, in other words, those that indicate what the article is about (*e.g.,* The relationship between A and B), or informative, in other words, those that inform readers of the findings (*e.g.,* A increases B). The journal's instructions for authors will inform you of the word or character limits, but you will probably need to browse a few issues to see whether they ever accept informative titles.

The titles of hypothesis-based studies should include the independent variable (if applicable), the dependent variable, and the population or animal studied. The following formats are often used:

- For indicative titles:
  - Effect of (independent variable) on (dependent variable) in (population):
    Effects of vasopressors on pulmonary vascular function in patients with liver transplants
  - (Dependent variable) in (population) in response to (independent variable):
    Pulmonary vascular function in patients with liver transplants in response to vasopressors

  Or when there is no clear independent variable:
  - (Dependent variable) in (population):
    Outcome after transmetatarsal amputation in patients with diabetic foot
- For informative titles:
  - (Independent variable) verb describing an effect (dependent variable) in (population):
    Vasopressors improve pulmonary vascular function in patients with liver transplants
  - (Dependent variable) verb describing an effect (independent variable) in (population):
    Pulmonary vascular function improves after vasopressor administration in patients with liver transplants
  - Adjective (Dependent variable) preposition (independent variable) in (population):
    Improved pulmonary vascular function after vasopressor administration in patients with liver transplants
    High rate of complications after transmetatarsal amputation in patients with diabetic foot

In addition to the title of your manuscript, many journals require you to provide a short title or "running head", which is usually limited to a maximum of 50 characters, including spaces. This abbreviated title will appear at the top of every page of your article.

Exercise 79

Rewrite the following titles to make them more concise.

1) A study of the pharmacodynamics and pharmacokinetics of intravenously administered digoxin and digitoxin
2) An investigation into the effects of XYZ39 on liver fibrosis in adult male Wistar rats
3) The nature of the interaction between norepinephrine and magnesium sulfate on cerebral vasoconstriction in rabbits' brains
4) A comparison of the normal findings in the elastic fibers in the musculature of the rectosigmoid colon in children compared with the findings in children with Hirschsprung's disease.
5) A description of the normal anatomy, anatomical variants, and common abnormalities of the cerebral vessels in the circle of Willis on magnetic resonance angiography

Exercise 80

Suggest how these titles might be improved.

1) Brain assessment in rats using micro positron emission tomography
2) Complications in babies resulting from anesthesia
3) Human losartan pharmacokinetic profile prediction based on in vitro uptake transport data
4) Preliminary results of a multicenter study on the ultrastructural changes in renal tissues brought about by mistoprostol in adults treated with cisplatin
5) Analysis of possible multiple sclerosis development predisposing factors

Exercise 81

Select the best title for these abstracts.

1) BACKGROUND: Enchondromatosis is characterized by multiple benign cartilage lesions in bone. While Ollier disease is typified by multiple enchondromas, in Maffucci syndrome these are associated with hemangiomas. Studies evaluating the predictive value of clinical symptoms for development of secondary chondrosarcoma are lacking. This multi-institute study evaluated the clinical characteristics of patients to gain insight into behavior of these diseases.
   METHOD: We retrospectively analyzed clinical data from 144 Ollier and 17 Maffucci patients from 13 European centers and one national databank supplied by members of the European Musculoskeletal Oncology Society.
   RESULTS: Patients had multiple enchondromas in the hands and feet only (group I, 18%), in long bones including scapula and pelvis only (group II, 39%), and in both small and long/flat bones (group III, 43%), respectively. The overall incidence of chondrosarcoma thus far is 40%. In group I, only 15% developed chondrosarcoma, in contrast to 43% in group II and 46% in group III, respectively. The risk of developing chondrosarcoma increases when enchondromas are located in the pelvis (odds ratio, 3.8; $p = 0.001$).
   CONCLUSIONS: Overall incidence of development of chondrosarcoma is 40%. Patients with enchondromas located in long bones or axial skeleton, especially the pelvis, have a seriously increased risk of developing chondrosarcoma and are need regular screening for early detection of malignant transformation.

a) Incidence of chondrosarcoma: A multicenter study of 161 patients
b) Prognosis of Chondrosarcoma in Patients with Ollier Disease and Maffucci Syndrome
c) Incidence and Predictive Factors of Chondrosarcoma in Patients with Ollier Disease and Maffucci Syndrome: An International Multicenter Study of 161 Patients
d) Incidence, severity, diagnosis, and prognosis of Chondrosarcoma in patients with Ollier Disease and Maffucci Syndrome: an international multicenter study of 161 patients

2) BACKGROUND/AIMS: The optimal timing of laparoscopic cholecystectomy (LC) in the treatment of acute cholecystitis remains controversial. This retrospective study was undertaken to assess the clinical outcomes and possible advantages and disadvantages of early versus delayed LC for acute cholecystitis.
MATERIALS AND METHODS: Records of all patients admitted for acute cholecystitis in whom LC was attempted between January 2004 and January 2006 at National Taiwan University Hospital were reviewed.
RESULTS: A total of 89 patients were recruited to the study. Of these, 56 patients received early LC, and 33 patients received delayed LC following conservative therapy. There were no intergroup differences in age, gender, or days of symptoms prior to presentation. Patients undergoing early LC experienced a significantly longer operation time (109 ± 37.59 minutes versus 77 ± 25.65 minutes, $p < 0.001$), more blood loss (76 ml versus 28 ml, $p = 0.006$), and a longer post-operation hospital stay (4.5 days versus 2.6 days, $p < 0.001$). The conversion rate to open cholecystectomy was not significantly different (4/56 versus 2/33, $p = 0.84$), and there were no biliary tract injury or other major complications in either group. However, patients with early LC had a shorter total hospital stay (4.53 days versus 7.79 days, $p < 0.001$) and fewer admissions (1 in early LC versus 2.4 in delayed LC, $p < 0.001$).
CONCLUSIONS: Both early and delayed LC appear to be effective and safe in the treatment of acute cholecystitis. Early LC may be more technically demanding and time-consuming, and may be associated with a higher rate of wound infections; however, it also tends to shorten the total length of hospital stay and reduce the risk of repeat cholecystitis. We recommend early LC for acute cholecystitis comparison with delayed LC.

a) Clinical outcomes, advantages, and complications of delayed laparoscopic cholecystectomy in the treatment of acute cholecystitis
b) Is early laparoscopic cholecystectomy safer than delayed cholecystectomy in the treatment of acute cholecystitis?
c) Evaluation of early versus delayed laparoscopic cholecystectomy in the treatment of acute cholecystitis
d) Both *b* and *c* are good titles for this abstract.

Abstracts

After the title, the abstract is the part of your paper that is most likely to be read. Just as only a small proportion of those who read your title will go on to read your abstract, only a small proportion of those who read your abstract will go on to read the entire article. Like your title, your abstract should give readers a realistic idea of what to expect in your article.

Abstracts can be classified into two basic types. A descriptive abstract is usually a single paragraph telling readers what to expect if they read the article. This type of abstract is usually reserved for review articles or case reports, which do not represent original research. Descriptive abstracts merely serve to help readers decide whether to read the full article; without the accompanying article, they are relatively useless. The other type of abstract, the informative abstract is much more common.

An informative abstract should be a condensed version of your article. It should be written to stand alone. Readers should be able to understand your abstract without reading the entire article; likewise, they should be able to understand your article without reading your abstract. The abstract is not an introduction. There should be no information in the abstract that does not appear in the article itself, yet all the most important information from the article should appear in the abstract.

Most journals use a version of the IMRaD format for indicative abstracts. This requires you to state the background or rationale for your study in one or two lines, followed by a brief but detailed statement of your objectives or hypothesis. You need to include enough information about your methods to orient your readers so they can understand your results. You need to highlight your most important results and sum them up in a succinct conclusion that shows your work is meaningful. Any conclusions in the abstract must be supported by information that also figures in the abstract—as mentioned above, the abstract must be completely intelligible without referring to the article.

The precepts that apply to all the other parts of a scientific paper are even more relevant in an abstract. Word limits force you to be concise, but you must be careful not to sacrifice clarity. Some journals forbid the use of abbreviations in abstracts, but most allow judicious use of abbreviations. Abbreviations are less likely to cause confusion in an abstract than in longer texts, because readers will have the definition fresh in mind and present on the same page if they need to refer back to it.

Exercise 82

Answer the questions about what is wrong with the following abstracts.

1) *What is missing from this abstract?*

BACKGROUND
Lithium is used to treat and prevent episodes of mania in people with bipolar disorder. Lithium-induced hyperparathyroidism (LIH) is a relatively underrecognized complication of long-term lithium treatment. Symptoms of LIH can be similar to those of bipolar disorder, delaying diagnosis of LIH. The first sign of LIH may be hypercalcemia, although it is often overlooked. We aimed to determine the prevalence of hypercalcemia in a cohort of patients with bipolar disorder.
METHODS
In this cross-sectional study, we collected data from 314 patients treated with lithium for bipolar disorder. Patients with bipolar disorder from the same clinics who had never been treated with lithium served as controls (n = 15).
RESULTS
In patients on lithium, mean serum calcium was 2.49 (SD 0.11) mmol/l and the point prevalence of hypercalcemia (> 2.60 mmol/l) was 15.6%. In controls, mean serum calcium level was 2.37 mmol/l, and none had hypercalcemia (p = 0.001). The duration of lithium treatment was the only significant predictor for the development of hypercalcemia (p = 0.002).
CONCLUSION
The prevalence of hypercalcemia was significantly higher in lithium-treated patients than in controls. Prevalence correlated with the cumulative time under lithium treatment.

2) *What is missing from this abstract?*

BACKGROUND
The objective of this research was to investigate the synergistic effects of two dietary components: docosahexaenoic acid (DHA), an omega-3 fatty acid present in cold-water fish, and curcumin (CCM), an herbal nutrient present in turmeric, in an ***in vivo*** model of DMBA-induced mammary tumorigenesis in mice.
METHODS
We used the carcinogen DMBA to induce breast tumors in SENCAR mice on control, CCM, DHA, or DHA + CCM diets. Appearance and tumor progression were monitored daily. The tumors were harvested 15 days following their first appearance for morphological and immunohistological analysis. Western analysis was performed to determine expression of maspin and survivin in the tumor tissues. Characterization of tumor growth was analyzed using appropriate statistical methods. Otherwise all other results are reported as mean ± SD and analyzed with one-way ANOVA and Tukey's post hoc procedure.
RESULTS
Analysis of gene microarray data indicates that combined treatment with DHA + CCM altered the profile of "PAM50" genes in the SK-BR-3 cell line from an ER–/Her-2+ to that resembling a "normal-like" phenotype. The *in vivo* studies demonstrated that DHA + CCM treatment reduced the incidence of breast tumors, delayed tumor initiation, and reduced progression of tumor growth. Dietary treatment had no effect on breast size development, but tumors from mice on a control diet (untreated) were less differentiated than tumors from mice fed CCM or DHA + CCM diets. The synergistic effects also led to increased expression of the pro-apoptotic protein, maspin, but reduced expression of the anti-apoptotic protein, survivin.

CONCLUSIONS

The SK-BR-3 cells and DMBA-induced tumors, both with an ER– and Her-2+ phenotype, were affected by the synergistic interaction of DHA and CCM. This suggests that the specific breast cancer phenotype is an important factor for predicting efficacy of these nutraceuticals. The combination of DHA and CCM is potentially a dietary supplemental treatment for some breast cancers, likely dependent upon the molecular phenotype of the cancer.

3) *What does not belong in this abstract?*

INTRODUCTION

The pathogenesis of juvenile dermatomyositis (JDM) remains poorly understood. Macrophages are often seen in muscle tissue very early in the disease process. We hypothesized that these cells secrete the pro-inflammatory myeloid-related protein (MRP) 8/14, which may then contribute to muscle pathology in JDM.

METHODS

We studied 56 patients with JDM. We compared serum MRP8/14 levels with clinical measures of disease activity. We used immunohistochemistry to determine the frequency and identity of MRP-expressing cells in muscle biopsies taken early in the disease process, and tested the effects of MRP stimulation and endoplasmic reticulum (ER) stress on muscle in vitro. We used multiplex immunoassay to analyze serum or supernatant levels of cytokines.

RESULTS

Serum MRP8/14 correlated with physician's global assessment of disease activity ($R=0.65$, $p=0.0003$) and of muscle strength/endurance measured by the Childhood Myositis Assessment Score ($R=-0.55$, $p=0.004$). MRP8/14 was widely expressed by CD68+ macrophages in JDM muscle tissue. Human myoblasts cultured with MRP8/14 secreted the cytokines MCP-1 and IL-6, and secretion increased after ER stress. Serum MCP-1 and IL-6 were significantly higher in JDM patients than in healthy controls.

CONCLUSIONS

Serum MRP8/14 is a potential biomarker for disease activity in JDM in clinical practice and research. MRP8/14 is easy to detect in serum even at low levels; it is already in clinical use to detect gut inflammation, and it is stable in clinical serum samples even when transported at room temperature. Tissue-infiltrating macrophages secreting MRP8/14 may contribute to myositis by stimulating the local production of cytokines directly from muscle.

4) *What does not belong in this abstract?*

BACKGROUND

Growing evidence suggests that alterations of the inflammatory/immune system contribute to the pathogenesis of depression. Peripheral and brain inflammatory markers are increased in depressed patients, and major depression often occurs together with other diseases associated with inflammatory alterations. We aimed to characterize the link between depression and inflammation by examining the inflammatory system alterations.

METHODS

We used homozygous rats with partial or total deletion of the serotonin transporter (SERT) gene as a genetic model of vulnerability for depression and wild-type, heterozygous rats as controls. We analyzed cytokine expression at baseline and after acute injection of lipopolysaccharide (LPS).

Continue

RESULTS

SERT mutant rats showed altered cytokine expression in the dorsal and ventral hippocampus at baseline and also displayed an exacerbated cytokine response to the LPS challenge. Moreover, mutant rats exhibit differences in the expression of markers for microglia activation.

CONCLUSION

Baseline or functional alterations of immune/inflammatory systems contribute to heightened susceptibility to depression. Failure to respond to antidepressant treatment may be due to increased cytokine expression.

5) *How can we improve the intelligibility of this abstract by moving the information from a single sentence?*

BACKGROUND

In assisted reproduction cycles, gonadotropins are administered to obtain a greater number of oocytes. Most patients have no adverse response, but 3% to 6% develop ovarian hyperstimulation syndrome (OHSS). Increased vascular permeability is central to OHSS. Metformin reduces the risk of OHSS, but little is known about its possible effects on OHSS or mechanisms of action. We evaluated whether metformin attenuates some of the ovarian adverse effects caused by OHSS and the mechanisms involved.

MATERIAL AND METHODS

We used a rat model of OHSS to investigate the effects of metformin administration, comparing rats administered gonadotropin to induce OHSS, rats pretreated with metformin before gonadotropin administration to induce OHSS, and control rats. Ovarian sections stained with Masson trichrome were examined histologically and follicles were counted. Vascular permeability was measured by the release of intravenously injected Evans Blue dye. Vascular endothelial growth factor (VEGF) levels were measured by immunosorbent assay. COX-2 protein expression was evaluated by western blot, and NOS levels were analyzed by immunohistochemistry.

RESULTS

Rats with gonadotropin-induced OHSS had pathophysiological characteristics similar to those seen in human OHSS: increased body weight, elevated progesterone and estradiol levels ($p < 0.001$), increased number of corpora lutea ($p < 0.001$), higher ovarian VEGF levels ($p < 0.001$), and greater vascular permeability ($p < 0.01$). Metformin prevented some of these effects. The vasoactive factors COX-2 and NOS were increased in the ovaries of animals with OHSS ($p < 0.05$ and $p < 0.01$) but not in those pretreated with metformin ($p < 0.05$), suggesting that metformin has a role preventing the increase in vascular permeability caused by the syndrome.

CONCLUSION

Metformin attenuates the increases in body weight, circulating progesterone and estradiol, and vascular permeability in OHSS. These effects are mediated by inhibiting the increase in the vasoactive molecules VEGF, COX-2, and partially NOS. These molecules are increased in OHSS and are responsible for many of the symptoms related to OHSS.

6) *What makes this abstract so hard to understand?*

BACKGROUND

M_3 muscarinic acetylcholine receptor (M_3-mAChR) is stably expressed in the myocardium, but its pathophysiological role remains largely undefined. This study aimed to investigate the role of M_3-mAChR in myocardial hypertrophy (MH) induced by angiotensin II (Ang II) and elucidate the underlying mechanisms.

METHODS

Cardiac-specific M_3-mAChR overexpression transgenic (TG) mice and rat H9c2 cardiomyoblasts (CM) with ectopic expression of M_3-mAChR were established. Models of myocardial hypertrophy (MH) were induced by transverse aortic constriction (TAC) or Ang II infusion in the TG mice ***in vivo***, and by isoproterenol (ISO) or Ang II treatment of H9c2 CM *in vitro*. MH was evaluated by electrocardiography (ECG) measurement, hemodynamic measurement, and histological analysis. mRNA and protein expression were detected by real-time RT-PCR and Western blot analysis (WBA).

RESULTS

M_3-mAChR was upregulated in MH, while M_2-mAChR expression did not change significantly. M_3-mAChR overexpression significantly attenuated the increased expression of atrial natriuretic peptide and β-myosin heavy chain induced by Ang II both *in vivo* and *in vitro*. In addition, M_3-mAChR overexpression downregulated AT_1 receptor expression and inhibited the activation of MAPK signaling in the heart.

CONCLUSION

The upregulation of M_3-mAChR during MH could relieve the hypertrophic response provoked by Ang II, and the mechanism may involve the inhibition of MAPK signaling through the downregulation of AT_1 receptor.

Exercise 83

Organize the following sentences into an abstract with the subsections Background, Methods, Results, and Conclusion.

PROTEIN INTERACTIONS OF THE TRANSCRIPTION FACTOR HOXA1

a) Other families of transcription factors, such as Smad or Stat, are signaling transducers.
b) Copurification confirmed 45 interactors, many of which were involved in cell-signaling transduction, cell adhesion, and vesicular trafficking.
c) We aimed to investigate the mode of action of mammalian Hox-A-1.
d) Whether Hox proteins are signaling transducers has never been investigated.
e) Screening identified 59 interactors.
f) Hox proteins are transcription factors involved in crucial processes during animal development.
g) The intracellular patterns for these interactions were consistent with the selective recruitment of Hox-A-1 by subgroups of partner proteins at vesicular, cytoplasmic, or nuclear compartments.
h) We used bimolecular fluorescence complementation (BFC) to determine where the interactions take place in live cells.
i) BFC detected 41 interactions.
j) Our characterization of the Hox-A-1 interactome suggests unexplored roles for Hox proteins in cell-to-cell communication and cell physiology.
k) We used systematic yeast two-hybrid screening against ~12,200 polypeptides derived from open reading frames to characterize the interactome of Hox-A-1.
l) BFC revealed distinctive intracellular patterns for these interactions.
m) Little is known about the mode of action of Hox proteins.
n) We used copurification and bimolecular fluorescence complementation to check the results of the screening.